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HEALTH RISK ANALYSIS IN THE STRATEGY OF STATE SOCIAL AND ECONOMIC DEVELOPMENT

Monograph

Under the general editorship of
member of the Russian Academy of Sciences G.G. Onishenko,
member of the Russian Academy of Sciences N.V. Zaitseva

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Writing team: G.G. Onishchenko, N.V. Zaitseva, I. V. Mai, P.Z. Shur, A.Yu. Popova, V.B. Alekseev, O. V. Dolgish, M.A. Zemlyanova, N.A. Lebedeva-Nesevrya, P.V. Trusov, T.V. Nurislamova, T.S. Ulanova, O.Yu. Ustinova, E.E. Andreeva, E.M. Vlasova, O.I. Goleva, D.A. Kiryanov, S.V. Klein, K.P. Luzhetsky, O.A. Maklalova, A.E. Nosov, N.G. Atiskova, A.O. Barg, S.A. Vekovshinina, M.R. Kamaltdinov, N.V. Nikiforova, A.S. Sboev, E.V. Seduysova, M.Yu. Tsinker, V.M. Chigvintsev, D.M. Shlyapnikov, V.G. Kostarev

Reviewers:
Member of the Russian Academy of Sciences, Doctor of Medicine, Professor, Director of the Research Institute of Nutrition of RAMS *V.A. Tutelian*;
the corresponding member of the Russian Academy of Sciences, Doctor of Medicine, Professor, Head of sanitary and epidemiological service management department of the First Moscow State Medical University named after I.M. Sechenov *E.N. Belyaev*

A64 **Health** risk analysis in the strategy of state social and economical development : monograph / G.G. Onishchenko, N.V. Zaitseva, I. V. Mai [and others] ; under the general editorship of G.G. Onishchenko, N.V. Zaitseva. – M.; Perm : Publishing house of the Perm National Research Polytechnic University, 2014. – 686 p.

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This monograph summarized the experience of scientific and methodological approaches to the health risk analysis and their use in solving strategical and tactical tasks of the state administration in the field of the assurance of sanitary and epidemiological welfare of the population and compliance of the consumer rights.

It covers the stages and prospectives of the development of health risk analysis methodology, states theoretical domestic and foreign approaches to various aspects of population health risk analysis. Taking into account the internationally recognized principles, this paper proposes methodical approaches to risk analysis and its evolution under the influence of various factors of the environment, products, environment and lifestyle on the health.

It indicates the peculiarities of the population health risk management including making management decisions based on the spatially-temporal modeling of risk distribution, economic evaluation, improvement of risk oriented model of the control and supervisory activities, medical-preventive technologies to reduce the effects when exposed to risk factors, represents the general principles, states the methods and model of risk communication.

It discusses the legal aspects of the health risk analysis in Russia and abroad. It summarizes approaches to optimize public health monitoring based on the health risk assessment, methodological approaches and practices to evidence the harm to health caused by exposure to risk factors, the practice of risk assessment and management using methods of evolutionary modeling.

The ways to improve the state policy in the field of risk minimization and integration of health risk analysis in the solution of strategic objectives of the state socio-economic development are presented here.

The publication is intended for professionals working in the field of public administration, at the bodies and institutions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance, scientific and educational institutions, interns, graduate students, doctoral students, and practitioners of preventive health.

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INTRODUCTION

The twenty first century brings many challenges in the field of sanitary and epidemiological welfare of the population and, at the same time provides new opportunities to overcome the threats to the security and health of citizens. For further development of the up to date existing socio-economic system in Russia, it is necessary to establish strategic guidelines and goals. These goals are indicated in the Concept of long-term socio-economic development of the Russian Federation for the period up to 2020 [The Concept, 2008]

In accordance with this document, "The strategic goal is to achieve a level of economic and social development according to Russia's status as a leading world power of the XXI century, with an attractive way of life, holding advanced positions in the global economic competition and reliably ensuring national security and the realization of the constitutional rights of citizens." A part of this goal and not the last condition for its successful implementation is to ensure the sanitary and epidemiological welfare of the population and the health of the citizens of Russia at a level corresponding to the level of leading world power development.

It should be noted that the start of an intensive socio-economic development of the Russian Federation took place in difficult conditions. On the one hand, the transition to a market economic system completed on the whole was associated with the need to ensure the social status of citizens under the condition of macroeconomic instability. To date, this has not fully solved all the pressing problems of social development against the background of changes in the structure of the economy in favor of industries focused on market demand. On the other hand, the return of Russia to the line of world powers takes place under the conditions of growth of politic instability and global competition, covering not only the traditional markets of goods, capital, technology, and labour, but also the system of national governance, support for innovation and the development of human potential.

Domestic sanitary science over the past centuries occupied a leading position in the world, highlighting the paradigm of a humanistic orientation ensuring human health in the present and future generations. Global changes relating to political, economic, and social systems of the state, that take place now transform the priorities which have been set for the scientific community, including those of hygiene; new strategic goals and objectives corresponding to the current situation in our country and the world community, require the development of new approaches to the achievement of these goals.

The representation of precious human life is in contradiction with the necessity of its economic assessment when it becomes necessary to select the measures and to determine their cost allowing saving as many lives as possible. The thesis "Save human life at any price", blasphemous though it might sound, cannot be applied, because any price is usually the price of life and the health of other people.

Modern trends in policy and strategy of the XXI century include the establishment of evidence-based policy and justification of investment and the creation of a such society that values health, recognizes the need to see the prospects, to indicate a strategic way, to put forward a set of priorities and a number of suggestions as to what measures are effective to improve health [Health 2020: Fundamentals of the European policy in support of the actions of the entire state and society in the interests of health and welfare, 2013]. It provides the

necessity to solve strategic objectives to develop the society on the supradepartmental level using universal tools in the field of sanitary and epidemiological welfare of a person and protection of consumers rights recognized in the world community.

The dominance of non-communicable diseases as cause of population mortality in developed countries, primarily in Europe, should be noted as another trend of the change in health of the current generation. High-level meeting on the prevention and control of Noncommunicable Diseases was held and the appropriate political declaration was made under the auspices of the General Assembly of the United Nations in September 2011 [Political Declaration of high-level meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. Only in the second time in history, after discussing the issue of HIV/AIDS in 2001, the General Assembly addressed the issue related to health at the global level, that shows extreme relevance of this problem study, identification of the factors forming i,t and preparation of solutions to overcome it on the basis of science-based forecasts of the evolution of noncommunicable diseases burden in connection with the prevalence and intensity of risk factors effect.

Demographic changes occurring in many countries require an effective strategy covering all stages of life and giving the priority to new approaches to health promotion and disease prevention. To reduce the burden of non-communicable diseases successfully, it is necessary to combine different approaches. A distinctive feature of communicable diseases prediction as the least developed area of health, in contrast to the prediction of infectious epidemiological processes, is the need to establish its dependence on the impact of different hazards. The basis of the application of a methodology for health risk analysis for the formation of the health state forecasts depending on the quality of the environment is information aggregated by national information systems, primarily in the framework of public health monitoring.

It is now widely recognized that the health of the population is influenced by various social and environmental determinants that lie outside the direct control of any of the individual ministries or other government agencies [Kickbusch I., Behrendt, 2014]. Therefore, Health-2020 policy supports the implementation of the integrated national approaches involving the whole society, which are reflected in other regional and global strategies [Health 2020: Fundamentals of the European policy in support of the actions of the entire state and society in the interests of health and welfare, 2014].

Experience shows that state regulation is required in order to achieve health protection objectives in the public interest. In order to be effective and legitimate, this regulation should be transparent, accountable, proportionate, consistent, and targeted [Karnani A., 2011]. The listed characteristics are perfectly consistent with the principles of the health risk analysis and allow positioning of this methodology as one of the best to justify management decisions at the state level.

This situation requires the creation and development of new innovative methodologies that meet modern requirements that address key strategic objectives ensuring socio-economic development of the country and sanitary and epidemiological welfare of its citizens. They include health risk analysis methodology. The aim of the health risk analysis, as a component part of preventive medicine and sanitary science, is the prediction and assessment of adverse changes in health status at the individual and population levels with justification including economic one, measures aimed at the prevention of diseases and creation of conditions that ensure the preservation of health.

The methodology of the health risk analysis can be considered as an instrument of coordination of law enforcement practice system of the state regulation to ensure the safety of life and health of the citizens of Russia, the main parts of which are technical regulation and hygienic rating systems. However, it is worth noting that the trend of environmental regulation taking into consideration only the best achievable technologies on technical and economic criteria is not always able to provide security for the life and health of the population. The usage of the best achievable technologies can create the conditions for violations of sanitary legislation, the consequences of which will lead to the formation of an unacceptable risk and harm to health.

The coordinating role of health risk analysis methodology should be emphasized, the results of its use are required to provide the safety of life and health of citizens in a number of economic sectors: urban planning, environmental protection, technical regulation, etc.

Health risk analysis methodology integrating achievements in medicine, biology, chemistry, mathematics, computer science, sociology, and other disciplines, allows generating conclusions determining the strategic management decisions affecting the territorial industrial development, technical regulation, social security, economic, and political status of the state. The cross-sectoral nature of this methodology makes it one of the most appropriate instruments to ensure harmonious social and economic development of the state.

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1. POPULATION HEALTH RISK ANALYSIS: THEORY, PARADIGM, STAGES AND DEVELOPMENT PROSPECTS

The generation of an optimal system of state administration requires using modern methodology to forecast various aspects of its development. First, it concerns the scope of the economy, but under the conditions of socially oriented policies of the Russian Federation, it is extremely important to improve methods of forecasting the social component of the country's development. This position is primarily concerned with the problem of increasing the labour force of the state, especially such an important part of these as human health and safety. One of the most appropriate instruments of prediction and control in the field of security provision for human life and health and its sanitary-epidemiological welfare is a health risk analysis methodology.

1.1. Theoretical aspects of health risk analysis: terminological identification of the definition "health risk", the place of health risk analysis in the general theory of risk analysis

The history of the "risk" concept emergence was considered in detail by various authors and their conclusions, as a rule, do not always coincide with each other. Nicholas Luhmann conducted a detailed and thorough study of this concept [Luhmann N., 1991]: "High cultures of antiquity ... did not need a word denoting what we now mean by risk." Therefore, the concept "risk" appeared only in a period of long transition from the Middle Ages to the early modern times. According to L.N. Telman (2002); there was no general concept denoting a risk in the middle ages. The risk meant luck and misfortune that was predetermined by a fate and fortune.

There are two main versions of the "risk" concept origin. According to one of them, the word "risk" is of Spanish-Portuguese origin and means "reef" (not in vain "risk" is similar to "reef"), i.e., danger [Abchuk V.A., 2001]. According to another version, the term "risk" comes from the Latin *risicare*, meaning "to decide" [Panfilova E.A., 2010]. Th first important areas of its application were seafaring and maritime trade. The following wordings can be found in the treaties governing who bears the risk in case of damage: «ad riscum et fortunam ...» (because of the risk and chance) or «pro securitate et risico ...» (for guarantees and according to risk) or «ad omnem risicum, periculum et fortunam Dei ...»(due every kind of risk, hazards and accidents sent down by the Lord) ... But also in other fields of application the word "risk" (from about 1500) has become increasingly common, apparently following the spread of book printing [Alekhin E.I., 2008].

The word «risk» came to English literature later in the middle of the XVIII century from France as the word «risque» (risky, doubtful). Entrepreneurship as an economic activity has become a key stimulus for the development of theoretical provisions of risk

analysis. French economist of Scottish descent R. Cantillon first considered the concept of risk in the XVII century as the functional characteristics of the business. According to R. Cantillon, an entrepreneur is any individual who has the foresight and willingness to take risks, looks to the future, whose actions are characterized by a hope to receive the income and a availability to losses.

Another representative of the German classical school, G. von Mangoldt, set the risk bearing as the most important role function of the entrepreneur in the center of its theoretical studies [Mangoldt G. von, 1855]. The American economist Frank Knight gave the fullest development to a risk factor as the most important component of the entrepreneurial function. According to F. Knight, risk represents an objective probability of a particular event and can be expressed quantitatively, in particular in the form of mathematical probability distribution of revenue. The more the probability of a standard deviation from the expected value in this distribution, the less the risk is, and vice versa. Apart from the risk - measurable uncertainty - there is an uncertainty, which in principle cannot be calculated based on a priori assumptions or statistical analysis of the available data. The great advantage of the concept by F. Knight [F.H. Knight, 2003] is the description of uncontrollable profit factors.

The above provisions apply to the economic risk which is determined as "a state of uncertainty of the results of the transaction, investment activities, buying or selling" [Modern Encyclopedic Dictionary, 1997]. However, as and when it is necessary to predict the situation, the risk assessment and management are developed in other areas. A vision of the political, industrial, emergency, social and other types of risks is formed along with the risk adjustment in the economy (investment, currency, tax, commercial, financial, etc.). Applications of the risk theory are virtually limitless. The most advanced financial areas of application are banking and insurance, management of market and credit risk, investment, business risks, and telecommunications. Non-financial applications associated with health risks, environmental risks, risk of accidents and environmental disasters, and other areas are also developed.

The mathematical risk theory is an intensively developing branch of probability theory which has numerous applications in economics, finance, and other areas of human activity related to decision-making under conditions of uncertainty [Novoselov A.A., 2001]. With the advent of the theory of probability, mathematical statistics, systems analysis, operations research, cybernetics, methods of analysis and evaluation of data, there were possibilities of risk evaluation, analysis and management as a key factor of human activity.

Risk analysis in its evaluation uses a particular mathematical apparatus: probability theory, the theory of fuzziness, interval mathematics, etc. The most common approach is based on the theory of probability (as a part of mathematics). A probability model of a real event is usually used in this approach (implementation of unwanted possibly, danger). According to this model, there are a probability of undesirable possibility (some authors call this probability a risk) and the random variable - accidental damage (severity of the hazard) in the case of its implementation. Various theoretical characteristics of random damage - mathematical expectation, variance, mean square deviation, variation coefficient, median value, quartiles, and interquartile distance, etc. are considered. Risk assessment is reduced to statistical estimation of parameters, characteristics, dependences included in the model. Risk management (*risk control*) can be implemented in various ways - intuitively, based on expert judgment, based on a mathematical model using various characteristics [.A.I Orlov, O.V. Pugach, 2012].

A.I. Orlov, O.V. Puhach (2012) showed that the same tools of the common risk theory can be advantageously used in the domains. The main conclusion: the common risk theory is designed in its main features, so there is no need to establish separate risk theories for specific application areas. Of course, some specific statements, models and methods for a particular subject area have a right of existence, but the general risk theory tools enables consistently solve the basic problems of risk analysis, assessment and management for all domains. One of the stages of risk analysis allowing further performance of the identification and assessment of risks, the development of methods of its management, is the risk distribution by groups based on classification criteria [Encyclopedic dictionary, 2001].

Since risk is a complex subject-object system, it is necessary to decompose it on different grounds. Risk classification determines the efficiency of the risk management organization. The risk classification should be understood as distribution of risk on specific groups according to certain criteria in order to achieve the stated goals.

Evidence-based risk classification allows the clear identification of the location of each risk in their overall system. It creates an opportunity for the effective application of appropriate methods and techniques of risk management. Each risk has its own corresponding system of management techniques.

However, currently, there is no any shared vision concerning the definition of "system" principle allowing arrangement of the distinguished risks in such a manner that the classification itself became a tool suitable for the study and practice risk management in literature. There are various solutions of the questions raised, which in most cases can be explained by the difference in the goals and objectives of classification. However, in some cases, it is proposed to use different, sometimes conflicting criteria of risk assignment to a particular group, even with the same classification characteristics [Alekhin E.I., 2008].

For example, according to Rao Kolluru [Kolluru R.V., 1996], there are five following types of risk:

- risks to safety;
- risks to health;
- risks to the environment;
- risks to the public welfare;
- financial risks.

Risks to safety are usually characterized by low probabilities, but severe consequences; they occur rapidly, in particular, they can include industrial accidents. Risks to health, on the contrary, have quite a high probability and often do not have the severe consequences, many of them appear with a certain delay. According to Rao Kolluru [Kolluru R.V., 1996], risks to the environment are a countless number of effects, interactions between the myriad of interactions between populations, communities, ecosystems at micro and macro levels in the presence of a very large uncertainties both in the effects themselves, and in their reasons. Risks to public welfare are due to the way in which the society perceives and evaluates the activities of the object (industrial, agricultural, military, etc.), the extent to which this activity is related to the rational use of natural resources, its affect on the state of the environment; negative perception of the activity of the object appears quickly and is stable. Financial risks are associated with the possible losses of property or income, non-receipt of the insurance premium or profit from investments (including investment in environmental protection measures) [Aizman R.I. et al., 2009].

Summarizing, supplementing and correcting the studied classifications, E.I. Alekhine (2008) presents the most important, in his opinion, elements that determine the risk sharing. Classification risk criteria and the composition of classification groups are shown below.

1. Depending on the nature of the consequences:

- pure risks (are characterized by the fact that they almost always carry the losses);
- speculative risks (are characterized by the possibility of obtaining both positive and negative results).

Net risks, in contrast to speculative ones, have a relatively constant manifestation nature. Methods of mathematical statistics and probability theory are widely used for their evaluation and analysis. Thanks to the stable nature, manifestation frequency and dynamics of the main indicators, pure risks are sometimes called *static risks*.

Speculative risks are in full defined by the management decision. As a rule, they have an uncertain manifestation nature and their analytical assessments change over time. More often, speculative risks are encountered in such areas of activity, which are dependent on market conditions. Because of this, speculative risks are sometimes called *dynamic risk management*. Unconventional methods of analysis and selection of management decisions (eg, technical analysis) is required to be used for study of speculative risks, which are characterized by a high variability of characteristics. A similar division into speculative and

non-speculative risks is seen in quite a large number of authors [Onishchenko G.G. et al., 2000; Bocharov S.A. et al., 2008; Zaitsev N.L., 2009].

The following risk classification by time of occurrence is known: the starting risk (when selecting one of the alternative action) and the final risk (occurrence of the most adverse effects of the already undertaken actions).

Short-term, long-term and permanent risk are allocated.

In terms of losses, it is proposed to classify the risk as acceptable, critical and catastrophic [Alekhine E.I., 2008].

Somewhat different classification of risks on various grounds is available at the web-site of the Peoples' Friendship University of Russia (Fig. 1.1).

♦ by the sources of risk:

– *technology-related* – the risk, the source of which is human economic activities, it is associated with the hazards arising from the technical facilities;

– *natural* –- the risk associated with the manifestation of the elemental forces of nature: earthquakes, floods, flooding, storms, etc.;

♦ by the type of risk source:

– *external* – that is, the existence or formation of which is not associated with the activity of this object of risk;

– *internal* – that which are directly dependent on the operation of the object;

– *risks associated with human factor* – errors of specific individuals (workers of the enterprise, designers, etc.);

♦ the nature of the damage caused:

– *environment* – the possibility of hazards or negative environmental changes which are caused by natural anthropogenic factors and lead to adverse social and economic impacts in society;

– *social* – dependence of the probability (or frequency) of adverse events associated with damage to certain groups of people exposed to a certain type of the impact in the implementation of the relevant hazards, on the size of these groups;

– *economic* – the possibility of losses due to the random nature of the results of the made economic decisions or actions;

– *individual* – the probability (frequency) of the damage to an individual as a result of the impact of the hazards being studied;

♦ by the size of damage:

– *acceptable* – the magnitude of a risk that is achievable according to technical, economic, and technological capabilities (10^{-6} is considered acceptable, that means the death of one person per 1 000 000 and corresponds to the risk of loss of life caused by natural hazards);

– extreme – the maximum risk that is not to be exceeded despite the expected result;

– *catastrophic (systemic)* –the risk effecting large areas at the same time;

♦ by the level of danger

– *unacceptable* – the risk level set by the administration of the company or the regulatory authorities as the maximum allowed level, which does not result in deterioration in the economic activity of the enterprise or the quality of life of the population under the existing social and economic conditions (risk level $>10^{-6}$);

– *acceptable* – the level of risk that is acceptable by the society as a whole in order to receive certain benefits as a result of its activities (10^{-6} < risk level $<10^{-8}$);

– *negligible*– the level of risk established by the administrative or regulatory authorities as a maximum one, it is necessary to take corrective actions when exceeding this level of risk;

Since the natural boundaries of risk to person is the range between 10^{-2} (the probability of morbidity per capita) и 10^{-6} (the lower level of risk of natural disaster or other serious hazard), technological risk is considered acceptable, if it is less than 10^{-6}.

♦ by exposure time:

– *short-term* – adverse effects does not exceed 1 hour, e.g., an explosion or a small fire;

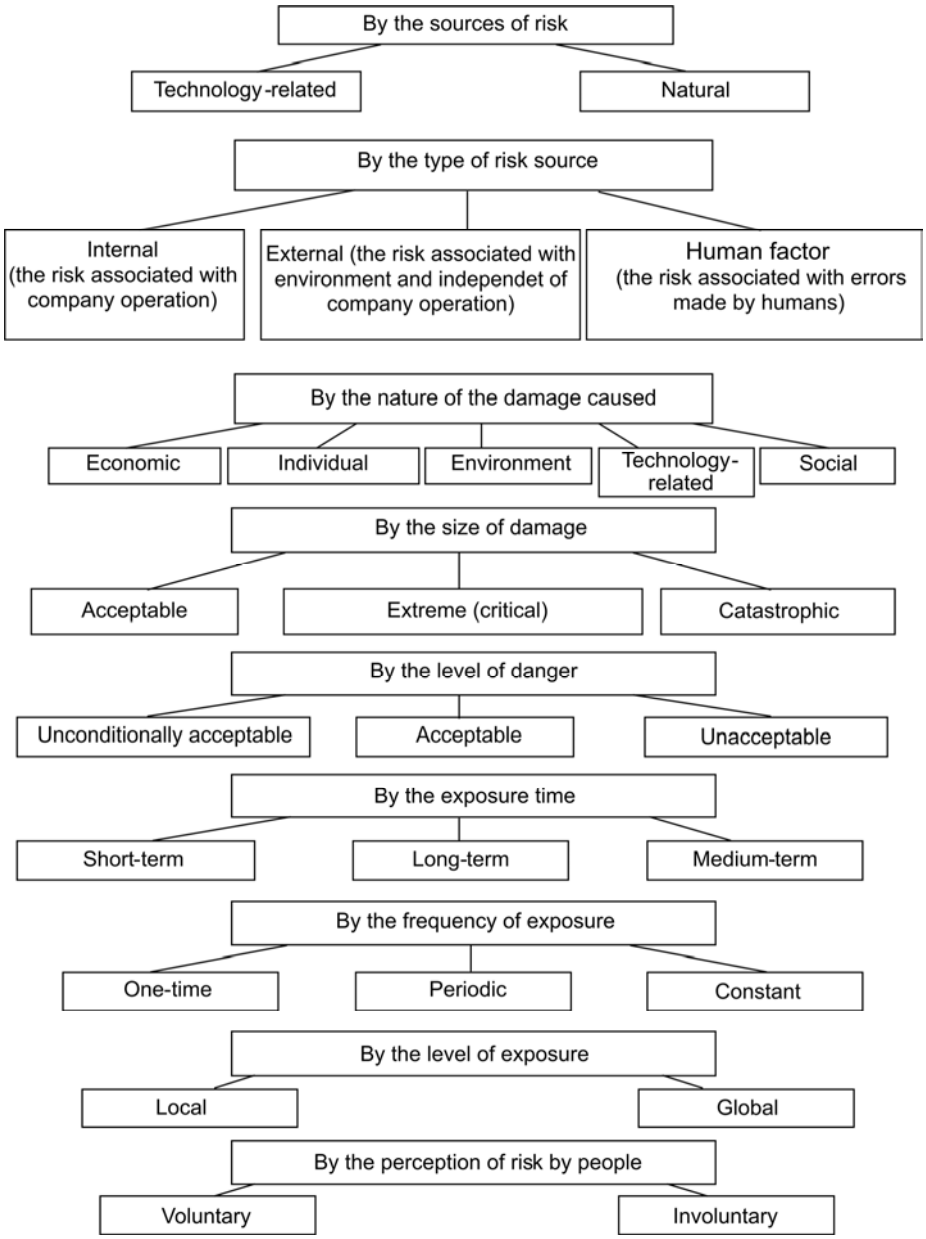

Fig. 1.1. Risk classification

– *medium and long-term* –associated with the emergence of radiation, destruction of flora and fauna, etc., the consequences of which may have an impact for a long time;

♦ by the frequency of exposure:

– *constant* – the risk the exposure of which has a constant effect;

– *periodic* – the risk arising from time to time (for example, when starting or stopping equipment);

– *one-time* – the risk appearing when creating an abnormal situation;

♦ by the level of exposure:

– *local* – the risk at the enterprise;

– *global* – the risk associated with the reflection of the situation in the country, in some sectors, regions;

♦ by the perception of risk by people:

– voluntary – the risk associated with the occurrence of accidents at the enterprise, for workers of this enterprise;

– *involuntary* – for the population living near the enterprise;

♦ by the nature of the impact on the various recipients:

– *social damage* – impact on a person;

– *economic damage* – the loss of material assets

– *environmental damage* – an adverse effect on the environment.

The most volumetric analysis of risk classification is given in the article by A.A. Bykov, B.N. Porfireva (2006). Classification of risks is a division of risks into categories using certain criteria. The choice of criteria depends on the objectives and characteristics of the procedure of risk analysis and management. The number of possible criteria for the classification of risk can be very large, so the classification criteria must be grouped. The main purpose of classification is the allocation of specific risk, and each of the specific risk measured by the frequency of occurrence and the size of the adverse effects (damage) is described by its standard features: danger associated with the risk, risk exposure, vulnerability (sensitivity to risk), as well as other additional parameters (characteristics) such as interaction with other risks, the degree of the risk homogeneity, the degree of predictability etc. [Porfirev B.N., 1988, 1991; Bykov A.A., Murzin N.V., 1997; Chernova G.V., Kudriavtsev A.A., 2003].

Depending on the degree of generality criterion and/or characteristics of risk, the risk classification can be divided into specific and general one.

Only the classifications related to health risk are reasonable to be considered further.

The most general and common to all types of risk characteristics can serve as criteria of the general classification:

1) sources, factors (occurrence environment) or reason (nature) of danger/damage;
2) object(s) of vulnerability to hazards;
3) the extent/levels of danger/effects;
4) dependence on the time factor;
5) generic character or regularity of a risk occurrence;
6) characteristics of the risk occurrence consequences;
7) characteristics of the interaction with other risks;
8) characteristics of the risk size/magnitude;
9) the possibility of free choice;
10) characteristic of the degree of measurability and predictability of risk.

1. According to the sources, factors or reasons (nature) of danger/damage, the following risks can be allocated: natural (geological, meteorological, etc.), associated with acts of elements and natural disasters (floods, earthquakes, storms, climatic disasters, etc.); anthropogenic, associated with human activities.

The following risks can be allocated according to this criterion

– sociogenic:

– social; the social risk is the risk of negative social phenomena such as crime, breach of facilities security, adverse social external effects, etc.;

– economic, related to the economic activity, i.e. business and results of economic processes;

– political or economic-political, associated with economic policy;

– technology-related (industrial, energy, transport, etc.) associated with the effects of the operation of technical systems and/or their violation (fires, changes in technology, the deterioration of the quality and production capacity, the specific risks of technology, errors in design and estimate documentation);

– combined (natural and anthropogenic, anthropogenic and natural, natural and technology-related, etc.), in particular, they include epidemic, ecological (environmental change) risks, etc.

By criteria: "What internal or external circumstances determine the risk", the following risks can be allocated:

- the internal ones, i.e. such as, for example, are related to the organization of the operation of the studied company on the activity of the studied person. In other words, these are the risks that may be affected by the management of the company. Examples of such risks are the breakdown of equipment, lack of the required goods at the store stocks, etc.;
- external, i.e. those that are determined by external circumstances. Examples also include the emergence of more efficient technology, environmental degradation, etc. of competitors. The risks of both types should be taken into account, but if you can control internal risks, than the external ones, in most cases are only accountable.

2. By the objects of vulnerability to hazards:

- social and political, where public relations are the object of vulnerability. The following risks can be allocated according to this criterion: individual; collective; general social; relating to domestic policy; foreign policy; general policy;
- ecological, where the object of vulnerability is the state of the environment. The following risks can be allocated according to this criterion: individual; generic (patrimonial, etc.); ecosystem;
- economic.

Economic risks associated with the following factors can be identified according to the object of vulnerability:

- the property (assets). Such risks are quite common and can be easily expressed in monetary terms. Of course, the features of specific risks depend on the type of property: immovable, movable, intangible assets. It is understood that the risks specific to the buildings are different from the risks that affect a car or copyright;
- income. These are quite specific risks as they arise only in the context of income (business) or distribution (for example, inheritance issues);
- staff. These risks often have a non-economic nature, so that they are difficult to assess in monetary terms. Often, this assessment is limited to the amount of negative financial consequences;
- responsibility. The associated risks are determined by the liability arising from an unforeseen event in relation to persons who at the time of risk assessment are not yet known. Examples include professional liability or risks associated with the environment. In some cases, one original event can affect a different number of the vulnerability objects exposed to risk.

The following risks can be identified by the criterion of the nature of the impact on the various vulnerability objects:

- overall risk – the risk affecting the various objects, sometimes causing negative consequences of a different nature. An example is a natural disaster causing loss of life, destruction of property, disruption of business, etc.;
- private risk – the risk affecting a single object or a person. As a rule, it is easier to collect the required information on general risks than on private ones, as many objects are exposed to adverse effects. The same applies to private mass risks.

The general risk is characterized by risks accumulation. The risk accumulation is a situation where one event can cause damage to different objects, but the responsibility for losses coverage in a whole or in part rests with one organization or person, so that the cumulative damage accumulates. An example is the insurance of real estate in an area exposed to the danger of flood.

After the flood, the insurance company may receive a large number of claims for losses associated with damage to the insured property.

3. By the extent/levels of danger/effects; By the criterion of the geographic scope, the risks can be divided into: local, regional, national, global.

By the criterion of the degree of danger/effects, the risks can be divided into: small (negligible), substantial, significant.

The following classification is possible by the criterion of scale or level of implementation in the social and economic system:

- risks arising at the level of the economic system of the country;
- risks arising at the level of administrative, economic, and regional entities;
- risks arising at the level of a separate household facility (the company);
- risks arising at the level of structural units;
- risks arising at the level of a separate work position.

Some of these risks can be influenced by others – they should be taken into account only when making decisions. The level of responsibility for risk does not necessarily coincide with the level at which it arose. In particular, the economic risks associated with business have the following levels of responsibility:

- project risks and or risks of division, i.e. associated with a specific project or a particular division of the company;
- risks of the company (enterprise), i.e. the risks specific to the company as a whole;
- industry risks, i.e. risks associated with the specifics of all companies in the industry (market conditions of production, etc.);
- general economic risks, i.e. risks of the entire economy (inflation, a crisis of overproduction or financial markets, etc.);
- global risks – risks of the global economy as a whole.

Each of the specified levels will have its own particularities in risk management analysis.

4. Depending on the time factor; Here, the classification criterion can be the extent of the time factor consideration, i.e. how long the risk will last.

The risk may take place for a limited time (for example, the risk of possible complications after surgery takes place only within a certain period after the corresponding surgery).

The following risks can be allocated according to the time factor: termless risks that do not have time limits; urgent risks, which in its turn includes long-term and short-term ones.

This classification is very important, since risk management must obviously have different policies regarding the termless, long-term and short-term risks.

The dependence of risk on time. The following risks can be allocated according to this criterion:

– static risks, i.e. risks that do not depend on time or this dependence was not be detected;

– dynamic risks, i.e. risks that change over time (e.g., increased risk of accidents in the increase of the equipment deterioration). The type and degree of dependence may vary for different risks.

Duration of identification and elimination of the negative effects.

As a rule, a risk with short or long term detection of adverse effects may be identified. In some cases, when it is caused by the specifics of risk, risks with the medium-term detection of negative consequences can be also identified.

Most risk refers to the group with a short-term detection of negative consequences: usually damage is identified immediately or within a few months. These are, in particular, the risk of fire or of exchange speculations. However, in some cases this is not possible.

Let us say, the identification of damage by risks associated with responsibility can occur after a sufficiently long period (with duration even up to several decades). A classic example of this risk is the situation with the use of asbestos in construction. A few decades ago, it was widely used in construction as it is non-flammable and is a good thermal insulator. However, it later became clear that asbestos dust is a carcinogen; it causes asbestosis (sclerosis of lung tissue due to asbestos dust).

5. By the generic character or regularity of a risk occurrence; Classification criterion is the extent of the generic character or regularity of the considered risk for this object and/or situation. The following risks can be allocated according to this criterion:

- fundamental risk, i.e. regular risk inherent (immanent) for this object and/or situation, as well as based on the natural or social principles. Relevant events are also random, but risk exposure is sufficiently high. These risks include, in particular, the risk of car accidents or hail damage to crops;
- sporadic or seasonal risk, i.e. irregular risk posed by extremely rare events and force majeure circumstances, the risk realized with a very low probability. An example is the destruction of property as a result of a meteoritic fall. When analyzing and managing risk, first of all, take into account the fundamental risks; sporadic risks should be considered only to the extent to which they are important according to other classification criteria.

6. By characteristics of the risk occurrence consequences; The consequences of risk occurrence is an important hazard characteristic posed to the studied object or process. The following risks are distinguished depending on the outcome of possible risk occurrences:

- pure risk, in which all outcomes, except for saving the current situation are related to the negative consequences. An example of this risk is a fire or robbery;
- speculative risk, i.e. risk, outcomes of which are related both to the negative ("loss") and positive ("win") effects. An example is the risk of gambling.

With regard to this classification it is important to identify the features of methods to control the specified risk. So, the pure risks are often controlled by insurance, and the speculative ones are controlled by hedging.

The following risks can be identified depending on who is affected by the negative effects of adverse events and who may suffer from the occurrence of the risk:

- unilateral risks;
- bilateral risks;
- multilateral risks.

An example of a unilateral risk is a mortality risk, bilateral – the risk of the insured event under contract with the deductible franchise, multilateral – the risk of inflation.

7. By the characteristics of the interaction with other risks; In practice, risks occur not separately but together. In some cases, the relationship of risks is a key aspect, since risks can strengthen or mitigate each other, induce or cause other risks. Prevalence of this risk can be a classification criterion here. The following risks can be identified:

- large-scale risks typical for a large number of similar objects (for example, the risks of car accidents). Even if the risk is small, it can occur quite often. It is easy to find information on such risks;
- unique risks encountered only in individual objects (e.g., nuclear risks).

Typically, this is a significant risk; otherwise, they are not worth time and resources. Due to the uniqueness of such risks, it is sometimes quite difficult to find information on them. Procedures and methods of analysis and management of these types of risk are fundamentally different.

The following risks can be identified using the criterion of the possibility to induce a “daisy chain” of risks:

- primary risks, i.e. directly related to the unfavorable initial event;
- secondary risks associated with the effects of the primary risks related to the unfavorable initial event;
- tertiary risks, etc.

An example of this initial event is an earthquake: destruction of property (e.g., dams) will correspond to primary risk, and consequences of flooding caused by the destruction of the dam will correspond to the secondary risk.

Another example is the influence of the natural and social environment on the economic risks. A similar effect cannot be observed (for example, there is unlikely to be any relationship between global climate change and fluctuations in the share price of the Microsoft company). If the natural and social environment affects the risk, the relationship can be either direct or indirect. In the case of global climate change, the example of a direct relationship will be the growth of aggregate losses from hurricanes, tornadoes and storms, and the example of a indirect one is the long-term impact on the stock price of "Gazprom". In this case, the impact of natural and social environment on the risk may strengthen or weaken it.

The criterion for the classification of economic risks may be a degree of their diversifiability. In this case, risks are divided into diversifiable and non-diversifiable.

Risk diversification, i.e. their redistribution in terms of volume, time and space, is considered the most effective way to reduce the risk, so the risk managers often seek to achieve the greatest possible degree of risk diversification. If the aggregate vulnerability is generally less than the vulnerability to the corresponding risks individually, than the risk is considered diversifiable, otherwise it is non-diversifiable.

8. By the characteristics of the risk magnitude (size); With regard to the magnitude of the risk it is extremely important to understand how to deal with the corresponding risk. The concept of the risk magnitude involves a coordinated analysis of the two characteristics – the frequency of occurrence and the extent of damage/effects. Classification criteria are:

a) the frequency of damage occurrence. It is an important characteristic of the risk magnitude, and it can be measured quantitatively or qualitatively. There are the following classes of risk in terms of frequency:

- rare risks which are characterized by a low frequency of risk occurrence, i.e. the low probability of damage occurrence;
- risks of medium frequency, which are characterized by a medium frequency of risk occurrence, i.e. the medium probability of damage occurrence;
- frequent risks which are characterized by a high frequency of risk occurrence, i.e. the high probability of damage occurrence;

b) the extent(severity) of damage/effects. The following risks can be allocated according to this criterion:

- low risks, i.e. the risks which have the low maximum damage;
- average risks, the maximum damage of which is characterized as average one;
- high risks, i.e. the risks with a large maximum damage;
- catastrophic risks characterized by exceptionally high maximum damage.

Such a classification is extremely important and widely used in practice.

According to the criterion of the acceptability, the risk magnitude can be divided into unacceptable; acceptable with significant limitations; acceptable without any significant limitations.

9. According to the criterion of the freedom of choice, the risks can be divided into: voluntary; imposed (including professional ones).

10. According to the characteristic of the degree of measurability and predictability of risk. The issue of the information provision is one of the key issues in the risk analysis and management, as its solution considerably provides the risk management process. Classification criteria here are the degree of measurability and predictability of risk, i.e. the possibility to assess and predict the risk, the availability of necessary information. The degree of predictability or predictability is an important characteristic of risk in terms of procedures and techniques to manage this risk. According to this criterion, risks can be divided into the following two groups:

- predictable (foreseeable) risks that can be predicted on the basis of economic theory and economic practice, but it is impossible to predict the time of their occurrence;
- unpredictable (unforeseeable) risks which are not known, so it is impossible to assess their impact on the extent and amount of risk.

Unpredictability can be associated both with full or partial lack of information (in particular, information about a unique object), and with the fundamental impossibility of quantitative or qualitative forecast (for example, in assessing the severity of some biotechnological researches). For predictable (foreseeable) risks, the further analysis is closely related to the acquisition of the necessary information.

Information can be:

- quantitative information, i.e. information expressed as numerical values of certain indicators; quantitative information can be processed using statistical methods, and used to estimate the parameters of mathematical models;
- qualitative information, i.e. information reflecting verbal description and/or value judgments concerning the object or process.

Both types of information may be useful in risk analysis and management, although the quantitative information is preferable, as it allows to numerically measure the studied risks.

The decision maker must clearly understand the degree of reliability of the information used, because the incorrect information may lead to wrong conclusions and errors in risk management, i.e. to an increase in potential damage. In most cases, the degree of information reliability can only be judged qualitatively, so that the question of the numerical measurement of the degree of reliability is not even worthwhile. Nevertheless, there are also approaches to quantitative assessment of these characteristics of the risk being studied [Bykov A.A., Porfirev B.N., 2006].

These examples of classification do not cover all the criteria and possibilities of risk classification. It is necessary to classify them according to different criteria in order to isolate the specific risks. It should be noted that the risks could be classified by many criteria. It is important to highlight a group of similar risks in the risk analysis. This has several important advantages. However, in practice it is not always possible to classify risks according to several criteria to such an extent that the risks in each group were virtually identical (homogeneous). This is due to limitations of the observed objects, a certain degree of risks uniqueness, incomplete information, and other factors. Therefore, the risks discussed in the framework of a selected group can be heterogeneous, which requires a more careful analysis of such risks at the subsequent stages.

A separate issue having a significant impact on the methodological frameworks of the assessment and management of risks, especially when trying to harmonize them, is the terminological identification of concepts and definitions. First, the definition of "health risk" is important for the purposes of the current study. On the one hand, this definition must not conflict with already well established and common terms in the field of mathematics, on the other it should take into account the particularities of hygienic terminology.

One of the most common definitions of the term "risk" is given in the Stanford Encyclopedia of Philosophy [Hansson S.O., 2012].

Risk is the potential of losing something of value, weighed against the potential to gain something of value. Values (such as physical health, social status, emotional well being or financial wealth) can be gained or lost when taking risk resulting from a given action, activity and/or inaction, foreseen or unforeseen. Risk can also be defined as the intentional interaction with uncertainty.

A sufficiently brief definition of the concept of "risk" is contained in the GOST R 51897-2002 and ISO Guide 73 : 2009 "Risk Management. Terms and Definitions". These documents cover risk because of the impact of uncertainty on the achievement of the stated objectives. At the same time, the ISO Guide 73: 2009 determines risk within a single division as the description of the possible (probable events) and its consequences, or combinations thereof (*Note 3, section 1*), or the consequences of possible events and the corresponding probability (*Note 4, section 1*).

ISO/IEC Guide 51:1999 treats the risk as a combination of the probability of harm (damage) and the severity of that harm.

The domestic legal framework establishes the concept of "risk" is in Article 2 of the Law "On Technical Regulation» (No. 184-ФЗ dated 27.12.2002). It defines the risk as the probability of harm to the life or health of citizens, property of individuals or legal entities, state or municipal property, environment, life or health of animals and plants, taking into account the severity of such harm. This definition integrates several diverse concepts of risk (risk to health, environment, damage to property), which corresponds to the overall risk.

According to one of the leading Russian scientists in the field of mathematical statistics, A.I. Orlov (2012), it is advisable to allocate a number of components to the concept of "risk". It is necessary to divide the event that implements the undesirable opportunity, in other words, the hazard and the assessment of this event (assessment of the intensity and severity of the hazard). Furthermore, A.I. Orlov includes the concept of "risk" and possible measures to reduce the undesirable effects (risk management using certain administrative decisions).

Thus, it should be noted that a single definition of the term "risk" has not yet been accepted. Moreover, some differences in the definition of "risk" are allowed even within the

same document. However, the presence of key concepts of the "event probability", caused "harm (damage)" resulting from this event should be noted in the vast majority of definitions.

Together with the above definitions of the term "risk", there are some definitions of risk with the differentiation by certain consequences (environmental, economic, demographic, etc.). Health risk has one of the first places. When it comes to the health risk arising out of or expected in connection with the adverse effect of certain environmental factors on it, it is necessary to identify terminologically this concept.

International documents such as the WHO Recommendations (1978) defines risk as "the expected frequency of adverse effects resulting from the given pollutant effects." According to the Glossary of the United States Environmental Protection Agency (US EPA) (2011), risk is "the probability of damage, disease or death in certain circumstances. Quantitatively risk is expressed as values from zero (reflecting the confidence that the harm will not be inflicted) to one (reflecting the confidence that the harm will be inflicted)."

With regard to the exposure of unfavorable environmental factors, risk is the expected frequency of harmful (adverse) effects in the population resulting from a given exposure to pollutant [WNO, 2000].

Adverse effect should be understood as the changes in morphology, physiology, growth, development or lifespan of an organism, population, or offspring appeared as the deterioration of functional capacity or the ability to compensate for an additional stress, or increase of sensitivity to the effects of other environmental factors. As a rule, the intensity of effects is taken into account in their assessment. The term "response" is used in the case of assessment of the portion of the exposed population, which has developed a specific effect, or the prevalence of studied adverse effects in the exposed population.

With regard to the risks associated with the consumption of food, "risk is the probability function of adverse health effects and the severity of such consequences due to the presence of a hazard (or hazards) in food" [WHO/FAO, 2010]. In the context of non-food products, the risk is defined as the probability and severity of an adverse effect/event that happened to a man as a result of the impact of risk sources under certain conditions [EC, 2004; Final Report, 2007].

The European documents proposed the following definition: "The risk is the function of probability and severity of adverse health effects due to the presence of danger" [EC, 2002], as well as "the risk is a balanced mix of risk and the probability of damage. Risk describes danger and probability not separately, but together and at the same time"[EU, 2010].

Russian regulatory and procedural documents defines the health risk as the probability of a threat to life or health of the person, or threat to the life or health of future generations due to the influence of living environment [R 2.1.10.1920-04].

Foreign guides consider risk as the probability of an adverse effect to a person, group of people, animals, plants, and/or ecology within a certain period of time in a certain area, which was exposed to an impact of the certain dose or concentration of a hazardous substance [Commonwealth of Australia, 2012], or as the probability of adverse effects on the body, system, or (sub)population when exposed to the agent under certain conditions [WHO, 2004]. However, the concepts of probability and severity are more often found simultaneously in the definition of "risk": risk is the probability and severity of an adverse effect/event that happen to a person or the environment as a result of the impact, under certain conditions [UKCC, 2007], risk is a combination of the probability or frequency of occurrence of a certain hazard and the magnitude of the incident consequences [UKCC, 2007].

Since the above definitions consider the probability and severity as basic essential risk characteristics, and also highlight the formation of risk under the influence of external factors, it is advisable to determine the health risk as the probability of adverse effects of different severity on the part of the human body and/or responses in the human population, stipulated by the factors exposure. This definition allows the consideration of the key aspects of health risk: probability, consequences of risk realization, their importance, individual and population character and the connection with the factors stipulating this risk.

Based on this definition of health risk, it can be classified as pure (non-speculative), fundamental, unilateral, large-scale, dynamic, and global one.

1.2. Paradigm and conceptual provisions of health risk analysis. The relation of paradigms of hygienic rating and health risk analysis

The concept of paradigm (comes from Greek παράδειγμα – "an example, a model, a sample" < παραδείκνυμι – "compare") in its modern sense was introduced by the American physicist and historian of science, Thomas Kuhn [Kuhn T.S., 1962], who highlights the various stages in the development of the scientific discipline:

- pre-paradigm stage (prior to the establishment of a paradigm);
- the stage of the paradigm domination (the so-called "normal science");
- crisis of normal science;
- the stage of the scientific revolution consisting of a paradigm shift, transition from one to another.

As a rule, the paradigm for many years determines the range of problems and methods of their solution in a particular field of science, the scientific school.

The need to formulate a paradigm of health risk analysis was formed by the beginning of the 1980s. At this time, studies were performed and the approaches to risk assessment and risk management were proposed in the United States, then they were adopted by the EPA (Environmental Protection Agency) and other agencies. The recommendations of this Committee are presented in the generalized form in Fig. 1.2 [Lipman M. et al., 2003].

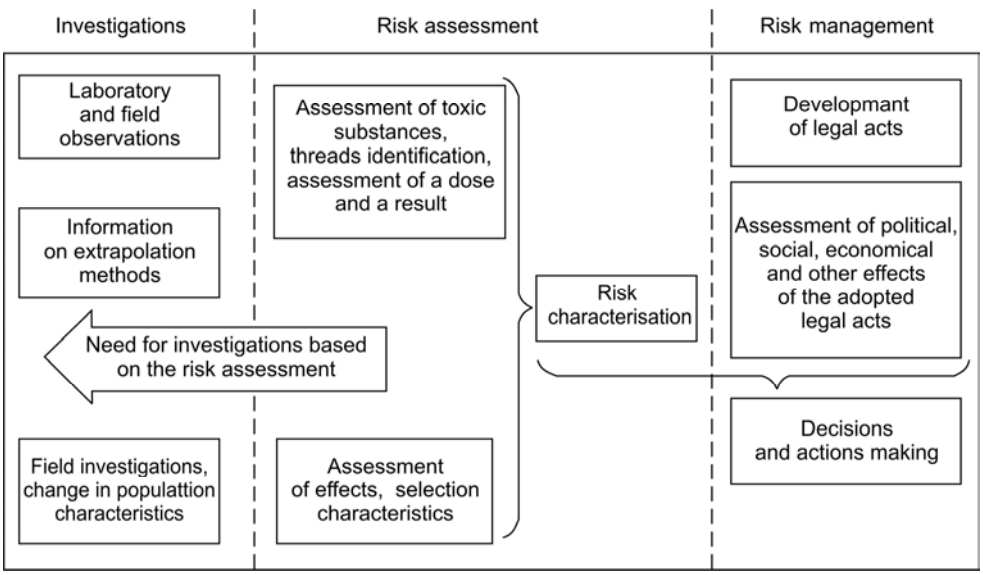

Fig. 1.2. The risk assessment is based on a assessment technique

The position on the division of risk assessment have been formulated according to the recommendations of the National Research Council, this risk assessment was based largely on the interpretation of scientific principles and data, and risk management, which is based on the decisions recognizing the nature and limitations of scientific risk assessment. The latter are influenced by limitations associated with legal aspects of responsibility, opportunity and cost of the intervention and control, as well as the expected availability of these features. The general idea was that scientists with the relevant expertise can carry out a risk assessment better, but they do not have to have a special or a dominant role in the choice of means and ways to implement projects to control the risks.

According to that which is stated above, the distinctive feature of the methodology of risk analysis is a functional separation of a stage of the research related to the health risk assessment and a stage of the risk management. The third element of risk analysis methodology is the information about the risk of all interested persons. All three elements of risk analysis are interconnected and only their combination allows not just identifying problems, developing ways to solve them, but also to create conditions for the implementation of these decisions (Fig. 1.3).

The paradigm of health risk analysis is presented in the form of diagrams describing this process with different degree of detail and application in various aspects (Fig. 1.4).

Fig. 1.3. The main components of health risk analysis [FAO/WHO, 1997]

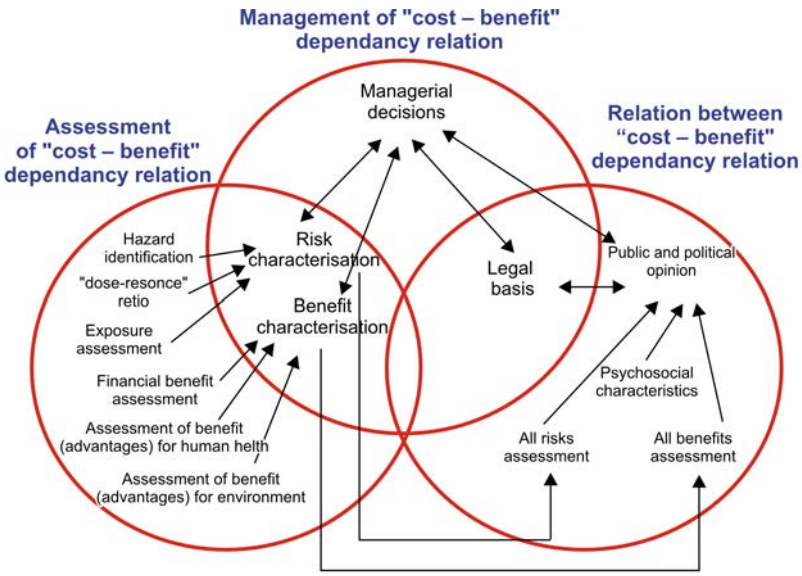

Fig. 1.4. Scheme to implement the health risk assessment paradigm in terms of the "cost – benefit" analysis

The probability of human health violation that is a consequence of exposure to a particular agent or combination of such agents, and can be expressed in different ways depending on the context, is considered as risk under the proposed paradigm. For example, the average annual risk for one person, the average risk for one person throughout life, the average number of people who are exposed within a given population, the average loss of life duration in people who have been exposed, etc.

Risk may be expressed either as an absolute risk (i.e., the absolute increase in the number or probability of negative effects), or as a relative risk (i.e., the relative increase in the initial frequency of the negative effects. The significance of a certain risk depends on the probability (frequency) of the analyzed effect and on its severity. Severity index includes such factors as the degree in accordance with which the effect is (or is not) symptomatic, painful, affecting the appearance leading to disability, irreversible, progressive, fatal, etc. In its broadest context, severity indicators are characterized not only by the impact on health, but also by other aspects including aesthetic, psychosocial, ethical, and economic impacts.

The paradigm of health risk assessment involves the use of a four-stage diagram of this process including hazard identification, assessment, "exposure – effect (response)" dependency relation, exposure assessment, risk characterization with the uncertainty estimation (Table 1.1) [Lipman M. et al., 2003].

This scheme provides for coordination with the process of health risk management (Fig. 1.5) [National Research Council., 1983].

Table 1.1

Four stages of risk assessment

Stage	Content
1. Threads identification	Analysis of relevant biological and chemical information indicating whether or not the agent is carcinogenic and whether the toxic effects will occur in the same situation as in other ones
2. Evaluation of relationship between the dose and the result	The process of the dose assessment and the assessment of its relationship with the frequency of adverse health effects
3. Impact assessment	Determination or assessment (quantitative or qualitative) of the amplitude, duration, and routes of exposure
4. Risk characterization	Integration and summation of the identified threats, assessment of the relationship between the dose and result. Impact assessment together with the assumptions and uncertainties. This final stage involves the assessment of the risks to public health and creates a structure to determine the significance of the risk.

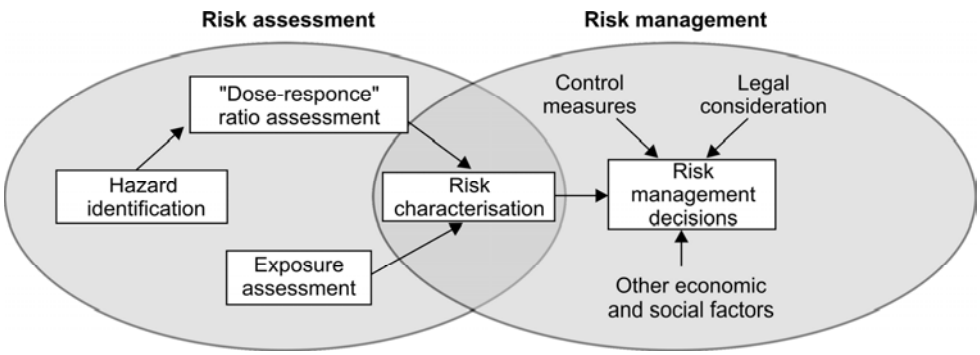

Fig. 1.5. Paradigm of the assessment/risk management
National Research Council (US EPA)

Schemes of the evaluation of other types of risk while maintaining the overall conceptual integrity are characterized by some differences. For example, a scheme for environmental risk assessment (Fig. 1.6), in addition to differences in the content of individual stages, involves an additional stage of the exposure point identification [Lipton J. et al., 1993]. This is due to the specific of the exposure targets – ecological systems.

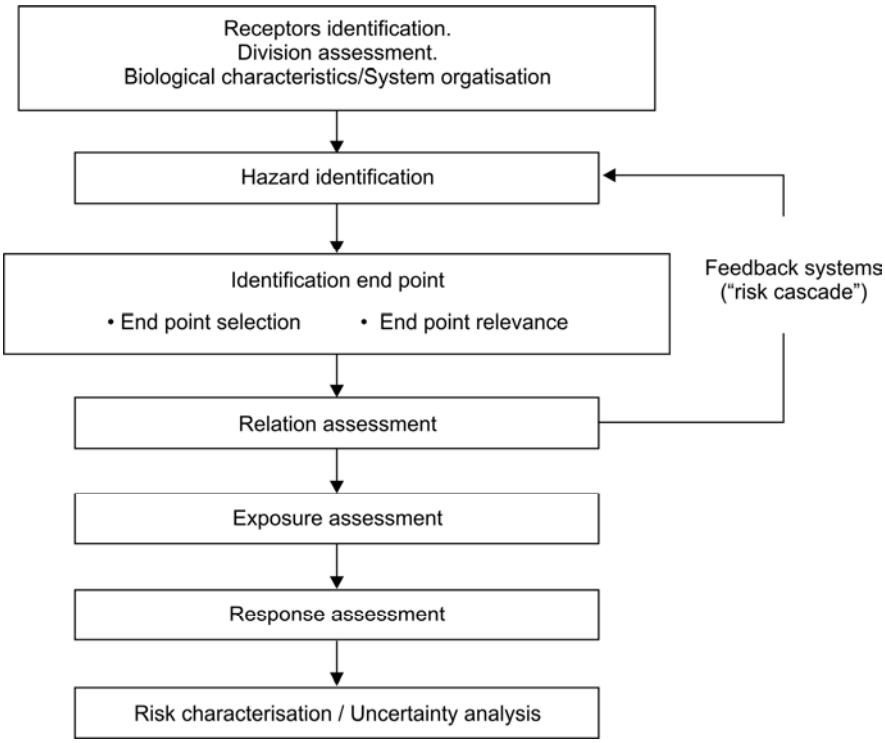

Fig. 1.6. Block diagram, describing the stages of the proposed paradigm for environmental risk assessment

The key provisions of the health risk assessment paradigm are:

– the priority of safety, health preservation over any other elements of life quality;

– the concept of a non-zero risk;

– consistent study based on hazard identification – qualitative description of risk factors and their corresponding effects, and the quantification assessment of "exposure – effect (response)";

– the presumption of the lack of the action threshold for a number of factors, such as the carcinogenic effect.

In the Russian Federation, the paradigm of health risk assessment is formed as a continuity one with regard to hygienic rating paradigm, the determining criterion of which is prevention of the harmful effects. This criterion must meet several requirements: it should be binding upon, have a comprehensive implementation, be available for control, and ensure the absence of direct, indirect or mediated harmful effects at the level of the modern scientific knowledge in the short and long periods.

When developing and validating hygienic standards, the paradigm of hygienic rating involves the use of a number of key provisions.

The principle of safety hygienic standard (the primacy of medical evidences) is based on the fact that in the justification of the standard of harmful factor in the environment, the

particularities of its effects on the human body and sanitary living conditions are taken into account first of all.

Advance principle of justification and implementation of preventive measures before the formation and (or) the impact of certain hazards. This principle is fundamental to the methodology of hygienic rating since the production and use of insufficiently studied potentially hazardous agents is associated with a risk to public health. In addition, the violation of the advance principle can result in significant economic losses due to production delays.

In practice, the implementation of the advance principle faces serious difficulties that are stipulated by the toxicological and hygienic studies arrearage of technological development due to the high cost and duration of the researches of the establishment of hygienic standards.

Thus, there is a contradiction between the needs of the practice in hygienic standards and the real possibilities of scientific institutions to justify them. It is obvious that hygienic standards cannot be based on the results of the investigations of community health exposed to harmful factors (multifactorial exposure, duration of the latency period of malignancies development). At the same time, experimental investigations carried out under the classic (full) schemes of hygienic rating, do not fully support the advance principle. According to the "International Program on Chemical Safety", even economically developed countries sufficiently investigated only a small part of commonly used potentially hazardous substances in terms of toxicology. Even the optimization of experimental studies (staging, turn-based strategy), sharing of data obtained in different sections of prophylactic toxicology, hygiene, environment, and the development of computational and express experimental methods of forecasting cannot fully solve the problem of environmental safety for human health under the intensification conditions of the new substances (often with unpredictable properties, e.g. nanocomponents) practical application.

The principle of unity of the molecular, structural, and functional changes as a basis for differentiation of hazardous and non-hazardous effects. The essence of this principle is that any one indicator of the health state, the changes of which are not pathological, but went beyond physiological fluctuations, cannot serve as a basis to judge the hazard or safety of the studied dose or concentration of the substance. The presence of integral shifts evaluated at the organismic level is a more significant in terms of the position of critical indicator of harm. Changes in the individual organs and systems, disturbances at the cellular and molecular levels are taken into account with regard to their nature and severity.

The criteria for harmful effects are: physiological and biochemical and morphological parallels, a study of the specificity and direction of the revealed shift, direction of changes over time (the presence or absence of shift progression in the continued exposure, the duration of changes during the recovery period following the termination of an exposure), a study of the state of metabolic transformations and kinetics of toxic substances in the body.

General biological critical indicators of harm: reduction in an average life expectancy, physical development disorder, changes in the central nervous system, impaired ability to adapt to the environment.

Criteria characterizing psychosocial disorders: violation of the mental functions, inhibition of the emotional sphere, a violation of interpersonal relationships, reduced ability to creative production activity, violation of dynamic behavioral stereotype.

Reproductive function disorders: change in the genetic material, effect on sperm, fertility, and infertility, pre- and postimplantation loss or delay in the development, biochemical, physiological and behavioral changes in the offspring, handicaps and other malformations.

Carcinogenic effects: an occurrence of tumors, an increased incidence of spontaneous tumors and reduced latency period of their development, the occurrence of tumors in the site other than one under the control.

Physiological criteria: functional activity of physiological systems (central nervous system, cardiovascular, respiratory, digestive, endocrine, etc.), adaptive (regulatory) mechanisms functions, premature aging, biological rhythms, behavioral responses.

Biochemical criteria: biochemical tissue constants, disorder of structure and spatial organization of nucleic acids and their chemical modifications.

Immunological criteria: nonspecific indicators of immunological reactivity, antibodies as a specific immune factors, immediate and (or) a delayed hypersensitivity.

Metabolic criteria: the rate of metabolism and substance excretion from the body, depending on its dose, substance accumulation in critical organs, depending on dose, the appearance of organotropic enzymes in the blood, activity inhibition and damage of key enzymes of metabolic systems, the activity of microsomal liver enzymes, changes in the activity of lysosomal enzymes in combination with labilization effect of lysosome membranes, a compensatory increase in the activity of the enzyme system for which the poison is a substrate, a violation of the enzyme systems interaction.

Morphological criteria: destructive and dystrophic changes in cell structures, biopolymers content in cells, changes in cell enzyme systems in histoenzymological analysis, the functional activity of intracellular organelles in electron and microscopic analysis, the activation of DNA-synthesizing cell function, microcirculation in organs, and increase in the degranulation index of mast cell system.

Statistical criteria: critical significance level of Student's shift is 0.1 for rigid biological indicators (variation coefficient of less than or equal to 10%); critical shift level is equal to 0.05 for plastic indicators (variation coefficient of 10–40%); critical shift significance level is 0.01 for superplastic indicators (variation coefficient of more than 40%).

According to I.V. Sanotsky and I.P. Ulanova (1983), the statistical harmful effects criterion must correspond to the dynamic overrange, i.e., overrange of the normal seasonal parameters variations (but not just a significant difference from the parallel control).

There are other critical indicators of harm, however, in this regard, it is crucially important to note that it is necessary to establish the border between the states of norms, adaptation, pre-pathology and pathology to form critical indicators of harm along with the definition of "norm".

When considering the range of all possible responses of the human body on chemical exposure, the following types of biological responses are differentiated; mortality, morbidity, physiological and biochemical signs of the disease, changes in the body of unknown etiology, the accumulation of xenobiotics in organs and tissues.

Criteria of harmful effects are closely related to two other principles of hygienic rating: threshold principle and principle of the "concentration/dose and time" effect dependency relation [Rumyantsev G.I., 2009].

Effect threshold principle isa fundamental principle of rating. It assumes the existence of doses/concentrations that do not exhibit toxicity or other adverse effects on the body. The possibility to establish a threshold of harmful effects for most types of chemical compounds is not in doubt. However, that question still remains controversial for mutagens and carcinogens. The vision of the thresholdless of genotoxic carcinogens impact was a consequence of the existence of a monomolecular mechanism of mutagen connection with nucleic acid bases.

The threshold principle is based on such fundamental provisions as the existence of a wide range of body responses to external impact, the possibility of an intermittent transition of minor quantitative changes in the organism state to new quality ones, the presence of constant renewal and regeneration of biological structures, processes of adaptation and compensation. A view that the physiological responses of adaptive nature and characteristic to a healthy body should be taken as a threshold level of exposure, was confirmed in modern domestic hygiene. They should be distinguished from compensatory physiological responses aimed to replace the disordered function, rather than to adapt a healthy body. Despite the clarity of the theoretic plan, the justification of the threshold doses/concentrations remains one of the most complex issues in the practice of hygienic rating in the evaluation of the experimental data obtained.

The threshold principle is inextricably connected with the other principle of hygienic rating – the principle of effect dependence on the concentration (dose) and the exposure time. The dose or concentration magnitude and the duration of exposure not only determine the time of the biological effect occurrence, but often affect its quality characteristics. The character of "dose – time – effect" dependence is defined by the processes of substance accumulation or its effects in the body – cumulation and the process of organism adaptation to this poison (adaptation, compensation). Differentiation of adaptation and compensation is

carried out using adequate mechanism of action of harmful substances, extreme and functional loads (pharmacological, physiological, etc.).

The principle of biological modeling to validate the degree of harm and danger of the standardized factor reflects the need for its advanced hygienic assessment before the use in economic activity. The possibility to obtain information about the extent and nature of the toxicity and hazards of chemicals directly in humans are very limited due to considerations of humanity. Experiments are conducted on humans only in some cases (such as when determining a certain threshold of irritant or olfactory action). Fundamental and basic model in the study of toxic and delayed effects are laboratory animals (mammals).

In most cases it is possible to choose an adequate laboratory model to run pathologic processes observed in humans. Quantitative transfer of data concerning the exposure levels that are effective for animals to human, is more complicated. Therefore, it is proposed to use the allometric ratio of sensitivity of different species of mammals and their body mass, to carry out the calculation of dose per a body surface area, to calculate the coefficient of species sensitivity, to consider a set of indicators (basal metabolic rate, the volume of cardiac activity, coefficient tserebratsii, body weight).

For a greater reliability of data extrapolation from laboratory animals to humans in the transition from the experiment to the value of the MPC, a safety factor determined on the basis of the indicators of substance hazard and toxicity, severity of species differences in sensitivity, is used. Rules to select the values of the safety factor are regulated for each of the environmental mediums (water, soil, air, workplace air, food).

Hygienic standards are set separately for each object in connection with the specificity and variability of physical and chemical properties of water, soil, air, food products of animal and vegetable origin, features of their effects on the human body (the principle of distribution of sanitary protection objects).

The principle of the limiting harm value is used when determining the final value of MPC; in accordance with it, the standard value is selected at the lowest concentration level set according to different critical indicator of harm (accounting principle of "weakest link" and "bottleneck").

Due to the fact that the complex of standard indicators (MAC, SRLI, APL, PL) is represented as simple numeric values, bearing the legal, medical, and many other features, the observation of *the principle of standardization of conditions and methods of hygienic rating* is of great importance. In practice, this principle is implemented in the form of guidelines, recommendations, state standards regulating conditions for researches, the methods used, the principles of assessment, etc.

The practical implementation of the advance principle, development and implementation of effective preventive measures are possible in observation of *the principle of stage-by-stage research*. This principle reflects the need to identify research strategies, highlight important steps carried out in strict sequence and, if possible simultaneously with the stages of the introduction of new substances and materials. Stages and rules for the conclusions (decisions) making at each stage depends on the environmental medium.

Considering the fact, that the results of experimental researches in any branch of science are only an approximation to the truth, to the extent allowed by the investigation methods used of, an important principle of hygienic regulation is *the principle of unity of experimental and field (hygiene, medical, epidemiological) studies* [Bolshakov A. M. et al., 2009].

MPCs of a number of substances have been reviewed taking into account this principle, for example, for water bodies, MPCs of lead and arsenic were reviewed and reduced, MPCs of zinc and stable strontium were increased, MPCs of a number of aliphatic alcohols were clarified.

These principles formed the basis of methodological research schemes on hygienic rating of harmful factors in the environmental medium.

Analysis of modern approaches to the safe management of environmental factors affecting the human body, has shown that the system of hygienic rating was considered as one of the most important instruments of state policy in the field of human health protection. There was an opinion that in our country, where hygienic rating was adopted as the world

first scientific basis for air protection against chemical pollution, it is inappropriate to consider the risk concept as an alternative to the concept of hygienic rating. It was noted that "the indicated concepts can be formally called alternative, because essentially they are organically connected not because they are aimed to protect the environment against chemical contamination, but also due to their approaches to solve these problems. These two concepts are, in fact, methodological alternatives to solve problems of air protection, etc." [Pinigin M.A., 2000]. However, the rating methodology as a set of principles, criteria, and methods of hygienic assessment of environmental factors is a matter of argument at the present stage. These arguments relate to some the basic principles of hygienic rating.

Comparison of key provisions of paradigms of hygienic rating and health risk analysis (Table 1.2) allows the identification of both their analogies and differences.

Table 1.2

Comparison of key provisions of paradigms of hygienic rating and health risk analysis

Paradigm of a hygienic rating	Health risk analysis paradigm
The principle of hygiene standard safety (the primacy of medical evidences) (principle of zero risk)	The priority of safety, health preservation over any other elements of life quality (the principle of the acceptable risk)
Advance principle of justification and implementation of preventive measures before the formation and (or) the impact of certain hazards.	Selection and justification for the evaluation factors from among the affecting ones
The principle of separation of sanitary protection objects (development of hygienic standards for the individual factors and objects of the living environment)	Impact assessment, including the multimedia and integral one, at the end point; the ways and sources are identified for management tasks
The principle of unity of the molecular, structural, and functional changes as a basis for differentiation of hazardous and non-hazardous exposure levels	Evaluation of molecular, structural and functional changes to validate risk assessment parameters (inactive levels and parameters of the "exposure – effect (response)" dependence
The principle of effect dependence on the concentration (dose) and the exposure time	"Exposure – effect (response)" dependency relation evaluation for various exposure scenarios
The principle of biological modeling to justify the degree of harm and danger of the standardized factor	Application of the results of the *in vitro* and *in vivo* experiments to validate the parameters of the risk assessment
The principle of the standardization of the conditions and methods of hygienic rating implemented in the form of guidelines, recommendations, state standards regulating conditions for researches, the methods used, the principles of assessment, etc.	Accepted principles of risk assessment procedures; the validated use of innovative approaches is allowed
The principle of stage-by-stage research (analysis of the factor properties, toxicity assessment, acute experiment, chronic experiment, the specific effects, epidemiological studies)	Stage-by-stage nature of the procedure (hazard identification, evaluation of "exposure – effect (response) dependency", exposure assessment, risk characterization)
The principle of unity of experimental and field (hygiene, medical, epidemiological) studies, review of the MPC of a number of substances according to the receipt of new scientific data	Revision of the final risk assessment through a comparison with independent data on population morbidity
Submission, review, and approval of the results at the departmental level	Transparency of assessment and the description of uncertainties as an integral part of the risk assessment

The coincidence of the main objectives of both paradigms is obvious; it is a minimization of the impact of environmental factors on human health. However, the conditions of hygienic rating paradigm formation suggested the setting of objectives that would be difficult to accomplish. For example, the solution of the problem of advanced industrial growth, which was supposed to be implemented in the middle of the last century due to extensive development, did not allow full compliance of hygienic standards of living environment quality. A significant deterrent role of hygienic rating in the formation of living environmental contamination in recent years and its importance for the development of hygienic science in Russia and worldwide should be noted. However, social and economic development of the country under the conditions of market economy requires an adjustment of a number of key provisions of this paradigm considering the validation and reality of their application in current conditions.

Health risk analysis paradigm proposes a priority of safety, health preservation as a key principle. Safety criterion is the absence of an unacceptable risk to human life and health. We should not forget that the acceptable risk levels are determined taking into account technological and economic capabilities of the state and society, and should be adjusted with the growth of these opportunities. This holds out a hope that the achievement of these levels at the present stage of economic development of the country is much more realistic than safety assurance (risk absence) by hygienic standards. The principle of safety is based on the avoidance of any adverse changes in health, even the most minimal ones. Since the risk is characterized by the probability of adverse effects occurrence and their severity, consideration of the effects severity is a fundamentally new aspect of the health risk analysis paradigm. It is obvious that the acceptable level of risk of serious disease and death should be considerably lower than the risk of reversible functional disorders.

Currently, the principle of hygienic rating involving an advance of the validation and implementation of preventive measures before the formation and (or) the impact of various harmful factors, require modification for reasons of pragmatism, It should be considered that the studies of a traditional methodology of hygienic rating require high costs and considerable time (from 1 to 3 years). For example, toxicological studies of on chemical substance cost about 500–600 thousand dollars in the USA. However, the workers in the United States are exposed to more than 650 thousand industrial chemicals, while acceptable exposure limits in this country are established for less than 1000 compounds. The growing number of new chemicals requires a thorough registration of all the existing compounds and compounds implemented in the production on the one hand, and a significant acceleration and increased expenditure for researches of hygienic standards validation on the other. The economic feasibility of such expenditures for the entire range of harmful environmental factors is difficult to validate. In world practice, researches to establish the parameters for the risk assessment are carried out only for priority, the most dangerous factors. Expediency of full-scale studies is the subject of individual developments; the criteria for selection of these factors recorded in legislative acts, are also discussed.

The use of a sanitary protection principle (development of hygienic standards for the individual factors and objects of living environment) in hygienic rating has led to the fact that hygienic standards do not take into account the full combined and united action of living environment factors. The content of chemicals in the air is regulated only for a few groups, e.g., 56 coefficients of a combined action (for 36 binary mixtures, 20 mixtures of 3–5 components) are established for atmospheric air of populated areas.

The development of methodological approaches to the recording of the combined action is carried out by determining the consolidated figures (contamination indices) using the principle of isoefficiency. However, in actual practice, one and the same toxicant may contaminate, for example, air, water, soil, and any food. In these cases, when supervising, it is difficult to focus on the hygienic standard designed to control the contamination of individual components of the environment. It is obvious that the existing methodological approaches solve the problem of quantitative assessment of the factors impact on human health only to a certain extent.

Examples of such an impact are provided quite often. Noise and vibration always enhance the toxic effect of industrial poisons. This is caused by changes in the functional state of the central nervous system (CNS) and cardiovascular system. The noise increases the toxic effect of carbon monoxide, styrene, etc.. Vibration increases the body's sensitivity to other factors by changing its reactivity, eg. cobalt, silicon dust, dichloroethane; carbon monoxide is also more toxic in combination with vibration.

Despite the fact that the sanitary science found quite large number of examples of the combined action of various factors, this was not reflected in setting standards.

In accordance with the risk analysis, the assessment of the impact, including the multimedia and integral one, is made at the end point, and the sources and routes of intake are identified in order to develop a detailed exposure scenario and to set management tasks. In addition to the assessment of a cumulative impact and conclusion about risk level tolerance, this allows revealing the mechanism of its formation and establishing the critical points for the control and minimization.

It should be noted that most of the key provisions that are part of the paradigm of hygienic rating, are used in the health risks analysis paradigm with some technical adjustments.

These include the principle of the unity of the molecular, structural and functional changes. If this principle was used as a basis for differentiation of hazardous and non-hazardous exposure levels in the hygienic rating, it is used to validate the risk assessment parameters in the health risks analysis both for no observed effect levels and characteristics of the "exposure – effect (response)" dependence at the level of living environment factors above the no observed ones. The paradigm of health risk analysis preserved both the principle of the effect dependence on the concentration (dose) and the exposure time.

Justification of the degree of harm and danger of the standardized factor on the basis of biological simulation in the hygienic rating has transformed into the application of the same principle using the results of experiments *in vitro* and *in vivo* to validate the parameters of the risk assessment.

The principle of stage-by-stage researches based on changes in the names of stages and their supplementation with a stage of risk characterization is considered to be one of the basic principles of human health risk analysis.

Some changes in the principle of standardization of terms and techniques have been made. If the guidelines, recommendations, state standards have quite strictly regulated conditions for researches, the used methods and principles of assessment within the paradigm of hygienic rating, then the risk analysis is based on the guidelines devoted to specific aspects of risk assessment and management formed according to the adopted principles of risk assessment procedures. However, the use of innovative approaches is allowed in the course of researches.

The principles related to the revision of the results of hygienic rating and health risk assessment coincide according to the receipt of new scientific data on the results of hygienic, medical, and epidemiological studies, as well as in the comparison with independent data on population morbidity.

Hygienic rating provides for mandatory disclosure of only final results of research (the established MPC, RC, etc.) reviewed and approved at the departmental level. The transparency principle recorded in the summary of the risk analysis paradigm involves mandatory publication of the assessments obtained with the possibility of wide discussion. Thus, the information forming the basis for the establishment of hygiene standards for the criteria of public health risk was published and available.

Thus, it can be said that the evolutionary change of paradigms occurs in terms of modification and continuity of the basic principles of hygienic rating and health risk assessment.

Naturally, the adaptation of the basic positions when changing paradigms reflected also on the paradigms applied in the framework of their methodological approaches (Table 1.3), hygiene criteria (Table 1.4) and the results of evaluations (Table 1.5) obtained by using them. Differences of paradigms concerning the regulation of procedures and sequence of hygienic rating and risk assessment are discussed when comparing the principles of standardization of methods and stage-by-stage nature of researches.

Table 1.3

Methodological approaches used within the paradigms of hygienic rating and analysis of health risk

Paradigm of a hygienic rating	Health risk analysis paradigm
The statutory procedure for standards establishment	Accepted principles of risk assessment procedures, the system of guides on specific aspects of risk analysis
The sequence of assessments according to types of effects (organoleptic/ reflectory, general toxic, specific)	Stage-by-stage nature of the assessment (hazard identification, evaluation of "exposure – effect (response) dependency", exposure assessment, risk characterization)
The use of safety factors according to the criteria of toxicity (hazard classes)	The use of uncertainty factors taking into account the conditions of the research (extrapolation from high to low exposure levels, from laboratory animals to human, the response of sensitive groups, etc.)
Sequential determination of the mean lethal, threshold and no observed exposure levels	Assessment of the threshold and zero-threshold (for a number of carcinogens and microbiological factors) effect
Differentiation by time of exposure (for ambient air) and scenarios of residential and work area	Assessment in accordance with the scenarios taking into account the intensity and duration of exposure for the studied cohorts
Application of the principle of the limiting limiting harm value	Establishment of the critical organs and body systems
–	Obligatory description of the uncertainties of all stages and risk assessment results

Table 1.4

The criteria used in the framework of paradigms of hygienic rating and health risk analysis

Paradigm of a hygienic rating	Health risk analysis paradigm
Toxicometry parameters (CL, DL, Lim_{ac} и пр.)	–
Minimum valid (threshold) concentration	LOEL, LOAEL
Maximum no observed effect concentration	NOEL, NOAEL
Safety factors	Uncertainty factors
–	The risk assessment parameters (reference doses/concentration (*RfD, RfC*), benchmark levels (BMD / BMC), the slope factors (*SF*), the unit risks (*UR*), etc.
Hygienic standards (MPC, RC, MRL, etc.)	Risk-based standards (ADI, MPL etc.)
The rate of the hygienic standard excess	Qualitative assessment: high, moderate, low risk, etc. A semi-quantitative assessment: hazard quotients (*HQ*), hazard indexes (*HI)* Quantitative assessment: the value of the individual, population risk (*CR, TCR*), the stated risk index ($\tilde{R}$) followed by classification

Table 1.5

The use of assessment results obtained in the framework of paradigms of hygienic rating and health risk analysis

Paradigm of a hygienic rating	Health risk analysis paradigm
Purpose for the adoption of command and control decisions(mandatory for all departments, bodies and organizations)	Justification of the differentiated effects on risk management depending on its degree
Legal responsibility for the infringement of hygienic standards	Assessment of social and economic feasibility of health risk management measures
Infeasibility of hygiene standards violation	Risk assessment at the exposure higher than inactive one
–	Conducting of population and economic assessments

Similar approaches are used within the methodological approaches to the establishment of harmlessness criteria during the hygienic rating and safety criteria in the health risk assessment. They involve the use of threshold, inactive, benchmark exposure levels adjusted using safety factors in the hygienic rating and uncertainty factors in the health risk assessment. The main differences relate to provisions governing the establishment of these values. Safety factors – the values showing in how many times the maximum allowable concentration of harmful substance established for a human is less than the threshold of the substance chronic effect established in animal experiments – are calculated, taking into account toxicological parameters, cumulative properties, the specific effects of the substance, the variability of species sensitivity. Uncertainty factors (modifying factors) take into account intraspecies uncertainty (the most sensitive groups), interspecies uncertainty (when transferring the results of laboratory experiments on humans), extrapolation of data obtained in acute, sub-chronic, chronic studies, for the period of a lifetime, the use of a threshold level instead of an inactive one, the use of incomplete data sets. The magnitude of safety factors ranging from 3 to 20, the total uncertainty factor can reach 1000.

There are some differences in the approaches to the modeling of "exposure – effect" dependence. These include, for example, focus to the threshold concept in hygienic rationing. The threshold concept has played an important role in the development of rating in general and hygiene rating in particular. But the development of science proved that it is in conflict with some regularities, which cannot be characterized only in the framework of its provisions. In particular, the majority of scientists and experts are of the opinion that ionizing radiation and many chemical carcinogens have no "harm threshold" in relation to radiation hazards, for example, the exposure to one gamma-quantum ray per cell of the body is sufficient for the occurrence of undesirable (adverse) effects which eventually may lead to remediless effects in the form of malignant tumors. Investigation of the influence of electromagnetic radiation from mobile phones showed the presence of chromosomal instability caused by chronic exposure to EMR, increase in the rate of cell proliferation, decrease in the melatonin secretion [Kudusova L.H., Dunayev V.N., 2013].

The health risk assessment methodology is supposed to use both threshold models of "exposure – effect" dependence, eg. in the non-carcinogenic chemical factors risk assessment, and non-threshold models to assess the carcinogenic risk and, in some cases, the risk associated with physical and microbiological factors.

Considerable attention in both paradigms is given to time parameters of hazards exposure. Basic understanding of the short-term (acute) and long-term (chronic) exposure are identical. However, there are some differences in the identification of periods of short-term exposure. For example, the one-time maximum allowable concentrations of harmful substances in the ambient air are set for 30-minute period in the hygienic rating, the reference levels assume the exposure time from 20 minutes to 24 hours in the acute inhalation exposure. The daily average MPC of atmospheric contaminations adopted in the

Russian Federation in accordance with the definition of MPC ensure that they do not cause pathological changes or diseases in everyday influence on the human body within a long time, established by modern research methods in all periods of life of the present and future generations. The concentrations with a mid-annual averaging, which are compared with the reference levels – daily levels of exposure to a chemical over a lifetime, which probably does not give rise to an unacceptable risk to the health of sensitive groups – are used within the assessment of risk associated with long-term intake of harmful substances from the ambient air. The health risk analysis paradigm provides more accurate assessments in the use of scenarios with variable exposure in the case of the accumulated dose calculation or the use of the risk evolution models. When assessing the exposure to occupational exposure factors, the hygienic rating system considers only one scenario: daily (except holidays) exposure within 8 hours but no more than 40 hours per week during the whole working life. The risk assessment paradigm enables the calculation of risk according to a given scenarios appropriate to real-time characteristics of the exposure of the studied cohorts. This may also considered a change in the exposure intensity over time.

The principle of limiting health hazard indicator in hygienic rationing is methodologically close to the establishment of critical organs and body systems in the development of reference exposure levels. The difference is that the list of hygienic standards indicates the type of indicator (for ambient air – reflectory, toxicological resorptive, for water – organoleptic, sanitary and toxicological, general sanitary), and the description of the reference values specify the certain organs and body systems which cannot be primarily affected by this hazard factor.

The comparison of criteria used in the framework of paradigms of hygienic rating and health risks analysis also allowed the establishing of the similarities and differences (Table 1.4). Comparison of methodological approaches with the establishment of the above criteria showed similarities in the use of threshold and no observed exposure levels, the justification of criteria and some differences in the determination of safety and uncertainty factors.

A key feature of the criteria system in the risk assessment is the use of the parameters characterizing the impact at the levels higher than those which were not observed ones compared to the hygienic regulation. This allows creating a criteria system, which can be expressed in the form of classification or risks scale. Moreover, each class and the range of scale defined fundamental recommendations on risk management.

This classification can be created based on the results of the qualitative risk assessment, for example, one provided by the guidance documents on the food microbiological risk assessment [MR 2.1.10.0067]. In addition, the classification can be based on quantitative or semi-quantitative parameters. An example of semi-quantitative parameters is the coefficients and hazard index calculated in the chemical factors risk assessment [Onishchenko G.G. et al., 2002]. A number of risk values takes into account the combined and complex effect (*HI, TCR*, $\tilde{R}$). Values of the individual carcinogenic risk are used for for the classification of quantitative indicators, evolutionary simulation risk indexes are specified for scaling [Zaitseva N,V, et al., 2011]. The developed criteria system established on the basis of risk assessment paradigm allows better decisions to be made in order to ensure human health safety.

The use of assessment results obtained within the framework of paradigms of hygienic rating and health risk analysis essentially differs (Table 1.5).

The hygienic rating paradigm was formed according to a predominantly administrative methods of state administration, when the problem of losses assessment including economic ones related to the negative impact of environmental factors was not set. Accordingly, the sanctions for violation of statutory regulations have an administrative nature and essentially did not consider the exposure intensity. It is necessary to quantify the effects of the impact of environmental factors to determine the feasibility and assess the effectiveness of public administration, including the establishment of hygienic standards in a market economy. Justification of the differentiated risk management action depending on its degree is one of the main results that can be obtained by applying the risk analysis paradigm.

The paradigm which is not hygienic rating did not highlight the assessment of losses associated with the pollution of the environment, even in the failure to comply with established standards. However, it was noted that the inclusion of the environmentally caused population health damage assessment to the hygienic assessment of life quality should be the basis of a new paradigm of the role of hygienic science in the social and economic development of Russia [Pinigin M.A. et al., 2003].

The paradigm of health risk analysis made it possible to implement the population-based risk assessments and economic assessments based on them. Consequently, this paradigm allows the assessment of the social and economic feasibility of health risk management measures, predicting their performance, choosing ones with the highest implementation priority and value for the social and economic development of countries.

The above provisions were an objective reason for the development of health risk assessment paradigm. Paradigms change is governed by the laws of society and science development as one of its components. The process usually takes place evolutionarily. It is important to preserve the achievements gained during the period of the previous paradigm, combined with new scientific knowledge. Thus, the development of health risk assessment methodology is not a rejection of the system of hygienic norms and standards, but improvement of their design and validation, including on the basis of the principles and criteria of acceptable risk to human health, adopted in the international community.

1.3. Main development stages of the theory and methodology of health risk analysis in Russia and abroad

The development of domestic hygienic science was characterized by the improvement of its fundamental basis, theoretical and methodological foundations in the Soviet Union after the solution of the acute problems of the elimination of epidemics and improvement of the sanitation conditions of the country in the second half of the XX century. This was a prerequisite for the development of a health risk analysis methodology in Russia. V.A. Ryazanov (1949) formulated hazard criteria and principles of hygienic rating. Methodological approaches used in the hygienic rating are quite similar to those used to assess health risk. Thus, a definition of the term "danger" – a set of substances properties determining the probability of a harmful effect in the real conditions of its industrial application [Izmerov N.F. et al., 1986] – contains elements of probability assessment.

The first stage of toxicological studies suggest a "literary development" aggregated the information about the chemical and physical properties of the substance, available toxicity parameters, estimated technologies of the production and use [Zaugolnikov S.D. et al., 1967]. The hazard identification phase is the health risk assessment stage with the same content.

Some hygiene fields, such as the hygiene of pesticides and polymer materials, widely use a concept of "exposure", and calculate the multimedia exposure in the pesticides hazard assessment. Much attention was paid to the exposure markers called "exposure tests " in Russia [Izmerov N.F. et al., 1986]. The dependence of the metabolites content in biological fluids on the dose (concentration) of harmful substances in the environment were set experimentally [Sanotsky I.V. et al., 1977; Sanotsky I.V. et al., 1978]. Results of the tests exposure investigation were parameterized and used to determine the thresholds of harmful effects [Sanotsky I.V., 1978; Maltseva N.M., 1979]. V.V. Kustov and L.A. Tiunov (1969) have shown that twice excess of the level of natural metabolites leads to harmful effects.

A number of studies have been devoted to study the "exposure – effect" relationships and their use in determining the no observed levels of harmful factors of production and ambient environment. This problem including dependencies mathematical simulation has been considered in a number of publications byleading Soviet hygienists [Kurlyandsky B.A., 1970; Krasovsky G.N., 1972; Golubev A.A. et al., 1973; Andreeshcheva N.G., 1973; Bushtueva K.A., 1976; Izmerov N.F., 1976; Shigan S.A., 1976; Sidorenko G.I., 1978; Krasovsky G.N.

et al., 1979]. The issues of effect nonlinearity and its causes were considered by V.A. Filov (1980). A number of assessment results of "exposure – response" dependencies was put into practice in the form of regulatory guidance documents (eg, "Guidelines for the establishment of quantitative relationships between the changes in the health status and the quality of the environment", 1983).

Indicators of the real danger – toxicometry parameters and their derivatives – were an analog of the indicators which are used when characterizing the risk: toxicity, the absolute values of the thresholds of harmful effect, the zones of acute, chronic, specific action. The concept of the zone of acute action was suggested by one of the founders of the Soviet industrial toxicology, N.S. Pravdin (1947). The indicator of irritant action zone is validated by I.V. Sanotsky (1964). The establishment of thresholds and no observed exposure levels allows assessing the safety or danger of the environmental factors influence.

At the same time, the concept of risk was used quite widely when evaluating the health impact of radiation factors. Unlike other toxic factors which have a completely harmless threshold of action, dose, and concentration (lower than the threshold ones), it is assumed that the additional exposure at any dose, no matter how low it is, carries a risk of late effects [Kirillov V.F. et al., 1988].

At this stage of hygiene development, ideological restrictions prevented the consideration and prediction of the probability of health damage due to environmental contamination at levels above the statutory maximum permissible ones. The theory of "zero risk" was supported as the dominant by government agencies, respectively, the idea of thresholdless and the approaches providing the establishment of acceptable risk levels have been criticized.

The first works in the field of health risk assessment were conducted in the United States Environmental Protection Agency (Environmental Protection Agency, EPA) in the 1970s. Risk assessment at the time was not yet a formally recognized process. The execution of the health risk assessment as a structured activity is taking place during the last 50 years, and it become more and more popular for management decisions validation [McClellan R.O., 1999].

EPA finished its first document relating risk assessment "Quantitative Risk Assessment for Community Exposure to Vinyl Chloride" [Arnold M.K., Robert E.M., 1975] in December 1975. In 1976 the following significant document appeared – "Interim Procedures and Guidelines for Health Risk and Economic Impact Assessments of Suspected Carcinogens". It was recommended that the medical data were analyzed independently of the analysis of the economic aspects.

In 1980, the EPA has submitted documents containing the water quality criteria for the 64 pollutants [US EPA, 1980]. This was the first use of the methods developed by the EPA for a large number of carcinogens, and the first EPA document describing quantitative procedures used in risk assessment. Clean Water Act (Section 304 (a) (1)) was a legal basis for the development of this document; the EPA is required to develop water quality criteria based on current scientific achievements in accordance with this Act. These criteria are based solely on scientific evidences and judgments with respect to the concentrations of the polluters and the effects on human health.

In 1983, the US National Council for Researches published a document entitled "Risk Assessment in the Federal Government: process control", which is often called the "Red Book" [NRC, 1983]. The next year, EPA issued a "Risk Assessment and Management: Framework for Decision Making) [US EPA, 1984], which emphasized the need for transparency and complete description of the risk assessment process, including its advantages and disadvantages, as well as possible alternatives.

In the 1980s, EPA implemented an Integrated Risk Information System (IRIS), a database of human health effects that may be developed under the influence of various substances [US EPA, 1989].

EPA issued a series of recommendations for risk assessment (eg, for the assessment of the risk of carcinogenic, mutagenic, reproductive effects, risk assessment under the influence of chemical mixtures, exposure assessment) following the publication of

the Red Book in the 90s [US EPA, 1986*a*; 1986*b*; 1986*c*; 1987; 1991*a*; 1992; 1996*a*, 1996*b*]. Although the efforts of EPA have focused primarily on the human health risk assessment, the base model was adapted to the environmental risk assessment in the 90s. The document "Guidance For Risk Characterization" was issued in 1995 [US EPA, 1995], it finally established the principle of separation of risk assessment and risk management.

A number of EPA documents aimed at the intradepartmental unification of risk assessment procedures and assessments transparency was issued and introduced by 2000 [US EPA, 1991*b*; 2000].

A methodology for risk analysis based on the principles of scientific validity, stage-by-stage nature of procedure (hazard identification, "exposure – effect" dependency assessment, the exposure assessment, risk characterization), transparency, separation of risk assessment and management was formed in the field of US environmental protection by the 2000s.

The documents of the World Health Organization relating to various areas of risk assessment are issued concurrently [WHO, 1995; WHO, 1999; 2009].

The European Union has developed a number of legal and procedural documents governing the principles and methodological approaches to assess the risks for living environment and production [EU, 2002; EU, 2003*a*; 2008; EFSA, 2009]. It should be noted that the European Union makes attempts to harmonize risk assessment procedures at this stage [EC, 2000; EU, 2003*b*].

A number of regulatory and procedural documents were established in the developed countries around the world, primarily in Canada and Australia [Health Canada, 2010*a*-*h*; Commonwealth of Australia, 2004].

The first studies on the risk assessment and management in the Russian Federation were model studies carried out in the framework of the "Project for environmental policy and environmental economics" with the financial support of the US Agency for International Development on the basis of the cooperation agreement. These studies implemented in the Moscow region, Volgograd, Perm, Yekaterinburg, Angarsk, Novokuznetsk, include a assessment of health risk caused by the impact of ambient air and water of utility and drinking water system network, as well as elements of risk management [Experience in the use of risk assessment methodology in Russia, 1997]. Significant contribution to the implementation of risk assessment methodology in Russia has been made by a study on the risk assessment in the Samara region [[Experience in the use of risk assessment methodology in Russia, 1999]. Monograph by G.G. Onischenko, S.M. Novikov, Yu.A. Rakhmanin, S.L. Avaliani, K.A. Bushtuevoy "A framework for assessing health risk when exposed to chemicals that pollute the environment" (2002) was published subsequently; it defined the basic principles and methodological approaches to the health risks assessment for the near term. The result of the health risk assessment best practice was the creation of the "Guidelines on the assessment of risk for public health at the impact of chemical substances contaminating the environment» [R 2.1.10.1920-04].

The methodological basis for public health risk assessment was also formed in the countries of the Customs Union almost at the same time. Instructions for the assessment of health risks when exposed to chemicals contaminating ambient air and noise in terms of settlements were developed in the Republic of Belarus under the auspices of the Medical Service [Instruction 2.1.6.11-9-29-2004; 2.1.8.10-12-3-2005]. "Methods for the assessment of risk for public health" was approved in the Republic of Kazakhstan by the decision of the Council for Sustainable Development of the Republic of Kazakhstan [The decision of the fourth meeting of the Council for Sustainable Development of the Republic of Kazakhstan No. 17-50 / 007606 dated 05.12.2007].

The vast majority of the above theoretical and methodological developments focused on the health risks assessment associated with exposure to hazardous chemicals. However, issues of quantitative characteristic of non-carcinogenic risks, detailed recording of temporal characteristics of the exposure and accumulation of negative effects under the complex exposure scenarios, eg. ones suggesting the intermittent activity, were not fully resolved in this area.

The task promoting the development of certain aspects and procedures for health risk assessment was set almost at the same period. It is an assessment of food safety. The

theoretical terms and procedure to analyse the risk of foods for the health of consumers were developed through the efforts of the FAO/WHO and Codex Alimentarius Commission. The main provisions and principles of risk assessment in this area are set out in the "Procedural Manual"published in 2013 for the twenty-first time. These principles do not differ from ones previously set in the United States. Thus, the "Working Principles for risk analysis" used by the Codex Alimentarius [FAO/WHO, 2012], establish that the health risks analysis should be carried out systematically and consistently, be open, transparent and well-documented, implemented in accordance with the Declaration of Principles concerning the role of science in decision-making, based and reviewed in term of newly acquired scientific data. It is noted that data of epidemiological surveillance, analytical and exposure data are particularly important data. In the absence of data for risk assessment, the document provides for the initiation of controlled research studies. "Working Principles ..." indicate that the risk assessment should take into account the probability of acute, chronic, long-term, and cumulative and/or combined adverse health effects depending on specific situations.

Definitions of risk analysis in food safety are adopted by the Codex Alimentarius Commission in 1997, they were revised in 1999, 2003, 2004. Risk analysis principles used by the Food Additives Codex Committee and the Foods Contaminants Committee were adopted in 2005, they were amended in 2007. Risk analysis principles applied by the Committee on Veterinary Drugs Residues in Foods and the risk assessment policy in the development of standards of the maximum permissible concentration of veterinary drug residues in food were adopted in 2007. The principles of risk analysis applied by the Committee on Pesticide Residues including the application "Risk Assessment Policy used by JMPR" were also established in 2007. The principles of food risk analysis and the guidance on their application in the work of the Committee of Codex on Special Dietary Nutrition were adopted in 2009.

In addition, the Codex Alimentarius Commission prepared and introduced documents relating to risk assessment features in chemical contamination of food with veterinary drugs residues, pesticides, chemical components, in microbiological contamination and the application of food additives [FAO/WHO, 1999; 2001; 2012; FAO, 2001; FAO/WHO, 2008; 2009; 2010*a*; 2010*b*].

The development of science and technology constantly sets new tasks requiring improvement of developed methodological approaches to the health risk assessment. This is primarily due to the emergence of new sources and types of human health hazards.

One of the most discussed issues is the health safety of genetically modified organisms (GMOs), the genotype of which is artificially changed using genetic engineering methods. Genetic changes are usually made for scientific or economic purposes. Genetic modification differs by targeted change in the genotype of the organism, in contrast to the random change characteristic for natural and artificial mutation. The use of transgenes to generate transgenic organisms currently is the main type of genetic modification. In the agriculture and the food industry, the GMO refers only to organisms modified through the introduction of one or more transgenes into their genome [FAO, 2001].

A commission involving the leading researchers in the field of molecular biology was established in 1974 in the United States to the study this issue. Three of the most well known scientific magazines (Science, Nature, Proceedings of the National Academy of Sciences) published the so-called "Breg's letter" which called for scientists to temporarily refrain from experiments in this field [Breg P. et al., 1974]. The Asilomar Conference was held in 1975. At this conference, biologists discussed the possible risks associated with the creation of GMOs [Breg et al., 1975].

In 1976, the National Institutes of Health (USA) has developed a system of rules strictly regulating the works with recombinant DNA. The rules have been mitigated by the early 1980s [B. Glick, J. Pasternak., 2002].

The main conclusion based on the efforts of more than 130 research projects covering 25 years of research and conducted with the participation of more than 500 independent research groups, summarized in the report of the Directorate General of

the European Commission for Science and Information, is that the biotechnologies, and, in particular GMOs are less dangerous than, for example, traditional plant breeding techniques [EC, 2010]. At the same time, a number of scholars indicate the possibility of negative effects to health in the use of GMOs. These include immunosuppression, the possibility of acute disruption in the organism functions, such as allergic reactions and metabolic disorders, as a result of direct action of transgenic proteins [Angurets A.V., 2004].

Effect of new proteins producing genes integrated in GMO is unknown. The man had never been made use of them, and that is why it is unknown whether they are allergens. About 25% of all so-called pathogenesis-dependent proteins that are actively used for GM plants, also have strong allergic properties [Beckie H.J. et al., 2001; Bernstain I.L. et al., 1999].

Adverse health effects can also occur due to the presence of "technological waste" including viral promoters, especially 35SH-promoter and bacterial terminators in the build-in DNA paragraph [Kuznetsov Vl.V., 2005].

The most of transgenic plants do not die in the mass use of agricultural chemicals and are able to accumulate them as mediated effect. There is an evidence that sugar beet is resistant to the herbicide glyphosate, it accumulates its toxic metabolites [Muller B.P. et al., 2001].

Probably, we should agree with the view expressed in the Science in 2000 [Domingo J.L., 2000] that there is extremely small amount of the data on the risks of GM foods for human health, the amount of judgments is much higher [Kopeikin V., Saksina T., 2005]. It defines one of the ways to improve the methodology of the health risks analysis at the present stage of its development – risk assessment and management with the use of GMOs taking into account both their direct and mediated impact.

An actual threat to human health is the spread of new chemically synthesized materials the impacts of which need to be studied both separately and as a whole under the conditions of the formation caused by their health risks. These include nanoparticles and nanomaterials.

Nanoparticles and nanomaterials have complex physical, chemical properties and biological effects that are often radically different from those of the same substance in the form of solid phases or macroscopic dispersion. The following physical and chemical behavior of substances can be highlighted in the nano-sized condition: an increase in the chemical potential of substances at the interphase boundary of high curvature (large curvature of the nanoparticles surface and the change in the topology of the atoms bound on the surface result in a change in their chemical potentials, thereby the solubility, reactivity and catalytic ability of nanoparticles and their components substantially changes); large specific surface of nanomaterials increasing their adsorption capacity, chemical reactivity and catalytic properties, and leads to the increase in the production of free radicals and reactive oxygen intermediates, and damage to biological structures); small size and diversity of nanoparticles (nanoparticles can bind to nucleic acids, proteins, built in the membranes, enter the cell organelles due to their small size and thus change the function of biological structures); high adsorption activity (due to the highly-developed surface, nanoparticles have properties of highly efficient adsorbents, and are capable of absorbing much more adsorbable substances per a unit of its weight than macroscopic dispersion); high ability to accumulate [MI 1.2.2520-09].

All of the above indicates that nanomaterials having different physicochemical properties and biological effect as compared to their conventional counterparts, should be attributed to new types of materials and products, which have a mandatory characteristic of the potential risk to human health and life.

Another feature of the present stage of development of production and consumption is an exponential growth of diverse hazards, resulting in risk to human health. Current sanitary-epidemiological situation is characterized by the combined influence of diverse environmental factors on human health. They include biological, chemical, physical, social, and other environmental factors that affect or may affect the man and (or) the health of future generations. A combination of hazards accompanies the person in the performance of production functions in everyday life, in the consumption (use) of consumer products, in contact with the objects of the living environment. These factors of different nature

(chemical, biological, physical) can provide simultaneous or sequential (combined) effect on the body.

The performed studies of joint action of factors and health risk assessment, conditioned by them are extremely insufficient and were conducted primarily to assess working conditions. In the field of health risk assessment, methodological approaches to the assessment of the combined action, including the multimedia receipt are considered mainly in relation to carcinogenic chemical factors and semiquantitative assessment of carcinogenic effects [R 2.1.10.1920-04]. The development of effects of different severity, functional interaction of organs and body systems are not considered in the framework of these approaches.

However, the accumulated experience in assessment of risk associated with exposure of diversified factors, combined with the existing mathematical tools could be a basis to solve a task on assessment the risk of effects formation of different severity in the simultaneous or sequential impact of diversified hazards.

A full analysis and use of the results of numerous studies aimed to the health risk assessment, is significantly complicated by the fact that these studies conducted in different countries and by different groups of professionals, are hard to compare because they differ in terminology, methodological approaches, procedures, criteria, and interpretation of the results. Development and implementation of key provisions of the harmonization of methods and criteria to assess the risk of products for the health of the population with international approaches is extremely important for the development of the domestic risk analysis methodology.

At the present stage of the health risk analysis development, there is a focus on the development of a theoretical basis to solve tasks on assessment of the risk associated with a combined, integrated and joint effect of the hazards both of the environment and products (goods), and also the assessment of the risk associated with new sources and types of hazards (genetically modified objects, nanomaterials, etc.). The adequate scientific and methodological support of procedures for health risk assessment is required for practical application of theory provisions.

The first steps to do this have already been taken. The first steps to do this have already been taken. A large number of regulatory and procedural documents have been developed and implemented in the Russian Federation in 2011–2013; it allows assessing the risk associated with the majority of environmental factors. They include guidelines on the quantitative assessment of non-carcinogenic risk in the impact of chemicals [MR 2.1.10.0062-12], these guidelines allow assessing the individual non-carcinogenic risk of specific effects (responses) development in terms of the health under the conditions of the intake of a certain chemical component as the multimedia one, and using one of the possible ways.

The issues the priority of reconstruction and modernization of various water supply systems, the achievement of a maximum result with minimum or optimum cost have become highly important in recent years. The implementation of this strategy requires the transfer from the existing system of drinking water quality assessment according to the principle "comply – does not comply", to the possibility to establish quantitative and/or qualitative characteristics of the adverse effects to human health, caused by the impact of environmental factors. For this purpose, it is reasonable to perform an integrated assessment of the drinking water quality according to the indicators of chemical safety based on the public health risk assessment methodology. A unified procedure and its algorithm was developed in order to ensure a single, science-based approach to the integrated assessment of the public health risks due to exposure to chemicals contained in drinking water [MR 2.1.4.0032-11].

The guidelines to assess the public health risk due to the exposure to traffic noise was developed to solve the problem of health risk assessment under the influence of physical factors [MR 2.1.10.0059-12]. These guidelines determine the procedure for health risk assessment of the population living within residential areas and exposed to external noise of a general and special-purpose transport: road, rail, and air transport. A similar document was also developed in the Republic of Belarus [Resolution of the Ministry of Health of the Republic of Belarus No. 199 dated 18.12. 2012].

The guidelines MR 2.1.10.0061-12 "Assessment of the public health risk when exposed to alternating electromagnetic fields (up to 300 GHz) in terms of settlements" (2012) are aimed to the assessment of health risk when exposed to alternating electromagnetic fields. This document states the approaches to the definition of the public health risk when exposed to alternating electromagnetic fields of different intensity in terms of settlements (places of permanent habitation of the population, including seasonal residence).

It should be noted that new methodological approaches actively developing the methodology and expanding the practice of human health risk assessment were proposed in the most of the above documents. Primarily, they refer to the use of mathematical simulation of the risk evolution taking into account its accumulation over the course of time.

The assessment of radiation risk is traditionally developed the Russian Federation. Recent methodological documents are dedicated to the assessment of low doses under long-term exposure [MI 2.1.10.3014].

In connection with the integration of Russia into the world community, a lot of attention is paid to assess the risk of products for the health of consumers. This procedure is obligatory in almost all developed countries. Methodological approaches to the assessment of the risk of food chemical contamination are developed first of all [MI 2.3.7.2519-09].

A number of guidance documents are dedicated to microbiological risk assessment. It is essential for food products. Methodological approaches specified in the guidelines for public health risk assessment under the influence of microbial factors, are based on the principles fully harmonized with similar documents of the Codex Alimentarius Commission [MR 2.1.10.0067].

Microbiological risk assessment are also being developed in relation to communicable diseases, including those transmitted by water [MR 2.1.10. 0031-11]. The study of flare and sporadic morbidity of intestinal infections transmitted by water has mainly a descriptive nature that does not allow establishing a quantitative relationship between sanitary and hygienic conditions and AEI morbidity.

In this regard, the method for epidemiological assessment of sanitary and hygienic conditions (utility and drinking water system, cultural and general water consumption, municipal improvement of settlements) which are directly related to the waterway transmission of intestinal infections was developed; it allows:

– validating the contribution of each specific indicator to an integrated risk assessment on the considered sanitary and hygienic factor;

– identifying factors facilitating or preventing the occurrence and spread of intestinal infections associated with water way of transmission, because the effect of one or a certain group of factors is possible in each settlement;

– providing a comprehensive assessment of the generalized indicator of microbial risk taking into account all sanitary and hygienic conditions within the settlement;

– predicting the sanitary and hygienic situation based on the obtained generalized data taking into account the integral and generalized risk indicators;

– developing measures to eliminate or reduce the negative impact of the adverse factors on the basis of the obtained data;

– determining the priority of measures to improve the sanitary and hygienic conditions of water consumption in a particular settlement in order to prevent intestinal infections due to water transmission factor;

– assessing the degree of microbial risk of acute intestinal infections and the possibility of waterway transmission.

According to the Climate Doctrine of the Russian Federation, adverse effects of the expected climate changes in the Russian Federation include increased public health risk (increase in morbidity and mortality level). Assessment of risks and associated losses is considered as an important component in the development and planning of measures to adapt to climate changes. Quantitative risk assessment allows determining the approximate value of the specific effects (diseases and premature death) in different scenarios.

The main risk factors associated with climate changes are high temperatures, extreme weather events, the propagation of infectious diseases, nutritional disorders, etc.

Heat and cold "waves" are considered one of the priority factors of climate change affecting the increase of population morbidity and mortality level in the Russian Federation. Elderly people and children are the most sensitive to the potential impact of these factors; the risk assessment can be carried out for these groups of population.

In connection with the global climate changes which appeared as unusual weather activity, the assessment of risks caused by them also became the subject of study and methodological developments in our country. Methodological approaches to the assessment of the risk of the increased level of morbidity and mortality under the influence of abnormal heat waves, set out in the relevant guidelines [MR 2.1.10.0057-12], contain methodological approaches to the collection and preparation of data, assessment of the impact of meteorological parameters on human health, assessment of economic damage associated with increased level of morbidity and mortality due to the climate-sensitive diseases in high-risk groups.

The main provisions of these guidelines are harmonized with methodological approaches set out in the documents of the World Health Organization [WHO, 2003; 2005*a*; 2005*b*; WHO, 2003] and can be used for:

– justification of the need to develop and implement measures on adaptation to climate change, consideration of the options of social, economic and technical measures to prevent and mitigate the potential adverse effects of climate change on public health;

– improvement of the monitoring system of the population and environment health status due to changes in climate for the prediction and prevention of diseases sensitive to climatic factors;

– rough assessment of the potential economic damage caused to human health and the reasonable expenditures for the implementation of measures to ensure the sanitary and epidemiological welfare;

– provision of the persons involved in the management decision-making, population, public organizations with the objective information about the levels of risk to public health due to the adverse effect of climate factors.

According the data of the World Health Organization, the impact of lifestyle factors determines the significant portion of morbidity and mortality of the population of the whole world. The living environment factors include chemical, physical, biological, social, and other environmental factors that affect or may affect the man and (or) the health of future generations. Actions to ensure the sanitary and epidemiological welfare include, in particular, the definition of cause-and-effect relationships between the population health and the impact of environmental factors using the methods and criteria to assesse the risk associated with this impact on human health. Methodological approaches to the assessment of risk associated with the impact of lifestyle factors on human health are developed when addressing the issues of sanitary and epidemiological welfare [MR 2.1.10.0033-11].

The application of these approaches allows obtaining the results containing:

– evidences of the fact that the risk assessment process actually identified effects associated with lifestyle factor;

– description of the adverse effects that may occur under the influence of lifestyle factors;

– reliability characteristic of quantitative information concerning the risks of adverse effects;

– characteristic of the main factors that reduce the validation and reliability of the results, including all the uncertainties of risk assessment;

– comparative analysis of the obtained data on risk assessment, the available information on the public health status, as well as the results of previous studies characterizing the risks and human health on similar areas.

The accumulated experience in developing of methodological approaches to health risks assessment associated with individual diversified factors, allowed formulation of the basic provisions of the integrated assessment of public health risk stipulated by the influence of the whole complex of environmental factors. Integral assessment of health risk is considered as a component of an integrated risk assessment as regards human health, and represents the process of assessment of the risk of adverse effects of different severity as a

result of the simultaneous effect of factors group of different nature on human. Integral health risk assessment develops and extends the system of the public health risk assessment when exposed to environmental factors, allowing quantifying the accumulation of risks taking into account the age and duration of exposure. The result of the integral risk assessment associated with the combined effects of chemical, physical, biological, and social environmental factors is its quantitative characteristic and classification as negligible, small, moderate, high, and very high risk, as well as the value of the reduction of the survival probability. Methodological aspects of integral risk assessment will be considered more detailed in Chapter 2

The conceptual provisions of the health risk assessment methodology, methods of identification and quantification of nanomaterials were developed at the present stage of development within the framework of solving the problem of risk assessment associated with new sources and types of hazards. The "Concept of toxicological studies, risk assessment methodology, methods of identification and quantification of nanomaterials" was approved in 2007 [Resolution of the Chief State Medical Officer of the Russian Federation No. 79 dated 31.10.2007].

The development of the approved Concept developed a number of guidance documents on the identification of nanomaterials, imposing a potential human health hazard and its assessment, the organization of nanomaterials control [MI 1.2.2520-09; MR 1.2.2522-09; MR 1.2.0054-11, MI 1.2.2966-11]. These documents noted that the report of the nanoparticles/nanomaterials control should include an assessment of the risks associated with human exposure, proposals on the composition and volume of activities aimed at reduction of human health risk imposed by nanomaterials. These documents noted that the report of the nanoparticles/nanomaterials control should include an assessment of the risks associated with human exposure, proposals on the composition and volume of activities aimed at reduction of human health risk imposed by nanomaterials.

– low degree of potential hazard. Toxicological assessment of nanomaterials is carried out in terms values recommended for its constituent components in the traditional form (macro-dispersive or as continuous phases). Researches on the specific biological effect of the components in the form of nanoparticles can be carried out selectively;

– medium degree of potential hazard. General toxical assessment of the material is carried out in the form of nanoparticles, and some kinds of special studies are carried if necessary;

– high degree of potential hazard. A full range of researches is carried out to study nanomaterials penetration through biological membranes and barriers of the body, distribution and accumulation in organs and tissues, elimination, general toxicity evaluation (acute, subchronic, and chronic toxicity), a set of special studies including testing for genotoxicity, mutagenicity, embryotoxicity, gonadotoxicity, teratogenicity, the impact of nanomaterials on the genome (gene expression), proteomic and metabolomic body profile, immunotoxicity, organotoxicity, the permeability of the gastrointestinal tract barrier, allergenicity.

A methodological approach to the implementation of these algorithms, which allows the definition of nanomaterials which posed a danger to human health, with the highest degree of reliability is the method of mathematical simulation described for technical, biological, and environmental substrates in the publication by V.G. Gmoshinsky (1972, 1977).

The risk assessment methodology relating to the assessment of risk of potential negative effect of genetically engineered organisms on human health has not been developed yet in the Russian Federation. The risk assessment methodology relating to the assessment of risk of potential negative effect of genetically engineered organisms on human health has not been developed yet in the Russian Federation. It was announced at the interdepartmental meeting on the regulation of the state environmental assessment concerning the release of GMOs into the environment in the Ministry of Natural Resources and Environment of the Russian Federation [Minutes of the interdepartmental meeting in the Ministry of Natural Resources and Environment of the Russian Federation dated 14.10.2013]. At the same time, methodological approaches allowing solving this problem to a certain extent were developed and implemented in the Republic of Belarus recently

[Resolution of the Council of Ministers of the Republic of Belarus No. 677 dated 04.05.2010; Resolution of the Ministry of Natural Resources and Environment of the Republic of Belarus No. 55 dated 29.08.2006]. These documents establish that the risk assessment defines:

– the safety of any effects resulting from the genetic modification;

– the safety of new proteins resulting from genetic modification (toxicity, allergenicity);

– the reduction of the nutrition value of genetically modified foods;

– the possibility of carrying of antibiotic resistance genes by the gastrointestinal tract microflora.

The current stage of development and implementation of health risk assessment methodology is characterized by a number of fundamentally new theoretical aspects of the stages of this process. At the stage of hazard identification, they should include provisions about a more complete, holistic nature of risk factors property evaluation.

Analysis of the impact of harmful factors on the environment objects within the health risk assessment is useful for the identification of indirect influence of these factors on the change in the mechanism of the exposure formation. For example, changes in the properties of genetically modified plants can promote the accumulation of toxic doses of pesticides and herbicides in them in contradistinction to traditionally cultivated plants.

Selection of negative and adverse effects that may be caused by the established hazards is supposed at the stage of hazard identification. Therefore it is reasonable to identify theoretically the concept of adverse effect.

Health adverse effect is the changes in morphology, physiology, growth, development or lifespan of an organism, population, or offspring appeared as the deterioration of functional capacity or the ability to compensate for an additional stress, or increase of sensitivity to the effects of other environmental factors [R 2.1.10.1920-04]. In its turn, the medical dictionary published by Webster's New World (2008) treated the adverse effect as a "negative impact: an adverse or abnormal effect. The negative impact may be caused by the treatment order or exposure to chemicals, and is defined as an unfavorable result, such as a disease or death" [Webster's New World™ Medical Dictionary, 2008].

A classification of adverse effects is given by R.P. Sherwin in his publication "What is the health adverse effect?" [Sherwin R.P., 1983]. In accordance with this, there are four categories of adverse effects: the first – the final category – death; the second is a disease, from the first, the most mild symptoms of ill health to incurable diseases; the third category is a subclinical form of the disease when a patient has no symptoms or do not pay attention to them, and the results of clinical tests do not allow to determine the diagnosis; the fourth category is a state of health accompanied by the depletion of cells, tissues, and organs of reserves, the so-called hypeinopenia [Sherwin R.P., 1974].

However, changes in health condition that are difficult to consider as harmful are recorded apart from these effects. They include changes in the laboratory tests results which show statistically significant differences under the exposure conditions compared with a control group of population or laboratory animals which are within biological standards. Responses to hazard exposure in the *in vitro* experiments in some cases are difficult to interpret as the adverse effects to human [EU, 2000].

Recorded and adverse effects are considered differentially in world practice of health risk assessment. This is reflected even in the title of the threshold levels of risk factors – NOAEL and NOEL. NOAEL (No-Observed-Adverse-Effect Level) – the level of exposure at which an adverse effect is not observed (similar to the term "maximal ineffective dose concentration") [R 2.1.10.1920-04]. NOEL (No-Observed-Effect Level) – the level of exposure at which there is no statistically or biologically significant increase in the frequency or severity of effect in the exposed population compared with the corresponding control (IRIS).

In the NOEL assessment, it is necessary to consider the hormesis phenomenon which characterize the situation where the response to the exposure effects in experimental animals or the population under study are statistically significantly less than the indicator background value in unexposed individuals [Calabrese E.J., Baldwin L.A., 1998]. The reverse situation is also possible. Though the importance of hormesis remains controversial, its biological plausibility is also noted [Sielken R.L.Jr. et al. 1995] because low impact can en-

courage cytoprotective and homeostatic processes in terms of added stress on body systems, and a measurable adverse effect may be expected in the exposure increase.

Thus, at the present stage, the theoretical provisions concerning hazard identification are supplemented by the provisions relating to the hazards establishment features characterized by unconventional properties (physico-chemical, toxic, etc.) considering their direct and indirect actions, as well as the effects of differentiation on the basis of their hazard to health.

Theoretical innovations at the stage of "exposure – effect (response)" dependency relation evaluation are associated with the use of conceptually new approaches to mathematical modeling of this dependency relation. The models of two groups: deterministic and probabilistic, are used at the present stage.

Almost exclusively determined approaches are used currently. This is associated with the fact that one of the main and the most valuable health risk management tools is standards that have a deterministic nature. At that, the description of the uncertainty of the risk assessment results, in fact, indicates the probabilistic nature of the assessments. The European Community considers whether deterministic risk degree assessment continues to be a principled approach to the risk degree assessment [EU, 2000].

When using deterministic approaches the "exposure – effect" dependency relation modeling in toxicology implies the choice of the optimal function to approximate the experimental data obtained, as a rule, in animal experiments for the problems of quantitative risk assessment [Wang Y., Liu M., 2008]. Approximation includes extrapolation beyond the studied range of doses, mostly towards low doses [Guo J. Jeff et al., 2010]. Methods for extrapolation of data can be divided into statistical and mechanistic ones. Statistical approaches are based on the assumption that each individual has their own level of sensitivity to chemical, the selection of the distribution function for this level determines the type of model. The most common distribution functions used to approximate data of the "dose – response" are "log-probit" and "log-logistic" models [Klaassen C.D., 2008] the diagrams of which has sigmoid form; curves are almost indistinguishable in the field of experimental data [Hartung R., 1987]. The mechanistic approach assumes that the toxic effect is a result of one or more random biological events. An example of a simple mechanistic model is the one-stage linear model of carcinogenesis, which requires only one critical cell interactions to change the cells.

The function of the lognormal distribution, log-logistic distribution and the function of extreme values distribution can be allocated from the two-parameter distribution functions used in microbiological risk assessment [Pinsky P.F., 2000; Kang S. et al., 2000]. Two-parameter distribution function of the beta-Poisson is widely used in microbiological risk assessment [Haas C.N. et al., 1993; Marks H.M. et al., 1998] in the models of the threshold dose level [Kodell R.L. et al., 2002]. In this case, it is preferable to use the log-logistic distribution function for the analysis of biological data [Holcomb D.L. et al., 1999]. We should also mention the beta-binomial model [Cassin M.H., 1998]. The model with Weibull-gamma distribution is the most common one from the three-parameter models [Farber J.M. et al., 1996].

In recent years, there are models, partly considering the time factor after the receipt of microbiological agents in the human body [Huang Y., Haas C.N., 2009]. Four modifications of exponential and beta-Poisson model are proposed, one of the coefficients of which is a function of time. Thus, the number of parameters in the models with respect to time is increased by one, which complicates an adequate solution to the problem of the coefficients identification.

The method of "exposure – response" models construction is used in the risk assessment, this method is based on probit analysis, which is used to determine the effect of a quantitative indicator for binary response. Probit analysis allows the estimation of the probability that the analyzed variables will be set to "1" for given factors values. The probit-function is modeled from the probability as a linear combination of factors in the probit analysis. The pre-calculated table values or built-in functions of specialized software packages are used for the practical conversion of probits into the probability (risk). This method is applicable, subject to the assumptions of "exposure – response" curve normality.
Regulatory guidance document adopted in the Republic of Belarus – Instruction 2.1.8.10-12-3-2005

"Assessment of health risk due to exposure to noise in terms of settlements" can be as an example of this method.

The essence of a probabilistic risk assessment is the determination of the range of possible values. In this case, these ranges allow consideration of the uncertainties.

The method of reliability theory refers to probabilistic methods. The reliability theory studies the probability of the system to perform its functions for a certain period of time and the patterns of failures distribution. Such logic and graphic methods as event tree analysis, decision tree analysis, fault tree analysis, analysis of structural reliability schemes, preliminary hazard analysis are applied to do this.

Stochastic methods are more complex, but at the same time accurate and informative ones [Li-ping He et al., 2002]. Stochastic methods are based on the processing of data in the event of a large volume of available information [Mofarrah A., Husain T., 2010]. In this case, probability distributions are used instead of the averaged (or maximum, minimum values and 95th percentile) values of the input parameters. Accordingly, the simulation results will provide the distribution of risk values with the corresponding statistical parameters - variance, standard deviation, etc. instead of point risk assessment [ILSI, 2013]. Monte Carlo and the Bayesian network methods can be distinguished among stochastic approaches.

All of the above approaches of the "exposure – effect (response)" dependency relation modeling characterize numerically determined relations of the separate hazards with specific effects and, as a rule, do not describe the effects on several biological targets simultaneously, even though such a situation occurs quite often. With regard to this, several factors may be involved in the formation of response.

This situation requires a multidimensional solution of health risk assessment problem in connection with the action of a variety of factors, distributed in time.

The formulation of such a task requires the use of the results of theoretical studies related to the description mechanism of damage accumulation in the body. Active development of theories in this area has led to the formation of the two main approaches explaining the loss of bodily functions in time: evolutionary theories and the theories based on random cell damage. A hypothesis explaining the loss of functions as a result of the evolution process was proposed by the German scientist Weisman A. [Weismann A., 1892] in 1891. The followers of evolutionary theories consider that the functions involution is not a necessary characteristic of living organisms, but the programmed process. Theories based on random cell damage were introduced by P. Medawar [Medawar P.B., 1952]. In 1952, he proposed a theory of mutations accumulation, considering the functions disruption as the by-product of natural selection. Damage theories suggest that the accumulation of disruptions is the result of a natural process of accumulation over the duration of damages that the body is trying to fight. The differences between these processes in different organisms are the result of varying effectiveness of this fight. At present, the latter approach is considered more reasonable.

Theoretical and methodological approaches to the analysis of the risk evolution taking into account the total (integral) impact of various factors on the formation of the risk of the effects of different severity were proposed in the development of these hypotheses for the analysis and quantitative evaluation of complex interactions. The fundamental provisions taken as a basis of simulation of the accumulation of disruptions in the organs and body systems functions related to the impact of risk factors are formulated.

– exposure of substances and energies affecting the processes inside the body disrupting the functioning of the organs and systems are formed by the living environment;

– the body is under a constant internal (between organs) and external (with the environment) metabolic processes of substances and energy;

– organs and systems are under a constant competition of functional damages and self-healing processes.

The accumulation model of disruptions in the organ functions and body systems functions is built as a evolutionary deterministic predictive mathematical model, including the possibility to consider the main processes occurring in the body. Section of the second

chapter of this monograph is dedicated to the methodological foundations for construction of evolutionary models.

Questions of conceptual tasks formulations of mathematical modeling are highly relevant for the exposure assessment stage. These tasks vary depending on the purpose of risk assessment. They may include the detailed modeling of exposure considering the time and spatial characteristics of the distribution of the hazards of separate sources, if it is necessary to validate decisions to minimize exposure and, consequently, the risk, or the simulation of exposure at a point of the factor contact with risk contingent considering a multifactor, multimedia exposure to plan measures to protect recipients. The objectives of risk assessment determine the spectrum of the used modeling methods. Thus, the models of direct action characterizing exposure without consideration of intermediate effects, and models of indirect action characterized by the presence of the intermediate media transferring the adverse effect can be used.

Examples of methods based on exposure models used in the assessment of the health risks associated with the factors of a different nature, are listed in Table 1.6.

Table 1.6

Examples of methods based on exposure models used in the assessment of the health risks

Risk factors		
Chemical	Physical	Biological
Methods to calculate the concentrations in water and air using diffusion equations. Methods to calculate the concentrations in water and air using mass balance equations. Methods to calculate the migration of substances from the surfaces. Methods to calculate the doses of chemical factors. Methods to calculate the levels of exposure markers in biological medium based on kinetic models	Methods to calculate the noise on the basis of the wave equation solution. Engineering methods to calculate noise levels. Methods to calculate the level of EMR based on Maxwell's equations solution. Engineering methods to calculate EMR levels	Method to calculate the concentration of microbiological agents in products based on the solution of bacteriological growth equation. Methods to calculate doses of microbiological agents originating from products

However, any use of modeling leads to an increase of uncertainty of the risk assessment results, so where it is possible, the use of direct methods of exposure assessment is preferable, including personal monitoring of the impact and identification of biological markers of exposure.

Currently, substantial efforts are taken to develop methods for chemical-analytical determination of chemical hazards in various biological mediums. As a result, more than 50 methods of quantitative identification of heavy metals and organic compounds in the blood, urine, milk, gastric juice and other biological mediums of human body are proposed in recent years to assess the exposure.

At the stage of risk characteristics, the classification of health risks and their scaling can be attributed to one of the least scientifically based positions.

A large number of classes names and risk scales have been proposed to date [GOST R 12.0.010-2009; MR 2.1.10.0067-12; Conroy R.M. et al., 2003]. This situation is related, primarily, to the lack of reasonable criteria for classification of the risk magnitude, agreed by all participants of the health risk assessment. A number of methods for risk assessment, for example, a qualitative assessment of microbiological risk is based on the expert assessments formed by the specialists conducting researches using risk descriptors, and does not involve quantitative parameters for scaling [FAO/WHO, 2009]. The statement that the risk is "small" (this can be interpreted as risk, that "do not differ from 0", or “as low as (is) reasonably achievable” – ALARA), "low", "medium", "high" and "very high" can be made on the basis

qualitative assessment of methodological recommendations. Quite often the classification during qualitative risk assessment means the recommendation to allocate three levels of risk "severity" (green – low, yellow – medium, red – high) to solve risk management tasks.

The full scale for semiquantitative assessment of results also has not been suggested because, in spite of the fact that the estimated coefficients show that the probability of adverse effects to human increases in proportion to the increase, however, it is impossible to indicate precisely the magnitude of this probability [R 2.1.10.1920-04].

The classification focused on the risk acceptability criteria system is commonly used regarding the results of a quantitative health risks assessment. In accordance with these criteria, the first range of risk (individual lifelong risk equal to or less than $1 \cdot 10^{-6}$), characterizes risk levels that are perceived by all people as negligible small, no different from ordinary, everyday risks (*de minimis* level). The second range (individual lifelong risk of more than $1 \cdot 10^{-6}$, but less than $1 \cdot 10^{-4}$) corresponds to the maximum permissible risk, i.e. the upper boundary of the acceptable risk. Most foreign hygienic standards are recommended by international organizations for the population as a whole was established at this level (for example, WHO uses a value of $1 \cdot 10^{-5}$ as acceptable risk for drinking water, and $1 \cdot 10^{-4}$ for air). The third range (individual lifelong risk of more than $1 \cdot 10^{-4}$, but less than $1 \cdot 10^{-3}$) is acceptable for professional groups and unacceptable for the population as a whole. The fourth range (individual lifelong risk equal to or more than $1 \cdot 10^{-3}$) is not acceptable either for population or for professional groups. This range is referred to as the *de manifestis* risk.

Parameters of the listed risk categories have been widely discussed up to present moment [Rhodes R. et al., 2011; Kocher D.C., 1993; Asante-Duah K., 2002; Ball D., 2006], but this classification is the most common for the current period.

The classification of risk levels using the performance indicators was proposed. For example, the listed risk indices are used when assessing the health risk with the use of evolutionary models [Zaitseva N.V. et al., 2013*d*]. According to this scale, the risk characterized by risk index of less than 0.05 is estimated as negligible small no different from ordinary, everyday risks 0.05–0.35 – as moderate risk, 0.35–0.6 – as high if the value of the index exceeds the level of 0.6, the risk is assessed as very high.

The differences in the assessment of risk levels, as well as a number of other theoretical and methodological aspects make it difficult to compare the results obtained by different researchers. Attempts to harmonize the process of health risk assessment are made in this regard. Thus, the substantial experience of harmonization of risk assessment procedures and normative acts regulating them are accumulated in the counties of the European Union [EU, 2000; EU, 2003*b*]. The documents of the European Commission emphasizes that the science-based risk assessment plays a crucial role in the preparation and improvement of legislation in the sphere of protection of the health of citizens.

European researchers mainly consider the harmonization in terms of social and economic relations and norms regulating them. This statement relates to the elimination of differences between the rules of the national law through the approximation. This refers to the achievement of a certain level of unity of legislation, or some kind of "rate band" that helps to set the common parameters for the adoption of legal acts by the state authorities, and "the movement of different countries to common standards and regulators" [Isaev D., 2005].

In this regard harmonization (unification) of terminology plays a key role in the process of harmonization of methods for health risk assessment. Attempts to harmonize the terminology in the field of risk assessment has been made repeatedly [Ahl AS et al., 1993; Kaplan S., 1997; IRIS], including in the Russian Federation during the implementation of health risk assessment methodology of United States Environmental Protection Agency (EPA) [Novikov S.M. et al., 1998].

However, the harmonization of methods and criteria for risk assessment used in the Russian Federation and the Customs Union with the internationally recognized methodology is considered to be important besides the terminology. Harmonization of methods and criteria for health risk assessment should be based on the harmonization of the legal framework and terminology. At the same time, the harmonization of methods, criteria and procedures of the health risk assessment is advisible to be carried out in the interdepart-

mental, regional, international (within the Customs Union and the Eurasian Economic Community), and global international aspects (with international organizations - WHO, WTO, FAO developed countries).

Summarizing the discussion of the present stage of development of the health risks analysis theory, the following can be noted as its main features: the involvement of new hazards to human health in the process of risk analysis, the clarification of effect hazards, the development of the conceptual foundations of the risk assessment with the combined impact of different factors on the formation of the effects of different severity, the heterogeneous of risk assessment classification and the drive to harmonize key definitions, principles, and criteria for health risk analysis, defining the main approaches to the management of this risk.

1.4. Prospective directions for the health risk analysis methodology development

The risk analysis shall be considered as the synthetic methodology integrating the fundamental provisions of a number of sciences for obtainment of required results according to the research objectives: hygiene, medicine, biology, chemistry, mathematics, sociology, social sciences, etc.

The fundamental principles of health risk analysis and prospective directions for the risk analysis methodology development are formed based on these provisions. First of all, they include the research and detailed elaboration of the risk formation mechanisms. As opposed to the description of the mechanisms of functioning and formation of the body systems pathology in the fundamental medicine the description of the risk formation mechanisms provides the use of complexes of deterministic and probabilistic characteristics. The time-dependent component of the investigation the role of which can be performed in two directions has significant meaning during the risk formation. First, to distinguish the negative reactions on the influence of environmental factors it is necessary to study the development of changes in the body functions conditioned by natural causes. Second, the information about the dynamics of mutual influence of the body organs and systems, which can be obtained during the special studies will allow for differentiating the risk of negative changes in the human health associated with the set of hazardous factors by the time of its implementation that is critical for developing the risk evolution research methodology and justification of the risk management measures.

For these tasks it is highly relevant to study the regularities of formation of the risk of the effects of varying severity in terms of integration of the mechanisms of disorders of the body systems and taking into account the possibilities of restoring the functions of the organism and its adaptive reserve for the periods of lowering the intensity of exposure or its absence. This direction of fundamental studies can be considered as one of priority for developing the risk assessment methods in terms of intermittent loads which are specific for the industrial exposure conditions, for example.

The study of adaptation processes also plays a significant role in the assessment of harmfulness of different effects that can make a decisive contribution to the clarification of the concept which health changes can be considered as harmful and which cannot be considered so. A detailed development of this provision will allow for substantive concretization of notions of thresholds of the risk factors and thus to develop the conceptual vision of the risk assessment methods and use of threshold "exposure – effect" dependence models.

The fundamental aspects of research which determine the principal positions in the health risk assessment methodology include the solution of problems concerning the evaluation of additivity properties of the risk factors activity, including the heterogeneous ones. Methodical approaches to the integration of probabilities in the general risk theory show that the probability of response to the simultaneous action of two risk factors always will be less than the sum of probabilities of responses under the separate influence of these

two factors. The theoretical provisions accepted in the modern toxicology allow both for additivity and potentiation (synergism) and antagonism of toxic action. The existing health risk assessment methods accept the supposition with regard to the additive action of factors justifying it by the fact that at the sufficiently low exposure levels which are met in the real situation taking the nature of combined action into account can be ignored. The determination of the real picture could become a basis for improving the methods of modeling the "exposure – effect" dependence.

The problem associated with formulating the basic provisions on the information platform of this methodology borders the fundamental aspects of the health risk analysis. These provisions shall provide the selection of information for the risk assessment, system for storing this information and guidance for access to it, organization of the information bases replenishment, and coordination with existing information resources.

The purpose of creating the national risk analysis information platform is the combination of the unified information space of entities carrying out the risk assessment and management, informing about the risk and methods for its minimization. The information platform is the tool for ensuring the implementation of the one of the main risk analysis principles – its transparency. By definition, the information platform is an information system, i.e. the aggregate of technical support, software and organizational assistance, as well as the personnel, designed for timely provision of certain people with required information in the field of health risk analysis. Such a definition complies with notion of information system recorded in the Federal Law of the Russian Federation No. 149-FZ dd. July 27, 2006 "On the Information, Information Technologies and Protection of Information": "information system is the aggregate of information contained in the databases and information technologies and technical facilities ensuring its processing" [Federal Law of the Russian Federation No. 149-FZ dd. July 27, 2006].

The creation and development of the national risk analysis information platform provides in accordance with health risk analysis structure the availability of three main structural components aimed at ensuring the risk assessment, risk management and risk informing.

The component which provides the risk assessment shall include the databases concerning the health risk factors for population, employees and consumers, information about the detected exposure levels of these factors, data on the types and parameters of the "effect – exposure" dependencies as well as in relation to the scientific information on which these data are based, information about the classes and scales of risks containing the data on the recommended measures equal to the level of established risk. This component can be supplemented by the relevant information about the health risk assessment experience and software for the health risk assessment procedure. It is feasible to provide the possibilities for referring to the information resources of international organizations (WHO, OCED, IPCS, etc.), foreign national information risk assessment systems, for example, IRIS, and domestic information sources, for example, the Federal State Statistics Service.

The information support relating to the risk management stipulates the economic block availability for calculating the risk value with further assessment of the efficacy of measures aimed at the risk management, databases on the most effective sanitary-technical and medical-preventive technologies, the system of health risk allowability criteria and hygiene standards justified under the health risk criteria, system for assessment of risks of potential danger of the types of economic activity for use during the planning of measures, including the control and supervisory measures.

The improvement of the fundamental information base shall be considered as the directions providing the risk analysis methodology development. They are the basis for directions having a more applied character. It is feasible to include into them the development of methods for forecasting the sanitary-epidemiological situation based on the evaluation of hazard and risk of health losses associated with the factors of living environment. Within this direction it is feasible to consider the system of chains of the cause-and-effect relationships each of which can be described using the complex of methods being the integral part of the health risk analysis paradigm. The principal diagram demonstrating the health risk assessment place in forecasting the sanitary-epidemiological situation and losses associated with negative changes of human health is shown in Fig. 1.7.

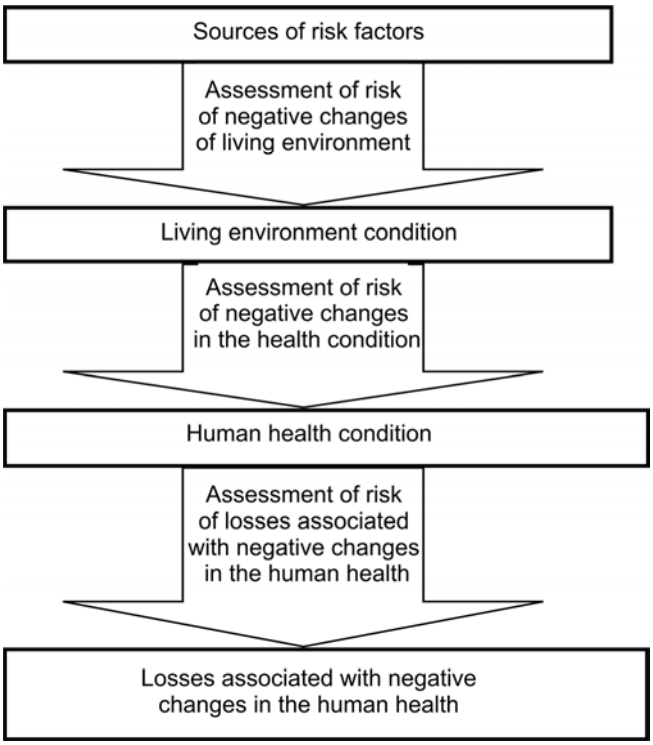

Fig. 1.7. Health risk assessment in forecasting the sanitary-epidemiological situation and losses associated with negative changes of human health

Practically each component of risk assessment requires methodical support improvement. Herewith the methodical techniques are characterized by the peculiarities which depend on the sources of hazard factors, the factors themselves, risk populations, living environment objects, exposure effects, etc. These peculiarities determine the types of health risk and shall be taken into account during the development of every type of the risk assessment methods. By now, the main methodical approaches to the assessment of health risk associated with traditional external environmental hazard factors (chemical, biological and physical) are developed quite completely. The methodology for assessing the other types of risk playing an important role in forming the sanitary-epidemiological situation requires the improvement and development; first of all, it relates to assessing the risk of products for health and some aspects of assessing the risk of the occupational diseases development.

Under the scale of prevalence and number of risk populations the assessment and management of the risk of products for health with no doubts can be included into the priority directions of the risk analysis methodology development. Herewith two aspects can be distinguished in this direction: the methodology for developing the hygiene standards meeting the acceptable risk criteria and methods for assessing the risk of products for the health of consumers in case of violating the hygiene requirements to the products with identification of the risk management measures equal to its level. The development of methodology for assessing the risk of products for health shall be carried out based on the harmonization of domestic approaches to the product risk analysis with main methodical techniques adopted at the international level and in the most developed countries of the world. The practical implementation of the methodology development results according to the first aspect is carried out when forming the hygiene standards within the technical regulations providing the safety of products for the health of the citizens of the Russian

Federation and member countries of the Customs Union. Improvement of the second aspect of the risk assessment methodology development allows for forecasting the health risk associated with consumption (use) of products (goods) and its contribution into the sanitary-epidemiological situation formation.

The development of the risk assessment methods and efficacy of their management using the exposure, response an sensitivity markers is one of the most science-intensive and at the same time prospective risk analysis directions.

The use of the biological markers of effect and exposure, according to the WHO experts opinion, is the main tool in assessing the individual and population public health risks associated with impact of chemical substances [WHO, 2006; 2011; CDC, 2011].

Approaches to the justification of the biological markers of exposure and effect of relationships are systemic and based on the aggregate results of scientific analysis of the hazard and risk associated with influence of the living environment factors on people, epidemiological studies, theoretical knowledge about the regularities and peculiarities of implementing the negative impact of outside environmental factors on the organismic, organic and tissue, cellular-subcellular and molecular-genetic levels.

By now, about 30 criteria of biochemical, immune, hematological and molecular-genetic markers of effects characterizing the polymorphism of genes, disorder of oxidation and anti-oxidative processes are justified and implemented into the practice of hygiene evaluations and expert opinions, including at the level of cell DNA, proteomic profile, bone metabolism, neuroendocrine regulation, hemapoiesis suppression, specific sensitization development, cell destruction activation, reflecting the pathomorphism of diseases of blood, respiratory system, gastrointestinal tract, cardio-vascular and central nervous system, genetic instability development and chromosomal abnormalities. Herewith the development and implementation of new highly sensitive analytical methods allows for studying the mechanisms of occurrence and development of the body response reactions at the earliest stages (cellular-molecular level) of their formation for the external environmental influence.

It is feasible to distinguish the following as the most prospective directions for the development of these studies:

- studying the proteomic and metabolic human profiles and consequences of internal molecular interaction (interactomics) in the conditions of external environmental and occupational impact of the risk factors. At the present moment the development and implementation of highly sensitive and highly selective biomolecular methods based on the hybrid technologies allowing for identifying the principally new direct "target biological markers" (target proteins, target metabolites) directly associated with the development of pathologic process and thus being the indicators of the early stages of health disorders are carried out. The building of proteomic and metabolic maps on the different hierarchic levels "individual – group – population" in the terms of negative influences of different intensity will allow for raising the diagnostic technologies of the population health risk factors to the new stage of development and increase the preventive measures efficacy;

- extraction, sorting and use of stem cells for identifying the effects of low-molecular haptens *in vitro*;

- genic polymorphism analysis at the DNA level in terms of influence of the chemical factors of the living environment;

- identification of specific antibodies to the extended list of allergenic toxicants.

Use of the methods for identifying the biological markers of effect will allow for improving the control over the the exposure of technogenic chemical factors carried out within the state social-hygiene monitoring system which is one of the components for increasing the sanitary and epidemiological wellbeing of population [Zemlyanova M.A., Dolgikh O.V., 2010].

The scope of tests allowing for identifying the negative body responses on the risk factors exposure extended significantly in recent years. A number of such tests with sufficient level of provenness can be included into the response markers. Mostly it refers to the indication of mutagenic, carcinogenic and genotoxic activity of factors. In terms of existing sanitary situation especially in the industrially developed cities the value of this type of markers cannot be underestimated. The expert and analytical study of agents released,

used and detected in the air of the one of cities of the Central Russia demonstrated that for 30.3% of the total number of substances there are the data on their mutagenic activity in the *in vitro* and/or *in vivo* experiments and for 42.5% of substances there are no data on their potential genotoxicity [Tsutsman T.E., 2000].

The development of modern toxicology allows for considering the following as the key directions for studying the markers: the DNA reparation and tumor formation risk, disorders of cell signal systems, peroxisomes activation, role of apoptosis in pathology, genetic polymorphism of the xenobiotics metabolosim ferments, genetic sensitivity to the occurrence of occupational diseases, some issues of chemical carcinogenesis, etc.

The use of modern methodical approaches for determining the nuclear genome structure allows for new evaluation of the common mechanisms of the genotoxic agents action. First of all, it relates to the sites of their direct influence on the nuclear genome and involvement into these processes of the secondary mechanisms aimed at the expression of the adequate adaptation response reflected in the level and direction of the detoxication reactions.

Due to the genetic heterogeneity of human population it contains the individuals the genetic peculiarities of which determine the increased sensitivity to the action of mutagens [Dolgikh O.V. et al., 2012*a*; Lanin D.V., 2013]. In this respect the actual problem is the detection of resistance of body of the separate human and population to the action of chemical agents associated with polymorphism of genes responsible for the biochemical and immunological homeostasis [Dolgikh O.V. et al., 2012*b*].

First of all, the genetic markers of sensitivity include:

- mutations in the genes of ferments of the 1st and 2nd phases of detoxification (metabolism and conjugation) of organic and organometallic compounds – a subfamily of cytochrome genes, metilentetrahydrophosphatereductase, glutathione transferase, coproporfirinoxidase, sulftransaminaza, superoxide dismutase 2, zinc-metallopeptidase;
- polymorphism of genes of proteins participating in the pathogenesis of disorders in the target organs (gene of elastase, gene of endothelial growth factor, ESR1-estrogen, DRD2-dophamine receptor, NO-synthase) and metabolic processes (TERT (telomerase), SIRT1 (sirtuin), the family of PRAR genes, APO-E-apolipoprotein, ACE-gene of angiotensine converting enzyme, GCCR-glucocorticoid receptor);
- genetic predisposition to oncoproliferative states BRCA (oncology of female reproductive system), MMP-metalloproteinase (oncology of lungs), TERT (general oncology), p53 (a transcription factor the presence of which prevents the oncological process development);
- immunogenetic markers TLR4 (toll-receptor 4), FAS, FOXP3, TNF-alpha, p53, HLA DR.

The development of methods for identifying the biological markers of sensitivity is vital in the view of the health risk assessment methods development at the individual level.

The individual health risk assessment can be distinguished as the separate direction for the risk analysis improvement. In association with this such assessment can be used as the basis for the personified risk mitigation measures. In the field of professional medicine such measures are used quite often and their validation is required. Thus, the transfer to another workplace not associated with high level of the hazard factor exposure, individual medical and preventive measures, etc. can be considered as the personified risk mitigation measures. [Izmerov N.F., Kasparov A.A., 2002].

The studies with regard to assessing the occupational and production-specific health risks are vital when the mortality rate for the working-age population in the Russian Federation exceeds the similar indicators of EU by 4.5 times [Izmerov N.F. et al., 2014].

It has been noted that with implementation of new safe technologies at the separate enterprises the risk of occurrence of bad cases of occupational diseases is mitigated, the diseases without clear biological markers based on the mixed (occupational and age-specific) genesis are registered more often. These are the subclinical diseases in the patients with big period of service (20 years and more of the work experience) for which the different age-specific health disorders are detected. Therefore, the definition of the average work experience risk threshold compared to the parameters of harmful occupational factors beyond which there is a risk of formation of "professionally conditioned" (induced) disease is

of very important meaning. This problem is actual also due to the fact that in recent years many employees even at the substantial exceedance of the maximum allowable limit of the harmful occupational factors regardless of the average work experience risk threshold continue to work in the harmful conditions exposing their health to danger. This practice is not allowed and so conscious ideas about health risks for different age groups are currently being examined [Onishchenko G.G., 2013].

The development of principal provisions of the risk management systems shall be considered as one of the key directions in the field of risk management. As of now the following is considered as the basic principles for forming the decision justification system:

- use and development of existing information base;
- establishment of quantitive parameters for the health risks management;
- detection of priorities of activity on the health hazard criteria;
- development of the management model taking into account the character and quantitative assessment of relation between the objects of management;
- identification of the indicative parameters of results of the management system activity;
- optimization of managerial decisions on the criterion of minimal sufficiency of the management system expenditures and use of the risk management methods corresponding to the situation;
- optimization of the state monitoring system.

Practically every sphere of state control (supervision) is characterized by the essential variety of controllable entities. Both large and small enterprises, which use the modern technologies and also work on the outdated equipment are acting in the majority of spheres [The concept for increasing the efficacy of control and supervisory activity of the state authorities and local self-governing bodies for 2014–2018 (draft)].

As a rule, at the same time, the scopes of production and corresponding risks are concentrated in the small group of companies (5–10%). Meanwhile the applicable legal framework in the majority of cases binds the control bodies to carry out with certain frequency the total audit of all companies, which results in the ineffective consumption of resources.

Simultaneously, the situation at which the number of controllable entities exceeds even the theoretical abilities of their auditing body is created that in turn results in the absence of possibility to ensure the safety through the state monitoring.

It should be noted that the global practice provides the evidence of active use of the risk assessment methods in order to decrease the total administrative load on the economic entities with simultaneous increase of the level of efficacy of the control and supervisory activity of the authorized executive bodies and regulatory activity in general.

In addition, the use of the risk assessment methods in the administrative practice allows for more accurate accounting of the peculiarities of economic activity in the one or another sphere of production or services.

At the same time the incorrect risk assessment often creates the probability of irrational use of administrative and material resources of the relevant control and supervisory bodies, their disproportional distribution and ineffective impact on the sources of risk.

Introduction of the risk-oriented model at carrying out the control and supervisory activity in a number of countries allowed for substantial differentiation of approach to the control measures implementation. In particular, under the data of Hampton report [Hampton P., 2005], which in the countries of Organization for Economic Cooperation and Development became the classical analytical resource in managing the control and supervisory activities; the reduction in the number of excessive inspections allowed for releasing of the sufficient quantity of resources for the implementation of measures on the mandatory requirements clarification.

Some of the principles for carrying out the control and supervisory activities covered in the specified report deserve special attention and can be taken into account to ensure the medical and sanitary wellbeing of the population:

- wide use of the risk assessment methods for the corresponding distribution and concentration of administrative resources of the authorized executive bodies;

- independence of making the decision by the authorized state control (supervision) bodies as well as the responsibility for the efficacy of carrying out the control and supervisory activities;

- absence of unjustified inspections;

- rapid detection and application of appropriate sanctions to the economic entities, which from time to time violate the mandatory requirements;

- the authorized executive bodies shall ensure the competent clarification of mandatory requirements in the easily available form;

- rational building of the structure of system of the control and supervisory bodies and no duplication of their powers;

- activity of the state control (supervision) bodies shall be aimed at ensuring and encouraging the economic progress; the interference into the activity of controllable persons is possible only in the strictly agreed cases.

In general, it is arguable that the above mentioned principles are used to a greater or lesser degree in a number of states with developed economy.

The risk-oriented strategies are widely used in such states as USA, UK, Australia and Canada. Some instruments of the risk-oriented model are used in the Scandinavian countries, Germany and other European countries in the certain spheres of activity, which includes the fields of natural resource management, ecology, employment and compliance with labour legislation, financial activity.

The information mentioned above stipulates the necessity for implementing the differential approach to the control measures implementation, depending on the level of risk of the ham (loss) infliction. The differential approach will allow for substantial increasing the efficacy of consumption of resources for the functioning of control and supervisory bodies through the concentration of efforts of the state supervision inspectors in the most important directions.

To organize the control and supervisory activity based on the risk management system it is necessary to create the system for classifying the state control (supervision) entities in order to assign the class of hazard, depending on the level of threat of infliction of harm to the life and health of citizens.

The development and implementation of system for assessing the risks of potential danger of the types of economic activity for the health and procedure of its use during the planning of control measures will allow for not only to organize more effective consumption of state funds for carrying out the control and supervisory activity but to encourage the economic entities, introduce the progressive safety systems at the facilities, which allow for reducing the key risk indicators as well as decreasing the influence of the state control (supervision) and municipal monitoring bodies on their own activity.

In the system of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance the actual directions for the analysis development are as follows: scientific-methodical and information support of the state sanitary and epidemiological supervision (harmonization of normative and methodical documents in the field of health risk analysis, development of domestic normative base ensuring the hygienic safety); justification of the target health risk levels at performing the state task for provision of the state services (works); development of methodical approaches to the assessment of efficacy of the activity of bodies and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance within their powers on ensuring the hygienic safety of population. Solving of these tasks will allow for establishing the priority health risks conditioned by the impact of the living environment factors and primary actions of bodies and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance on the mitigation of existing risks to the allowable level.

It is feasible to consider the following as the priority ranking criteria for the risks analysis: the significance of effects/responses in relation to reducing the expected lifespan, prevalence of the risk factors impact on the health of population, provenness of cause-and-effect relationships and possibility of the health risk management. Thus, the diseases of the circulatory system, neoplasms, external causes, diseases of the digestive and respiratory

system forming the largest contribution to the reduction of the expected lifespan of population of the Russian Federation require the highest attention. Respectively, the factors of living environment conditioning the risk of these health disorders are considered as the priority for the assessment and management.

The optimization of managerial solutions under the criterion of minimum sufficiency of expenses for them, including in the system of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance is currently complicated due to the insufficiently complete solving of issue concerning the health risk economic assessment. The certain methodical approaches to the cost risk assessment especially of its population indicators were proposed in general [Bobylev S.N, 2002: MP 5.1.0029-11; Karnachev I.P., 2011; Zaytseva N.V. et al., 2012]. But these approaches can be supplemented during the improvement of the economic assessment of the groups health loss risk, which were not taken into account in full up to the present moment.

The assessment theory provides three main approaches: income, cost and comparative. Thus, the most apparent became the approach (within the income approach in the assessment theory) in which the population is considered as the labor resources of state, i.e. from the point of view of future money flows generated by them. The assessment is based on the disability period (the disability period reduction) and it is proposed to assess namely this period. The state can assess the cost of the human economic activity period (i.e. the reduction of this period) through the influence of the economic activity period value on the main social and economic indicators (gross domestic product for the country and gross regional product for the region).

The existing practices of economic assessment of losses for the life and health of population are also based on the cost estimate of the disability period. At the same time the social function of the state provides the creation of conditions for the life of all members of society (including the incapacitated persons). As of now the "Methodology for calculating the economic losses from mortality, morbidity and incapacitation of population" is applicable [Order of the Ministry of Economic Development of the Russian Federation, the Ministry of Health and Social development of the Russian Federation, the Ministry of Finance of the Russian Federation, Federal State Statistics Service No. 192/323н/45н/113 dd. April 10, 2012] but the proposed methodology allows for performing the calculations of economic losses from the population mortality only from the point of view "human – labor resource", on the one hand, and does not consider the issues on assessing the prevented losses, on the other hand.

Considering the role of humans in the economy (exclusively from the utility point of view) it should be noted that the population today is not only the labor resources; looking forward the human is able to reproduce the labor resources that shall be also taken into account in the calculations. In other words, not only the future work in favor of the state but also the "future (potential) children" shall be taken into account during the economic assessment of losses from the children's population mortality. In addition, the human not only "produces" but also "consumes". That is, besides that the human produces the public product contributing into its total volume it is also a consumer in the economy (that is very critical for understanding the economic role of the nonworking population). The growth of consumption increases the demand and leads to the growth in the scope of the gross domestic product. Herewith the expenses increase the scope of production by the value bigger than the scope of expenses. The multiplier effect – the ability of expenses to cause the growth of incomes bigger than the expenses caused this growth – is working [Goleva O.I., 2014].

The economic assessment of such losses associated with risk in full, especially the ones avoided at the expense of eliminating the violations of the sanitary legislation, shall be considered as the separate direction in the health risk analysis methodology.

Traditionally, the health risk management measures include the actions aimed at the exposure reduction. The risk management scenarios can include the different types of measures: regulating and supervisory, organizational and managerial, technical and technological, etc. [MP 5.1.0029-11].

To ensure the health risk mitigation for the period of implementation of sanitary-technical and other measures aimed at decreasing the level of exposure the most actual is

the risk analysis development direction, which provides the development and implementation of medical and preventive technologies for the health risk management.

The technologies for prevention of diseases associated with the influence of hazard factors are based on the following:

- recovery of membrane cell mechanisms for biotransformation of chemical substances of technogenic origin;
- stimulation of the natural mechanisms for eliminating the chemical substances of technogenic origin and their metabolites;
- recovery of balance of oxidation and anti-oxidative processes at the systemic level at the expense of stimulation of the functional activity at the cell and subcell level;
- stimulation of factors of immunological protection and non-specific reactivity;
- recovery of adaptation reserves and vegetative reactivity of body;
- correction of pathophysiological and pathomorphological disorders in the target organs [Zaytseva N.V. et al., 2013*b*].

The medical-preventive health risk management technologies allow for solving the following tasks:

- distinguishing the target risk groups for rendering the specialized targeted preventive aid;
- early detection (at the stage of functional disorders) of somatic pathology associated with influence of the hazard factors;
- optimization of the organizational and functional model for rendering the preventive aid under the influence of risk factors with implementation of ethiopathogenetically justified preventive technologies;
- long-term planning of preventive activity based on the assessment of the efficacy of technologies;
- revision and extension of the normative documents on rendering the preventive aid to the population with diseases associated with the influence of technogenic chemical factors of living environment (standards, protocols, consensuses, etc.) [Ustinova O.Yu. et al., 2012].

The implementation of such programs provides the preliminary risk-oriented clinical and laboratory examination of risk groups, chemical and analytical investigation, complex of functional and laboratory tests aimed at identifying the response factors equal to the risk factors [Zaytseva N.V. et al., 2011*a*]. Thus, it provides the targeted application of specialized medical-preventive technologies and preventive programs that results in their sufficiently high efficacy.

The results of studies of pathogenetic mechanisms for forming the diseases development risks associated with influence of the living environment factors is used as the fundamental basis of the risk management medical-preventive technologies that first of all provides the pathogenetic orientation of the preventive programs.

The development of effective specialized preventive measures requires the solution of the whole number of tasks: establishing the "threshold" for adaptation abilities of different groups of children's population to the different chemical factors; studying the peculiarities of the clinical manifestation of pathological conditions modified by the risk factors; identifying the biological markers of the external environmental impact and developing the methods for their determination based not only on the standard approaches but also on the cell, molecular, proteomic and nanotechnologies; assessing the system of relationships between the level of influence of the environmental factors and the human health condition.

Separate approaches to application of the medical-preventive technologies are already proposed. Thus, there are the publications describing the approaches to organizing the preventive aid for the children's population [Zemlyanova M.A., 2011; Zaytseva N.V. et al., 2013*c*]. The application of these approaches was succeeded by the detailed assessment of risk of occurrence, progress and chronization of diseases associated with the impact of chemical factors of the living environment, confirmation of exposure, including with the help of identification of the biological markers and effect based on the cellular-molecular, proteomic and nanotechnologies, analysis of systemic relationships of the markers of

exposure with the negative response markers [Avaliani S.L., 1992; Grishkin I.G., 1995; Zaytseva N.V., 2011*a*; 2011*c*]. The used medical-preventive technologies can and shall be unified and provided with standards and protocols for rendering of preventive as well as specialized aid. It is feasible to develop the same technologies in relation to the other risk groups and factors.

It should be noted that in all cases rendering the preventive aid shall be carried out based on the hygienic and medical-biological criteria, which take into account the availability of risk factors, exposure value, disease development risk characteristic, level of biological markers of exposure and negative effects hierarchically structured under the level of the body response reactions (molecular-cellular, organic and tissue, systemic, organismic), clinical manifestation, pathomorphism, severity and stage of pathology.

Therefore, it is feasible to distinguish the following as the main prospective directions for the health risk analysis methodology development:

- development of fundamental provisions on which the methodology is based;
- creation of information platform for the health risk analysis;
- development of methods for forecasting the sanitary and epidemiological situation based on the assessment of hazard and risk of health losses;
- formation of the risk-oriented population health management technologies as the element of stable social and economic development of the state;
- development of methodology for justifying the effective preventive programs.

1.5. Principles for harmonizing the health risk analysis methodology in the international aspect

When integrating into the global society the development and implementation of main provisions for harmonizing the principles, methods and criteria of the population health risk assessment with international approaches is the necessary condition for ensuring the economic and social development of the state. This will allow for transferring to the harmonization of hygiene regulations developed based on the health risk criteria. Because in the Russian Federation hygiene regulations are a component part of the sanitary legislation this health risk analysis aspect will receive legal support.

The documents of European Committee underline that the scientifically justified risk assessment plays the exclusive role during the preparation and improvement of legislation in the field of protection of the rights of citizens and especially of their health. In addition, the provision on that the risk assessment conduction in accordance with internationally recognized procedures provides the grounds for defending the normative acts in a judicial proceeding, for example, in the European Court of Human Rights in case of disagreement with rules of the World Trade Organization [EC, 1997] is distinguished. In this relation the Directorate General of the European Committee for Health and Consumer Protection with participation of the scientific steering committee and eight additional expert committees under the different risk assessment fields carries out the development of recommendations on the harmonization of procedures for the health risk and environment assessment. The main harmonization principles were formulated in the European Union within the health risk assessment procedure [EU, 2000].

In relation to the food products risk assessment the common food products risk assessment principles are specified in the procedural manual of Committee Codex Alimentarius in the Section V "Risk Analysis Working Principles" where the main working risk assessment principles used by the Codex Alimentarius are listed [World Health Organization / UN Food and Agriculture Organization, 2010]. The same principles are formulated also in the European Union [EU, 2002*a*]. The documents of Committee Codex Alimentarius describe the common principles for the microbiological risk assessment based on the procedural manual.

The main goals of the risk assessment methods harmonization include:

- risk level assessment orientation in the context of human health;
- unification of main principles and key steps of the risk level assessment;
- identification of the range of important problems, common interests involved into ensuring the compliance of the risk level assessments in the scientific committees;
- submission of recommendations for the harmonization development.

The work group of experts of the European Community countries emphasized that the following is required to harmonize the risk assessment methods at the international level:

- harmonization of terminology in the field of risk assessment;
- cross-sectoral harmonization in the field of risk assessment, which is carried out by the different establishments;
- horizontal harmonization in the assessment of risk of different factors (for example, the quantitative assessment of microbiological risk and risk associated with the impact of chemical substances);
- ensuring the mutual understanding between the bodies / experts on the risk assessment and management.

The analysis of legislative and normative-methodical health risk assessment basis demonstrated the applicability for harmonizing the risk assessment methods and criteria used in the Russian Federation and Customs Union with the internationally recognized methodology.

The experience in harmonizing the risk assessment principles of Committee Codex Alimentarius and European Community countries allowed for identifying the main health risk assessment principles, which though they are not formulated in the separate document are used in practice in the Russian Federation and member countries of the Customs Union:

- scientific justification of methods and criteria for the products risk assessment;
- development of available information sources for using the methods and criteria for the products risk assessment;
- openness of the products risk assessment;
- products risk assessment by the independent experts;
- discussion by all member countries of the methods and criteria for the products risk assessment.

It is feasible to start the harmonization of terminology from the unification of understanding of the term "harmonization" itself. Common definition of this term is contained in the Big Economic Dictionary: "Harmonization is the mutual agreement, systemization, unification, coordination, normalization and ensuring of the mutual compliance of processes, relations, goods, taxes, etc." [Borisov A.B., 2003]. Determination of the notion "harmonization" specified in the WTO agreement on the application of sanitary and phytosanitary measures: "Harmonization is the establishment, recognition and application of common sanitary and phytosanitary measures (SPM) by different members" [WTO, 1995].

International unification (harmonization) of the national legislation of separate states through the adoption of international acts differs from the changes in the national legislation in general by that the unification (to a lesser degree – harmonization) results in change in the form of adoption in the separate states of the same, textually equal legal norms [Veliyaminov G.M., 2004]. In this relation the harmonization (unification) of terminology plays one of the key roles in the health risk assessment methods harmonization.

The harmonization of terminology, together with the legislative base harmonization, is the basic condition for harmonizing the health risk assessment methods and criteria.

As it was mentioned above, the attempts to normalize the terminology in the field of risk assessment were taken repeatedly [Ahl A.S. et al., 1993; Kaplan S., 1997; IRIS], including in the Russian Federation during the period of implementing the health risk assessment methodology of the U.S. Environmental Protection Agency (EPA) [Novikov S.M. et al., 1998].

The first document of the harmonization project "The Risk Assessment Terminology of the International Program on Chemical Safety" [WHO, 2004] is issued in 2004 within the activity of the International Program on Chemical Safety (IPCS).

When harmonizing the terminology in the field of the public health risk assessment in the Russian Federation it is feasible to be oriented on the harmonized terminology of the World Health Organization and European Committee for Health and Consumer Protection.

The notions "hazard" and "risk" are distinguished in the European Union countries as the priority terms requiring the harmonization. Under the WHO data, in the scientific literature there are not less than 18 definitions of term "hazard" and 22 definitions of term "risk" [EU, 2000].

The same understanding of definitions as well as the correct translation of terms and definitions plays the essential role within the global interstate harmonization of terminology. The second report on harmonizing the risk assessment procedures in the EU countries [EU, 2003*b*] distinguishes the provisions on that one term can describe the different notions or one term stipulates a large number of interpretations.

In this relation within the terminology harmonization it is feasible to identify the categories of the risk levels described not in the numerical form, identify the conditions for using of terms, select the terms, which are mostly used by translators from amongst the same terms, identify the translation of meaning of the selected terms taking into account the complete message, provide the harmonized terms to the experts for use in their work.

The translation of the main terms used for the risk assessment into the languages of the member countries of the European Community was performed [EU, 2000]. The example of this translation supplemented by the translation of terms into the Russian language is presented in the Table 1.7.

The harmonization of notions reflecting the sense of terms is the most complicated and requiring the detailed discussion. For example, only in the documents of European countries 18 terms describing the risk at the *de minimis* level were detected.

Table 1.7

The translation of the main terms used for the risk assessment into the languages of the member countries of the European Community supplemented by the Russian language

English	**Hazard**	**Risk**	**Risk analysis**	**Risk assessment**	**Hazard identifcation**	**Hazard characterization**
French	Danger	Risque	Analyse du risque	Estimation du risque	Identification du danger	Caracterisation du danger
German	Gefahr	Risiko	Risikoanalyse	Risiko bewertung	Gefährlichkeitser mittlung	Gefährlichkeits-Charakterisierung
Nederlands	Gevaar	Risico	Risico analyse	Risicobeoordel ing	Identificatie vangevaar	Karakterisering van het gevaar
Español	Peligro	Riesgo	Análisis de Riesgo	Evaluación de Riesgo	Identificación de la Peligrosidad	Caracterización de la peligrosidad
Dansk	Fare	Risiko	Risiko analyse	Risiko-vur-dering	Identificeringaf sundheds-fare	Karakteristikaf sundhedsfare
Suomi	Vaara	Riski	Riski-analyysi	Riskinarviointi	Vaaran tun-nistaminen	Vaaran ku-vaaminen
Islandsk	Hætta	Áhætta	Áhættugreining	Áhættumat	Hættukennsl	Hættulýsing
Norsk	Fare	Risiko	Risiko analyse	Risiko vurdering	Identificering af sundhedsfar	Karakteristik af sundhedsfare
Svensk	Fara	Risk	Riskanalys	Riskvärdering	Faroidentifiering	Farokarak-tärisering
Русский	Опасность	Риск	Анализ степени риска	Оценка риска	Идентификация опасности	Характеристика опасности

End of Table 1.7

English	Risk assessment policy	Risk characterization	Risk communication	Risk evaluation	Risk management
French	Politique d'estimation du risque	Caractérisation du risque	Communication sur le risque	Appréciation du risque	Gestion du risque
German	Risikobewertungs Grundsätze	Risiko-charakterisier ung	Risikokom-munikation	Risiko Risikobeurteilug	Risikomanagemt
Nederlands	Risico (beoordelings) - beleid	Risicokarakterise-ring	Risicocommuni-catie	Risicoevaluatie	Risicomanagemn
Español	Polí tica de la evaluación del riesgo	Caracterización del riesgo	Comunicación il riesgo	Valoración del riesgo	Gestión del Riesgo
Dansk	Risiko-vurderings-politik	Risikokarakteristik	Risiko-kommunikation	Risiko-evaluering	Risikohåndtering
Suomi	Riskinar-vioinnintoiminta-periaatteet	Riskin kuvaaminen	Riskiviestintä	Riskokonais-arviointi	Riskinhallinta
Islandsk	Áhættumats-stefna	Áhættulýsing	Áhættukynning	Áhættuskoðun	Áhættustjórnun
Norsk	Rsiko vurde-ringspolitik/-retningslinjer	Risiko karakteri-sering sering	Risiko kommunication	Risiko evaluering	Risiko håndtering
Svensk	Riskvärde-ringspolicy	Riskkaraktäri-sering	Riskkommunikation	Riskevaluering	Riskhantering
Русский	Политика оценки риска	Характеристика риска	Информирование о риске	Расчет риска	Управление риском

The problem of unification of the acceptable risk notion is of special interest in the products risk assessment field. The toxicological dictionary of the US National Institute of Health besides determining the risk *de minimis – "the risk, which is negligible and very small to be of the social interest"* provides the quantitative expression of this risk (the probability is less than 10^{-5} or 10^{-6}). Herewith, it is noted that the use of this term in the legal practice stipulates the negligible risk for individual [ISO/IEC, 1999].

The same interpretation of the term "acceptable (allowable) risk" is specified in the "Guidelines on the assessment of risk for public health at the impact of chemical substances contaminating the environment: "The acceptable risk is the adverse effect development risk level, which does not require the implementation of long-term measures for its mitigation and assessed as the independent and negligible in relation to the risks existing in the daily activities and life of the population" [P 2.2.1.10-1904].

The documents of the International Organization for Standardization use the notion "endurable risk" but the contains the definition of the same term "acceptable risk" – the risk, which is endurable in the certain context and based on the valuable existing in the society at the current moment [ISO/IEC, 1999]. The Russian Federation patented the method for determining the integral acceptable risk of the separate classes and types of consumer products for the human health. This invention determines the integral acceptable risk of products, which does not result in the consistent change of background values of the health indicators (patent of the Russian Federation No. 2368322 dd. September 27, 2009). This formulation to the maximum extent complies with notions of acceptable risk adopted in the world and allows for developing the methods, which can be used in practice.

Thus, in order to harmonize the terminology in the health risk assessment field it is feasible to develop the glossary of terms and definitions in the Russian language. For global interstate harmonization it will be necessary to create the same document with translation

into the official languages adopted for publishing the UN documents. When harmonizing the terminology it is feasible to use the experience in this field accumulated in the European Community countries.

It is necessary to distinguish the risk assessment provisions, which can be actual for the health risk assessment and consider them as the priority objects of harmonization. It is feasible to consider the health risk assessment harmonization objects in general and for the separate risk assessment stages.

The harmonization of methodical approaches to the risk assessment stipulates the unification of this process. In relation to the health risk assessment stage-by-stage approach the differences between the domestic methodical approaches to the health risk assessment and methodology adopted in the majority developed countries are negligible. The majority of methodical developments dedicated to the assessment of risk associated with the impact of chemical, microbiological, physical, social and other factors recommend the implementation of four stages: hazard identification, hazard characterization ("exposure – effect" dependence assessment), exposure assessment, risk characteristics.

The task of the horizontal harmonization of methodical approaches to the assessment of risk associated with the impact of chemical and microbiological factors was set within the risk assessment methods harmonization in the European Union [EU, 2000]. Within the development of methodology for assessing the risk of products for the health of population it is feasible to extend and formulate the horizontal harmonization task as the harmonization of methodical approaches to the risk assessment, including the products, associated with the impact of chemical, physical and microbiological factors as well as to the assessment of integral risk associated with different factors.

The main methodical approaches used at the separate stages of risk assessment, including the products, are specified in Table 1.8.

Table 1.8

Harmonization of content of the risk assessment stages for the health risk assessment tasks

Risk assessment stage	Risk factors			Recommendations on the content of stage for the harmonized risk assessment methods
	Chemical	Micro biological	Physical	
1	2	3	4	5
Hazard identification	Establishment of priority harmful chemical risk factors Determination of possible negative effects of influence of the established factors. Hazard indicators selection. Determination of affected population. Forming the preliminary exposure scenario	Establishment of probability for the presence of known pathogenic microorganism or microbial toxins. Assessment of their potential to cause the adverse effects. Risk profile formulation. Establishment of the risk group and population, which probably contacts with pathogenic microorganism.	Characterization of the sources of influence. Determination of possible negative effects of influence. Detection of peculiarities of spatial and time distribution. Determination of the number of population affected by the harmful influence.	Identification of the principal scenarios. Establishment of the types and factors of the products risk in accordance with scenarios for including into the further assessment procedure. Determination of possible negative effects of influence. Risk groups identification. Assessment of possibility

Continuation of Table 1.8

1	2	3	4	5
	determination of routes and ways of influence. Assessment of possibility and combined action	Assessment of reproductive capacity		combined action of different factors
Hazard characterization (assessment of dependence "exposure – effect (response)")	Justification of safe (referential) levels of impact based on the maximum non-acting, threshold and reference values. Simulation of dependence "exposure – effect (response)", including with the use of extrapolation of results of toxicological studies from high levels of exposure to low, results of epidemiological studies from high levels of exposure to low	Determination of the minimum infecting doses of microorganisms. Simulation of dependence "exposure – effect (response)", including taking into account the susceptible groups of population. Use of extrapolation of results of toxicological studies from high levels of exposure to low	Determination of the threshold criteria of observed effect taking into account the duration and level of influence. Separate assessment of effects	Use of pair mathematical models of dependence "exposure – effect" for every factor and type of effect in order to establish the non-acting levels. Identification of non-acting levels of the separate hazard factors, including for different groups. Use of established non-acting levels and parameters of mathematical models of dependence "exposure – effect" for the risk evolution mathematical models. Use of the risk evolution mathematical models for calculating the integral risk of the different factors of products for health in accordance with scenario
Exposure assessment	Use of scenario approach (especially for the food products). Deterministic approach to the exposure assessment. Calculation of dose (preferentially) and concentration of the chemical factor. Use of the exposure markers. Calculation of the chemical agent dose at the multi-environmental intake by different ways. Use of mathematical models for the exposure calculation.	Scenario approach (especially for the food products). Probabilistic and deterministic exposure assessment. Calculation of concentration (preferentially) and dose. Use of mathematical models for the exposure calculation.	Assessment of exposure in different ranges. Deterministic approach to the exposure assessment. Influence frequency assessment. Use of mathematical models for the exposure calculation.	Use of scenario approach. Calculation of exposure level for every factor at the different scenarios of impact and consumption of products (maximum, recommended, actual). Exposure probability assessment, including for different groups – at the different scenarios of impact and consumption of products

End of Table 1.8

1	2	3	4	5
Risk characte-rization	Comparison of exposure to the allowable (referen-tial) levels of impact. Calculation of the risk values for separate effects (responses) and its comparison to the acceptable (allowable) level. The calculation of risk at the multienvironmental intake of chemical agent by different ways and at the combined action. Semi-quantitative and quantitative assessment and classification of risks. Calculation of the population risk levels	Comparison of exposure to the allowable levels Risk establish-ment and description Qualitative, semi-quantitative and quantitative assessment and classification of risks. Calculation of the population risk levels	Comparison of exposure to the allowable levels. Quantitative risk assessment, classification of risks. Calculation of the population risk levels	Description of risks as the probabilities of separate effects with their quantitative characterization at the different types and ways of impact as well as for the separate classes and types of products. Integral health risk assessment under the influence of different factors. Comparison of results of quantitative assessment to the acceptable levels of risks. Classification of the level of risks. Calculation of the population health risk levels

At the hazard identification stage during the assessment of risk practically for all types of factors for inclusion into further assessment procedure the certain risk factors are established in accordance with principal impact scenarios as well as the possible public health disorders associated with the risk factors; the risk groups identification is conducted. In addition, the possibility of combined action is assessed for the chemical risk factors. At this stage for the health risk assessment methods it is feasible to recommend the identification of principal scenarios for establishment of the types and factors of risk in accordance with scenarios for inclusion into the further assessment procedure, determining the possible negative effects of influence of the different factors as well as consumption of products, identification of groups, assessment of possibility of the combined action and determination of critical points for the hazard formation.

The hazard characterization in assessing the risk of different factors stipulates the determination of safe levels of their impact for the factors possessing the threshold action and parametrization of dependence "exposure – effect (response)" for the non-threshold factors and at the levels beyond the safe ones. The information about the maximum non-acting and minimally acting exposure levels under the data of experiments and about the benchmark levels under the data of epidemiological studies is used for the safe levels determination. Most often the pair mathematical models of dependence "exposure – effect" for every factor and type of effect are used. The determination of the safe levels of impact is carried out taking into account the duration of impact and the most susceptible groups of population [WHO, 2010; US EPA, 2012].

Simulation of dependence "exposure – effect", which allows for conducting the quantitative risk assessment is the most developed for the chemical, physical (radiation) and a number of microbiological factors as well as in relation to the carcinogenic effects of electromagnetic radiations. The separate simulation elements are used in relation to effects

from the noise exposure [WHO, 2009*a*; 2009*b*; Holcomb D.L., 1999; Verkasalo P.K. et al., 1993, 1996; Stansfeld S.A. et al., 2005].

For the chemical and physical factors there is the experience of using the risk evolution mathematical models for calculating the integral risk of different factors for the health. In this case the parameters established for the pair models of dependence of the human health changes on the exposure of separate factors are used. This type of models allows for more precise accounting of duration and change in the exposure intensity in accordance with scenario [MP 2.1.10.0059-12; MP 2.1.10.0062-12].

In the health risk assessment methods at the hazard characterization stage it is feasible to use the pair mathematical models of dependence "exposure – effect" for every factor and type of effect in order to establish the non-acting levels, identify the non-acting levels of different factors, including for different risk groups, use the established non-acting levels and parameters of mathematical models of dependence "exposure – effect" for the risk evolution mathematical models, application of the risk evolution mathematical models for calculating the integral risk of different factors for health in accordance with scenarios.

During the assessment of exposure of different factors the scenario approach is used at which the exposure level calculation for every factor is performed in accordance with different exposure scenarios taking into account the most susceptible groups. Herewith the deterministic approach is applied to the chemical and physical factors, and the deterministic and probabilistic exposure assessment is applied to the microbiological factors [Nogawa K., Kido T., 1993; WHO/IPCS, 2008; МУ 2.3.7.2519-09; Torre G. et al., 2007].

To assess the exposure during the health risk assessment it is recommended to use the scenario approach to the calculation of exposure for every factor at the different scenarios (for example, consumption of products – maximum, recommended, actual). The exposure assessment for different groups is performed at the different scenarios. Within the risk assessment methods harmonization it is feasible to take into account the issues of combining the deterministic and probabilistic exposure assessment.

The risk characterization stage provides for all factors the description of risks as the probabilities of separate effects with their quantitative or semi-quantitative characterization. This stage provides the risk level acceptability assessment and its classification. The methodical documents applicable at the current moment do not provide the integral characterization of risk of health disorders of different severity level under the influence of different factors, however, for example, the risk of products for health in general is formed as the integral. In this connection when developing the methods for assessing the risk of products for health it is necessary at the risk characterization stage to provide the comparison of the qualitative assessment results with acceptable levels of risks both for separate factors and for the products in general, with use of integral risk assessment from the influence of the different factors of products. It is necessary to assess both the individual and population risk. To justify the making of decisions on the risk management their levels at the risk characterization stage shall be classified.

The issues of inclusion of a number of effects to the negative ones is considered as one of the main problems of harmonization at the hazard identification stage. The European Community experience demonstrated that the formalization of this stage could result in the exclusion of important information had the qualitative character from the assessment.

The approaches to determining the non-acting levels shall be considered as the main subject of harmonization during the hazard characterization, especially the uncertainty factors used at it and used models of dependence "exposure – effect", including for the most susceptible groups of population.

The methodical approaches to the assessment of health risk associated with different factors have a number of peculiarities. The harmonization of methods for assessing the health risk associated with different factors is critical during the formation of the health risk assessment methods. However, currently in the global practice the health risk assessment is carried out only in relation to the separate factors. In this connection the harmonization and adaptation of existing health risk methods and criteria to the use in the health risk assessment methods associated with different factors (chemical, physical, microbiological, social, etc.) is critical.

The health risk assessment methods harmonization includes:

- use for performance of stages for hazard identification, assessment of dependences "exposure – effect (response)" of the relevant information contained in the internationally recognized sources and databases;
- application during the exposure assessment of adequate and internationally recognized methods for measurement and simulation of the hazard factors intensity;
- use during the characterization of risks of comparable risk classification scales, including the level of acceptable risk, taking into account the already proposed levels of negligible risk of serious diseases or death.

The harmonization of criteria for assessing the risk of products to health covers several issues:

- the necessity for establishment of such criteria;
- the harmonization of acceptable health risk levels;
- the risk classification harmonization.

Some documents on establishing the safety criteria, in particular, the microbiological ones, contain the provision on that in order to conduct the health risk assessment to establish the criteria it is necessary to have the evidence that such criteria are necessary for practice. The results of epidemiological studies or evidences of the health risk availability are considered as such proof [FAO/WHO, 2010].

The exposure values of these factors, which provide the absence of unacceptable risk is used during the products risk assessment as the safety criteria of separate factors for health in the technical regulations. For chemical factors of food products these are the maximum permissible levels (maximum concentration limits) of pollutants, pesticides, residual quantities of veterinary preparations, for physical factors these are maximum allowable limits, for microbiological – the number of colony-forming units or their absence in the weight unit of product.

In relation to the products the safety criteria are the regulations contained in the "Unified Sanitary Requirements" [Decision of the Customs Union Committee No. 299 dd. May 28, 2010] for 23 types of products, for example, for food products these are the acceptable levels of chemical and microbiological indicators, for children's goods – the requirements of microbiological (content of microorganisms in 1 g (for 1 cm^2)) and chemical (migration ratios) safety, for perfumes and cosmetics and oral hygiene products – the retirements of microbiological (content of microorganisms in 1 g (for 1 cm^2)) safety and toxicological safety indicators determined at the laboratory and alternative biological models *in vitro*. Herewith, only the separate regulations contained in the "Unified Sanitary Requirements" are justified under the acceptable risk criteria.

This provision complicates the use of these regulations as the criteria for assessing the risk of products for health. Currently the justification of hygiene regulations under the public health risk criteria is conducted. This procedure is already completed for the residual content of tetracycline antibiotics, nitrates and ractopamine in the food products, acceptable levels of content of *L. monocytogenes* in the separate groups of products.

The harmonization of the regulations scope of application is the essential issue during the harmonization of safety of the separate factors of products for health. Some regulations at the release from manufacturer and marketing differ substantially. Thus, in the semi-smoked sausage products in accordance with regulations EC 1441-2007 [the Regulations of Committee (EU) No. 1441/2007 dd. December 5, 2007] the content during the control at the end of technology (the presence of *L. monocytogenes* in 5 samples from batch with size of 25 g each is not allowed) differs substantially from regulation during the control at the market (100 CFU/g, not more than, in each of 5 samples from the batch). The regulations of the Customs Union provide that the regulations of the Unified Sanitary Requirements shall be observed both during the control at the end of technology and during the marketing of products.

One of the most important issues of the health risk assessment criteria harmonization is the common recognition of levels of acceptable risk for the health of population. Such levels are presented in some methodical documents. The "Guidelines on the assessment of

risk for public health at the impact of chemical substances contaminating the environment" the value of the individual risk of serious disease or death $1 \cdot 10^{-4}$ is considered as the upper limit of acceptable (allowable) risk. This value practically corresponds to the values specified in the majority of methodical US and EU documents.

The draft of instruction "Assessing the Risk for the Health of Population from the Influence of Chemical Substances Contaminating the Ambient Air" [Instruction 2.1.6.11-9-29-2004] proposes to assess the value of potential risk of immediate (reflectory) action of up to 2% (or up to 0.02 in the unit fractions) and risk of long-term (chronic) exposure of up to 5% (or up to 0.05 in the unit fractions) as acceptable. Herewith, it is stipulated that the risk on non-specific responses is suggested. Unfortunately, the severity of these responses is not identified. The same document proposes the acceptable and allowable levels of carcinogenic risk equal to the classification of risks specified in the manual P 2.1.10.1920-04.

The provision specified in the "Methods for Assessing the Risk for the Condition of Health of Population from the Environment Contamination" applicable in the Republic of Kazakhstan (approved by the order of the Minister for the Environment of the Republic of Kazakhstan No. 139-п dd. June 6, 2008) shall be taken into account. Expression of the specialist opinion during the expert evaluation of the public health risk assessment: the level of risk one case per million - it is considered that the influence of the expert evaluation object on the public health condition is practically absent.

When assessing the integral health risk associated with the living environment factors the value of the specified health risk index that is less than 0.05 can be assessed as the negligible risk not differing from the common daily risks.

It should be noted that many documents do not provide the numerical values of the acceptable risk for health but specify, for example, that it is the level of risk of the adverse effect development, which does not require the implementation of additional measures for its mitigation evaluated as the independent and negligible in relation to the risks existing in the daily activity and life of the population.

When harmonizing the acceptable health risk levels it is feasible to compare the values which are already available taking into account the severity of effects for which they are proposed. Taking into account that the acceptable risk levels depend on such factors as the social and economic situation, perception of risks by population, social responsibility of regulatory bodies and business community and other which can be changed it is necessary to consider the issue on the methods for justifying the acceptable levels of the risk of products for the health of population.

The problem of the risk levels classification is closely connected with the problem of harmonization of the acceptable health risk levels. As a rule, such classifications include the acceptable (allowable) levels. The risk ranges classification specified in the "Guidelines on the assessment of risk for public health at the impact of chemical substances contaminating the environment" reflects the most often used in the global practice system of criteria of the individual life-long risk associated with the external environmental factors.

In accordance with these criteria the first risk range (individual risk during the whole life equal to or less than $1 \cdot 10^{-6}$ that corresponds to one additional case of serious disease or death per 1 mln. of exposed persons) characterizes such levels of risk, which are accepted by all people as *negligible*, not differing from the common daily risks (level *de minimis*). Such risks do not require any additional measures on their mitigation and their levels are subject to the periodical control only.

The second range (individual risk during the whole life of more than $1 \cdot 10^{-6}$ but less than $1 \cdot 10^{-4}$) corresponds to the maximum acceptable risk, i.e. the upper limit of acceptable risk. Namely at this level the majority of the foreign and recommended by the international organizations hygiene regulations for population in general are established (for example, for drinking water the WHO as the acceptable risk uses the value $1 \cdot 10^{-5}$, for ambient air – $1 \cdot 10^{-4}$). These levels are subject to the permanent control. In some cases at such levels of risk the additional measures on their mitigation can be taken.

The third range (individual risk during the whole life of more than $1 \cdot 10^{-4}$ but less than $1 \cdot 10^{-3}$) is acceptable for professional groups and not acceptable for the population in general. The occurrence of such risk requires the development and implementation of the planned recreational measures. The planning of measures on the mitigation of risks in this case shall be based on the results of deeper assessment of different aspects of existing problems and establishment of the level of their priority in relation to the other hygienic, ecological, social and economic problems at this territory.

The fourth range (individual risk during the whole life equal or more than $1 \cdot 10^{-3}$) is not acceptable both for population and professional groups. This range is defined as the de manifestis risk and if it is reached it is necessary to provide the recommendations for persons making the decisions on the implementation of emergency recreational measures for the risk mitigation.

The Republic of Belarus adopted the hygienic regulations "Criteria for Assessment and Degree of Risk of Harmful Influence on Human of the Acoustic Load at the Populated Areas" [Resolution of the Ministry of Health of the Republic of Belarus No. 199 dd. December 18, 2012] in accordance with which the classification of risks is performed (Table 1.9). Bu this document does not determine the risk of which effects (responses) is characterized.

Table 1.9

Criteria for Assessment and Degree of Risk of Harmful Influence on Human of the Acoustic Load at the Populated Areas

Parameter	Values				
Assessment criterion – specific acoustic load, dBA	up to 50	51–60	61–70	71–80	more than 80
Harmful influence risk	None	Small	Average	High	Very high
Assessment in points	1	2	3	4	5

The draft of instruction "Assessing the Risk for the Health of Population from the Influence of Chemical Substances Contaminating the Ambient Air" (the Republic of Belarus) provides quite sufficient classification of the levels of risk and hazard [Instruction 2.1.6.11-9-29-2004].

The value of potential risk of immediate (reflectory) action is assessed under the following criteria specified below.

- Acceptable – up to 2% (or up to 0.02 in the unit fractions). The growth of the population morbidity associated with the impact of assessed factor is practically excluded, and the discomfort condition can occur only in the individual cases at the highly-sensitive persons.
- Satisfactory – from 2 to 16% (or 0.02–0.16 in the unit fractions). The frequent cases of complaints of the population on the different discomfort conditions associated with the influence of assessed factors (unpleasant odors, reflectory reactions, etc.) are possible; the tendency to the growth of total morbidity, which is usually tracked under the medical statistics data or during the conduction of special studies as a rule does not have the verifiable character.
- Unsatisfactory – from 16 to 50% (or 0.16–0.50 in the unit fractions). The systematic complaints of the population on the different discomfort conditions associated with the influence of assessed factors (unpleasant odors, reflectory reactions, etc.) at the tendency to the growth of total morbidity, which as a rule has the verifiable character are possible.
- Hazardous – more than 50% (more than 0.50 in the unit fractions). The mass cases of complaints of the population on the different discomfort conditions associated with the influence of assessed factor at the verifiable tendency to the growth of total morbidity as well as the occurrence of other effects of harmful influence (appearance of pathology specifically associated with the type of influencing factor, etc.) are possible.
- Extremely hazardous – close to 100% (or 1). The pollution of environment in this case has transferred to other qualitative condition (occurrence of cases of acute poisoning, change in the structure of morbidity, tendency to the growth of mortality, etc.), which shall be assessed with the help of other, more specific, models.

The value of potential risk of long-term (chronic) exposure shall be assessed under the following criteria:

- acceptable – up to 5 % (or up to 0.02 in the unit fractions). As a rule, the adverse medical and ecological tendencies are absent;
- satisfactory – from 5 to 16% (or 0.05–0.16 in the unit fractions). As a rule, a tendency to the growth of non-specific pathology occurs.
- unsatisfactory – from 16 to 50% (or 0.16–0.50 in the unit fractions). As a rule, a verifiable tendency to the growth of non-specific pathology occurs at the appearance of individual cases of the specific pathology;
- hazardous – from 50 to 84% (or 0.50–0.84 in the unit fractions). The verifiable growth of non-specific pathology occurs at the appearance of the substantial number of cases of specific pathology as well as the tendency to increasing the population mortality;
- extremely hazardous – close to 100% (or 1). The pollution of environment in this case has transferred to other qualitative condition (occurrence of cases of acute poisoning, change in the structure of morbidity, verifiable tendency to the growth of mortality, etc.), which shall be assessed with the help of other, more specific, models.

In accordance with same document the hazard quotient value is assessed under the following criteria:

– extremely high >10;
– high 5–10;
– average 1–5;
– low 0.1–1.0;
– minimum <0.1.

The methodical recommendations adopted in the Russian Federation also proppose the risk levels classification, including the risk calculated using the risk evolution simulation. For example, the recommendations on the health disorders risk management associated with the action of negative factors of the living environment can be developed taking into account the evaluation scale of the specified risk index $\tilde{R}$.

- The value $\tilde{R}$ is less than 0.05 that can be assessed as the *negligible risk* not differing from the common daily risks. It is recommended to use the measures on organizing the reduced (random) monitoring of load, the planning of measures, which can be implemented in the longer term (5 years and more). The planned revision of the risk levels shall be carried out not less than once in every five years as well as during the placement at the territory of new sources of contamination and change in the town-planning situation. The value 0.05 corresponds to the upper bound of acceptable risk.

- Value $\tilde{R}$ is in the range of more than 0.05–0.35 that can be assessed as the *moderate risk*. It is recommended to use the measures for organizing the permanent load monitoring. The measures on the chemical load reduction shall be developed taking into account the average and short term perspective (1–3 years). The planned revision of the risk levels shall be carried out not less than once in every three years. The measures on the risk mitigation shall be developed taking into account the average and short term perspective (1–3 years). The risk degree shall be revised every year.

- Value $\tilde{R}$ is in the range of more than 0.35–0.6 that can be assessed as the *high risk*. It is recommended to use the measures on organizing the extended load monitoring program with conduction of additional studies at the places and/or in the periods of the maximum levels of load. The risk mitigation measures shall be developed for the nearest short-term perspective during one year. The risk degree shall be revised every year.

- Value $\tilde{R}$ exceeds the level of 0.6 that is assessed as the very high risk. It is recommended to use the measures on the immediate termination of activity of the main contamination sources or evacuation of population from the harmful impact area. It is recommended to revise the degree of risk after taking the measures on the public health preservation.

The classifications of the risk levels of products are specified in the methodical documents on the assessment of microbiological risk for the food products [FAO/WHO, 1999; MP 2.1.10.0067–12]. Thus, when assessing the microbiological risk for solving the risk management tasks it is recommended to distinguish three levels of the risk "severity" (green – low, yellow – average, red – high).

The same classification can be carried out using the evaluation scale (Table 1.10).

Table 1.10

Evaluation scale for the public health risk level characterization at the influence of the microbial factors contained in the food products

Risk category indicator (RI_{cat})	Risk level
$9 \le RI_{cat} \le 27$	High (red)
$3 \le RI_{cat} < 9$	Average (yellow)
$1 \le RI_{cat} < 3$	Low (green)

High level of risk ($9 \le RI_{cat} \le 27$): high risk of development of serious, long-term and widely spread adverse changes in health within the probable scenarios of exposure as a result of established contact with microorganisms. In case of such health risk level it is recommended to develop and implement the risk control and management measures in the form of development and/or correction of sanitary and epidemiological standards and guidelines, hygienic regulations, standards for improving the systems for control of quality and safety at production, development of inter-industry target settings (terms for elimination or reduction of the diseases risk level), increase the efficacy of sanitary training and promulgation, hygienic education of employees.

Simultaneously, under these results the priority directions of studies aimed at the reduction of uncertainties and development of new control or prevention strategies are determined.

Average level of risk ($3 \le RI_{cat} < 9$): adverse changes in the public health within the probable scenarios of exposure are presented mainly by the individually solved cases of average severity. It is recommended to develop and implement the risk control and management measures in the form of improving the systems for control of quality and safety at production, development of recommendations for industry, trade, consumers, hygienic education and training of employees of the food industry and catering enterprises and population.

Low level of risk ($1 \le RI_{cat} < 3$): adverse changes in the public health within the probable scenarios of exposure are presented by the quite rare, individually solved, cases of light degree. It is recommended to develop and use the risk control and management measures in the form of hygienic education and training of population.

It should be noted that practically all risk levels classifications contain the principal recommendations for persons making the risk management decisions.

The analysis of legislative and normative-methodical health risk assessment basis demonstrated the applicability for harmonizing the risk assessment methods and criteria used in the Russian Federation with the internationally recognized methodology.

The experience in harmonizing the risk assessment principles of Committee Codex Alimentarius and European Community countries allowed for offering the main principles for the health risk assessment in the countries of EurAsEC and Customs Union:

- scientific justification of methods and criteria for the risk assessment;
- development of available information sources for using the methods and criteria for the risk assessment;
- openness of the risk assessment;
- risk assessment by the independent experts;
- discussion by all member countries of the methods and criteria for the risk assessment.

The health risk assessment methods and criteria harmonization shall be based on harmonizing the legislative basis and terminology. As the main directions for harmonizing the legislative basis regulating the assessment of the risk of products for health, it is feasible to distinguish the harmonization of provisions on the risk assessment in the technical regulations with the same provisions of top level documents, documents of EU and international organizations. These provisions cover:

- risk assessment places during the design, production evaluation of compliance with safety criteria and implementation of control and supervisory measures;
- determination of the acceptable risk level or necessity to develop the methods for its level determination;
- responsibility of concerned parties for carrying out the risk assessment and if necessary - for the mitigation of risks to the acceptable level; informing about the unacceptable risks in case of objective impossibility of their prevention;

To harmonize the terminology in the health risk assessment field in general and to assess the risk of products for health in particular it is feasible to develop the glossary of terms and definitions in the Russian language with further translation into the official languages adopted for publishing the UN documents. When harmonizing the terminology it is feasible to use the experience in this field accumulated in the European Community countries.

The health risk assessment methods and criteria harmonization includes:

- use for performance of stages for the products hazard identification, assessment of dependences "exposure – effect (response)" of the relevant information contained in the internationally recognized sources and databases;
- application during the exposure assessment of adequate and internationally recognized methods for measurement and simulation of the hazard factors intensity;
- use during the characterization of risks of comparable risk classification scales, including the level of acceptable risk, taking into account the already proposed levels of negligible risk of serious diseases or death.

When harmonizing the acceptable health risk levels it is feasible to compare the already available values taking into account the severity of effects for which they are proposed. Taking into account that the acceptable risk levels depend on such factors as the social and economic situation, perception of risks by population and other it is necessary to consider the issue on the methods for justifying the acceptable levels of the risk of products for the health of population.

Within the risk classifications harmonization, it is feasible to provide the comparison of the health risk levels and ranges taking into account the severity of effects. When adopting the unified classification of risks it is necessary to standardize the management actions at each health risk level.

The harmonization of the product safety standards has a special meaning and also the methodological basis for their establishment with the application of the health risk criteria. Herewith it is feasible to use the experience of hygienic standardization and assessment of risk of influence of chemical, physical and biological factors accumulated in the Soviet Union and Russian Federation for justifying the product safety standards.

It is feasible to prepare the document establishing the harmonized forms for submission of results of the conducted studies of risks and their assessment for public discussion, expert evaluation, assessment of compliance, control and supervisory measures, and development of technical regulations.

An object of separate interest is the harmonization of hygienic regulations with regulations recognized in the developed countries based on the harmonized principles for establishing the referential exposure levels (time averaging, uncertainty factors, accounting of results of the health risk assessment and epidemiological studies). The solving of this task will provide the possibility to consider the increased health risk as the violation of sanitary legislation and will allow for transferring to the establishment of harm to health associated with negative influence on the living environment.

1.6. Conceptual setting of strategic health risk analysis tasks in the ensuring the social and economic development of the state

The setting of strategic health risk analysis tasks cannot be performed without the concept of long-term social and economic development of the Russian Federation developed in 2008 in accordance with instructions of the President of the Russian Federation [The Concept of Long-Term Social and Economic Development of the Russian Federation for the Period to 2020, 2008]. The content of this Concept determines the ways and methods for ensuring in the longer term to 2020 of stable increase in the wellbeing of the Russian citizens, national security, dynamic development of economy and strengthening of the positions of Russia in the global community.

The strategic directions of the long-term social and economic development are formulated in the Concept: They include:

- high human wellbeing standards;
- social wellbeing and consent;
- economy of leadership and innovations;
- balanced spatial development;
- economy able to meet competition at the global level;
- institutes of economic freedom and justice;
- safety of citizens and society.

It is feasible to structure the setting of health risk analysis strategic tasks in the field of ensuring the social and economic development of the state namely in relation to the specified directions.

The personal security standards play an essential role in ensuring the high human wellbeing standards. Safety in the Russian and international legislation is interpreted as the absence of unacceptable risk for life and health. The risk analysis methodology is one of the most effective tools for detecting the fields of activity where the probability of health disorders under the influence of the living environment factors is the highest and justification of decisions, which allows for minimizing of this probability. The cost of errors in this field is sufficiently high. The underestimation of risk and understatement of hazard can result in future in the substantial losses and the consequence of its overestimation will be the unjustified labor and financial expenses, which are extremely undesirable, especially during the period of insufficient economic stability. In this connection as the one of the main conceptual tasks of the risk analysis it is necessary to determine the health risk analysis methodology improvement aimed at increasing the accuracy of assessments and efficacy of actions on the risk minimization.

The provision of equal possibilities, including the human development, requires the creation of equal conditions, which include the equal degree of sanitary and epidemiological wellbeing both industrial and domestic. The equal degree of sanitary and epidemiological wellbeing means the for all citizens of the country it is necessary to provide the living environment conditions in which there is no harmful influence of the living environment factors on human and the favorable conditions for life activity are provided. The absence of unacceptable health risk in many countries is considered as the criterion of such condition.

The legislation of USA as well as the European countries includes the human life and health risk assessment aspects in the field of environment protection and safety of consumer products [TSCA, 1976; RACBA, 1995; US EPA, 1996*c*; 2008; FHSA, 2011; EC, 2002*b*; EC, 2006]. Currently the health risk assessment methodology is an integral part of the safety analysis and generally recognized tool for justification of making the managerial decisions in the field of the population life and health protection and consumer rights defense.

The sysem of sanitary and epidemiological standardization in the Soviet Union and later in the Russian Federation as the component of legislation historically was not aimed at the risk assessment methodology. In the modern stage of the risk theory development even at the sufficiently high degree of uncertainty this methodology becomes the basis for making the decisions in the field of finance, policy, and production management. However,

regardless of that for 2009–2012 the Russian Federation practically created the basis for the development of system of normative-legal and methodical documents in the field of health risk analysis until now the use of the health risk analysis methodology did not obtain the legislative fixation in full. Under these conditions the developments of areas for law enforcement of the health risk analysis methodology in the field of protection of consumer rights to the safety of goods and services for health and ensuring the sanitary and epidemiological wellbeing of population shall be considered as the strategis health risk analysis task in the field of ensuring the social and economic development.

The economy of leadership and innovations is considered as one of the directions of the long-term social and economic development. This sphere includes also the leadership in the field of knowledge. The health risk analysis can also contribute into the achievement of this goal. For the quite short compared to the developed countries period of development of the health risk analysis methodology in Russia even in the conditions of limited legislative support it was possible to accumulate the scientific experience, which allows for practical application of this methodology. The risk analysis development level is such that currently Russia can defend its positions at the global arena. For example, this concerns the preservation of hygienic standards for content of veterinary preparations in the food products justified under the health risk assessment criteria. In a number of the risk analysis directions the Russian scientists offer the effective approaches. This relates to such fields as the integral risk assessment, economic assessment of losses associated with the health risk. At the same time the study of these aspects is not finished. Due to the urgency and relevance of developments the improvement of the economic aspects of the health risk analysis and forecasting of measures aimed at reducing the losses associated with negative changes in the health of citizens can also be attributed to the strategic health risk analysis tasks.

The balanced spatial development of the state is also identified as one of goals of the long-term social and economic development. It is obvious that the formation of new regional growth centers both in the areas of development of new raw materials and during the formation of points of development of innovative technologies shall not be accompanied by an increased risk to health. This provision is difficult to implement without the broad application of the risk analysis methodology, which allows for using the already accumulated and developing approaches to forecasting and situational simulation of consequences of growth of industrial and agricultural potential across the state, the individual zones of economic growth and specific regions and territories. The existing methods for estimating the spatial distribution of risk allow on the basis of its comparative assessment to determine and predict the areas of the largest hazard for health and take into account the possibility of negative changes in the conditions of health at the population level, which can lead to the significant reduction of the labor potential in the areas of economic growth.

When building an economy which is competitive at global level it is necessary to provide also the creation of scientific base competitive at the global level, including the security of development and harmonious increasing of all types of resources, including labor. As a priority activity in accordance with this guideline it is feasible to consider the leadership in the integration processes in the Eurasian space, which implies also the leadership in relation to the fundamental and applied development on the health risk analysis. As part of the integration it is necessary to guarantee for all participants of this process the maximum level of sanitary-epidemiological security, which can be achieved only through a broad application of the human health risk analysis methodology. At this stage, a significant amount of methodological developments on the assessment and management of health risk determines the potential priority of the Russian Federation in the Eurasian region in this field and can be the basis for the mutual harmonized development of this methodology. The examples of such development are already available. Thus, a number of scientific institutions of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare and the Academy of Sciences of the Russian Federation at the active cooperation with scientific organizations of the Republic of Belarus and the Republic of Kazakhstan proposed the methodology for assessing the risks to the health of population when exposed to the chemical, physical and biological factors to determine the parameters

for the safety of products (goods), which is considered as the basic for the common economic space.

Within the priority of economic freedom and justice the policy of the state will be focused on expanding the entrepreneurship freedom, ensuring the effectiveness of the public administration system, maintaining the social justice. Under these conditions the task of the health risk analysis methodology development is the justification of optimal state control measures, including under the performance criteria. In the field of consumer rights protection and human wellbeing the state control measures includes primarily the control and supervisory measures. "The concept for increasing the efficacy of control and supervisory activity of the state authorities and local self-governing bodies for 2014–2018" (draft) provides the development of system for assessment of risks of potential danger of the types of economic activities and the procedures for its use in planning the control measures. The methodical approaches to the assessment of risks of the potential danger providing the analysis of probability of violations of sanitary legislation, severity and possible distribution of negative changes in the health status of different population groups associated with these disorders are proposed. The results of the implementation of such approaches shall be used when creating a classification of the types of economic activities and individual supervision objects, which, in accordance with the health risk level will determine the frequency and intensity of control and supervisory measures. This shall lead to the reduction of excessive control over the objects of small danger and to the increase of focus on the objects the activities of which contribute to the high health risk levels.

Modernization of methods for forecasting the threats and ensuring the economic development of the areas of the economy and territories of the Russian Federation as the strategic benchmark of the long-term social and economic development can be implemented at the national level within the targeted programs. An example of such implementation is the Federal Target Program "National System of Chemical and Biological Safety of the Russian Federation" – interconnected system of program activities on minimizing the chemical and biological risks. In some cases, attempts to solve the problems related to ensuring the chemical and biological safety without the use of the program-target method could lead to the increase in the negative influence of hazardous chemical substances and biological agents on the population. The lack or untimely addressing the issues in the field of chemical and biological safety can damage the observance of the internal interests of the country, including the economic ones. The purpose of this program is to develop a national system of chemical and biological safety consistently providing a decrease to the acceptable level of risk of influence of hazardous factors on the population. To achieve the goal a number of tasks that have direct relevance to the health risk analysis methodology are solved. First of all, they include the detection, forecasting, providing of criteria and ranking of external and internal risks of objects to the health of population in the country. A number of measures is provided within the direction of activity on solving of this task, including:

- a comprehensive analysis of the situation, identification and assessment of new chemical and biological threats and hazards;
- scientific, information-analytical, criterial and methodical support of the risks assessment for the population, ecological systems and the technosphere generated by the sources of chemical and biological hazard;
- scientific and methodological support for the assessment of harm, damage and insurance of risks associated with the activities of objects – sources of chemical and biological hazard;
- methodological support of state supervision, inspection, verification and monitoring of hazardous chemical and biological factors at the objects of the ambient and production environment;
- scientific and methodological justification of the response measures at all levels of governance and cooperation in the field of ensuring the chemical and biological safety on the basis of situational and simulation modeling of parameters of chemical and biological safety in terms of legislative, structural and functional and other changes in the Russian Federation;

- development and harmonization with international standards of hygienic regulations for content of chemical and biological agents in the objects of living environment and biological environments of human, including under the risk criteria.

The development and harmonization of hygienic regulations are aimed at the protection of the rights of citizens of the Russian Federation for health under the economy globalization conditions. To date, there are the examples of successful use of domestic developments in the field of health risk analysis methodology for promoting the interests of the state at the international level. Thus, the justification of hygienic regulations under the risk criteria prevented the threats for the health of citizens of Russia associated with attempts to impose the use of food products containing the residues of veterinary preparations (antibiotics of tetracycline group, ractopamine), which cause the unacceptable risk of diseases of the gastrointestinal tract, cardiovascular system and other both for the whole population and for the most sensitive subpopulations. Justification of acceptable levels for content in the foods products of *L. monocytogenes* allowed for preventing the unacceptable risk of such disease as listeriosis.

Ensuring a high level of security of the state is a necessary prerequisite for the transition to the innovative socially-oriented type of economic development. Such transition is impossible without the implementation of the priority directions of the country development, which include the preservation and strengthening of the health of population, increase in the role of disease prevention and promotion of healthy lifestyles.

The preservation of the health of population and strengthening the diseases prevention require the conduction of applied scientific and epidemiological studies to justify the improvement of the legislation of the Russian Federation and methodological framework, including the health risk analysis and the introduction of modern medical-preventive technologies to prevent this risk.

The healthy lifestyle formation shall be the most important area of policy in the field of health protection. In this case, the basis for promoting a healthy lifestyle, along with informing about the health risk associated with low physical activity, irrational and unbalanced nutrition, consumption of alcohol, tobacco, drugs and toxic substances shall be the training in skills to minimize these risks by means of the efforts of the population. This is possible only at the upgrading of this component of risk analysis as the health risk communication.

Therefore, the strategic health risk analysis tasks in the ensuring the social and economic development of the state are as follows:

- improving the health risk analysis methodology aimed at increasing the accuracy of assessments and efficacy of actions on the risk minimization;
- development of the law enforcement fields for the health risk analysis methodology to protect the rights of consumers to the safety of goods and services for health and ensure the sanitary and epidemiological welfare of the population;
- improving the economic aspects of the health risk analysis and forecasting the measures aimed at reducing the losses associated with negative changes in the health of citizens;
- ensuring the balanced development of economic and labor potential of the state;
- modernization of methods for forecasting the threats and ensuring the safety of economic development of the areas of economy and territories of the Russian Federation;
- protection of the rights of citizens of the Russian Federation for health under the economy globalization conditions.

This list of tasks is not exhaustive. The possibilities of risk analysis allow for formulating the wide range of tasks the fulfillment of which without security based on this methodological platform will be difficult.

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2. METHODOLOGICAL ASPECTS OF RISK ANALYSIS AND ITS EVOLUTION UNDER THE INFLUENCE OF VARIOUS FACTORS OF LIVING ENVIRONMENT, LIVING CONDITIONS AND STYLE ON HEALTH

2.1. Systemic approach to health risk analysis

The formation of the optimal economic system in the state requires systemic researches – is one of the most modern and new research directions. At the present time, they are represented by the systemic approach, general or abstract systems theory and systemic analysis. Results obtained by these components are applicable to the whole complexes of scientific and technical disciplines [Gvishiani D.M., 1979]. A systemic approach, which has methodological nature and general scientific interdisciplinary nature, is main among these components [Brekhovskikh S.M., 1986].

There are several similar definitions – "systemic analysis", "systemic approach", etc. Some of them are discussed below.

Systemic analysis is a set of methods of scientific knowledge, which is a sequence of actions to establish the structural relationships between variables or elements of the system under study. It is based on a set of general scientific, experimental, natural methods. N.N. Moiseev (1989) presents a narrow definition of systemic analysis: "Systemic analysis is a set of methods based on computer use and study-oriented complex systems – technical, economic, environmental, etc. The result of systemic studies is the choice of a well-defined alternatives, as a rule: region development plan, design parameters, and so on".

Systemic approach is a methodological direction of research, which is based on the consideration of the object as a complete set of elements in a set of relationships and connections between them, that is the consideration of the object as a system. Concerning a systemic approach, we can talk about some method of organization of actions that covers any kind of activity, identifying regularities and relationships to achieve more efficient use [Matorin S.I., Zimovets O.A., 2012].

Generalizing theoretical concept in the consideration of health in recent decades has become a systemic approach as a natural stage in the development of biological sciences. Modern systemic approach allows considering the hierarchical structure of biosocial essence of man and outline a methodological strategy in the development of the concept of health as a state of a biological system – the body, which is also a component of the social system – a society.

Theoretical aspects of health risk analysis suppose consideration of risk analysis as a conceptual methodology of management of such socio-economic system, such as human health under the conditions of the living environment.

Characteristic features of the development of socio-economic systems are:

- integration of scientific knowledge, growth of number of interdisciplinary issues;
- the complexity of the problems and the need to study them in the unity of technical, economic, social, psychological, and other aspects of management;
- complexity of problems and objects to be solved;
- increase in the number of connections between objects;

- dynamism of changing situations;
- deficiency of resources;
- increase of the level of standardization and automation of production and management processes components;
- globalization of competition, production, cooperation, standardization, etc.;
- strengthening the role of the human factor in the management, etc.

These listed features cause the inevitability of application of systemic approach, because, in our opinion, only this basis can ensure the quality of management decisions.

The systemic approach is a direction of methodology of scientific cognition, which is based on the consideration of the object as a system: an integral complex of interrelated elements [Blauberg I.V. et al., 1970, 1978; Sadovsky V.N., 1980].

The systemic approach supposes a comprehensive study of the phenomenon or process as an integrated whole from the perspectives of systemic analysis, i.e. clarification of complex issues and their structuring in a series of issues to be solved with the help of mathematical methods, finding the criteria for their solving, detailing the objectives, designing effective organization to achieve the goals. The systemic approach means not a separate analysis, but in the system one**,** i.e. certain coupling of elements of this system.

The systemic analysis includes an analysis and description of principles of design and operation of the system as a whole, analysis of features of all system components, their interrelationships and internal structure, transfer of certain properties of the model on the properties of the system under study according to certain rules.

The main principles of the systemic approach:

- integrity, which allows considering both the system as a whole and at the same time as a subsystem for higher levels;
- hierarchy principle of structure, i.e. the presence of multiple (at least two) elements disposed on the basis of the submission of lower level elements to higher level elements. The implementation of this principle is well illustrated by any particular organization. As is known, any organization is the interaction of two subsystems: controlling and controlled one. One is governed by the other;
- structuring, allowing analyzing the elements of the system and their relationships within a particular organizational structure. Typically, the process of the system operation is not due to the properties of its individual elements but the properties of the structure;
- multiplicity, which allows using a lot of cybernetic, economic and mathematical models to describe the individual elements and the system as a whole;
- systemacity is object property to have all the characteristics of the system.

The systemic approach is an approach in which any system (object) is considered as a set of interrelated elements (components) having an output (target), an input (resources), communication with the external environment, feedback. It is the most complex approach. Its essence is the implementation of the requirements of general systems theory, according to which every object in the course of its research should be considered as a large and complex system, and at the same time as an element of a total system. A detailed definition of the systemic approach also includes a compulsory study and practical application of the following eight aspects:

- system-element or system-complex, which consists of an identification of elements that make up this system. In all social systems, it is possible to found real components (means of production and articles of consumption), processes (economic, social, political, spiritual, etc.) and ideas, scientific and conscious interests of people and their communities;
- system-structural, which consists of an identification of internal relationships and - relationships between the elements of this system and provides a picture of the internal organization (structure) of the system being studied;
- system-functional, which is intended to identify functions the performance of which it has been created and for which there exist appropriate systems;
- system-target, meaning the need for a scientific definition of goals and sub-goals of the system, their mutual coordination among themselves;

♦ system-resource, which consist of the careful identification of the resources required for the functioning of the system, for solving of one or another problem by the system;

♦ system-integration, which consists of the determination of the set of qualitative properties of the system, which ensure its integrity and feature;

♦ system-communication, which means the need to identify external relations of this system with others, that is, its relations with the environment;

♦ system-historical, allowing determining the conditions in the time of occurrence of the system under study, passed steps, current state and possible future developments.

The most important tasks of the systemic approach are: 1) development of means of presentation of the objects under study as systems; 2) development of generalized models of the system, models of different classes and specific properties of the systems; 3) study of the structure of systems theory and various system concepts and developments.

In the systemic study, the object being analyzed is considered as a specific set of elements, the relationship of which makes holistic properties of this set. The main emphasis is on identification of the variety of connections and relationships that occur inside the object, as well as in its relations with the external environment. The properties of the object as a whole system are determined not only by summing the properties of its individual elements as properties of its structure, specific systemically important, integrative bonds of the object under study. The essential value of the systemic approach is given to the determination of the probabilistic nature of the behavior of the objects under study. An important feature of the systemic approach is that not only the object, but also the process of study acts as a complex system, a task of which, in particular, consists in combination of different models of the object [Prokhorov B.B., 2005].

A systemic approach to risk analysis is based on the block diagram of health risk analysis area (Fig. 2.1), which determines the major subsystems, their elements and inter-system connections. The role of risk analysis as a methodology describing and characterizing the relationship between the individual subsystems and their elements, consists in modeling of the system state at changing of the state of one or more of its elements.

In the context of the health risks analysis as a major subsystems (blocks), it is advisable to allocate living environment, human health, population health, subsystem of economic parameters and management. In its turn, each subsystem includes a number of elements. It should be noted that the allocation of the individual subsystems and elements is rather conditional and is not regarded as an exhaustive description of the system. In the frameworks of the health risk analysis, intra-system communications between the individual elements and subsystems are identified, parameterized, on the basis of which the solutions optimizing the state of the system as a whole are validated.

Inter-system communications are presented as links between subsystems (interblock communications), as well as between the individual elements of these subsystems (intra-bloc communications).

Human health depending on the level of contamination of the living environment can serve as examples of interblock connections. In these examples, the interblock connections can be characterized by health risk values: individual risk for the living environment connection with the health of the individual and population – with the health values of entire contingents. If dependence models constructed mainly using data obtained in toxicological experiments is used for identification and parameterization of the first models, models based on the results of epidemiological studies are more appropriate for assessments of connections at the population level.

Parameters of population health can significantly affect the economic parameters of the country's development. Losses of the period of labor activity due to additional morbidity, disablement and premature mortality of the population associated with impact of living environment risk factors, lead to a decrease in the volume of goods and services produced and, ultimately, to a reduction in the total budget of the country. It should be noted that the reduction and changing of consumption structure due to additional morbidity and premature mortality, might also adversely affect the pace of economic development. Mathematical

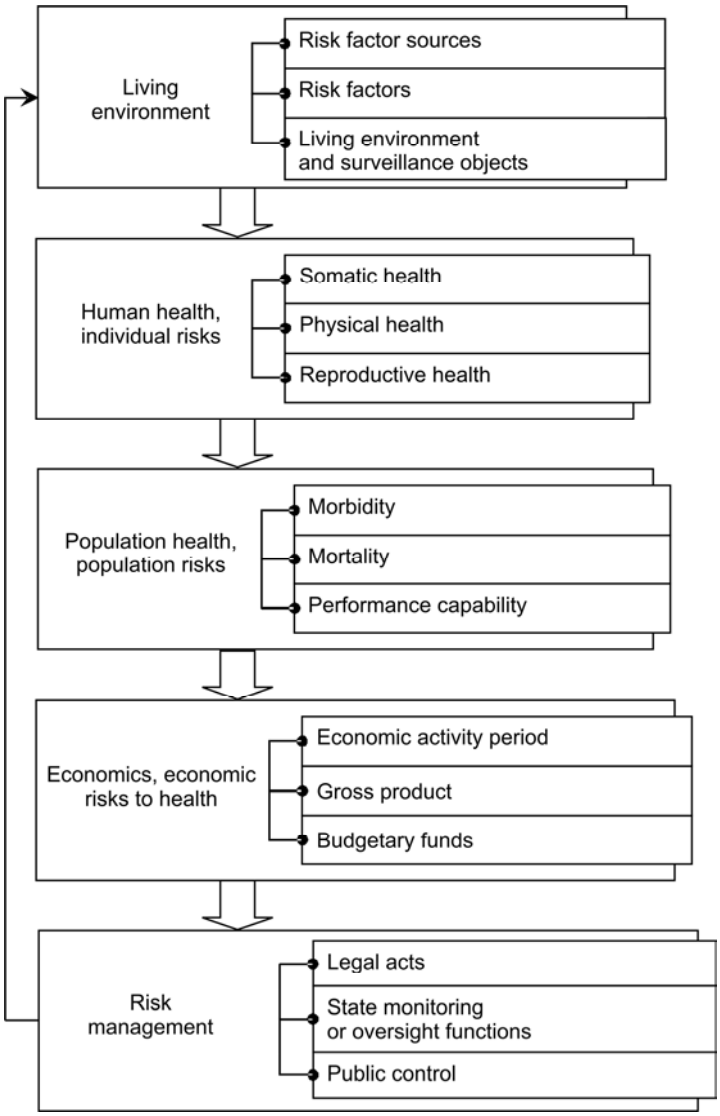


Fig. 2.1. The schematic block diagram of health risk analysis

description of this kind of connections in respect of the working population is now reflected in a number of regulatory documents [The methodology for economic losses calculation, 2012]. In the strategic perspective changes of human health, which determine negative population trends, reduce the employment potential of the state, component of which is population health.

In its turn, macroeconomic parameters may influence the management system. For example, optimization of state control and supervision functions in the case of reduction of the intensity of supervision will require significant economic investments in material resources and training of highly skilled professionals to ensure safety of life and health of citizens. Only in this case, reduction of the number of supervisory actions may be compensated by an increase in their efficiency.

The area of health risk analysis presented in the form of a system, in addition to the hierarchy, is characterized by the presence of feedback, i.e. final subsystems may affect subsystems of other levels. Therefore, it is obvious that health risk management system must be associated with the quality of the living environment. Improvement and enhancement of efficiency of the management should improve the quality of the media or stabilize it at an acceptable level. This, in its turn, will affect all of the following subsystems.

To optimize the management of such systems, it is extremely important to determine the critical points of management, the impact of which may lead to maximum effect. The concept of HACCP – Hazard Analysis and Critical Control Points is based on similar principles. It provides for the systematic identification, assessment and management of hazards that significantly affect the safety of the product [GOST R 51705.1-2001] To establish the critical points of risk management it is reasonable to allocate individual elements of subsystems. The elements of individual subsystems (blocks) are also interconnected, and intra-block connections for management tasks require identification and parameterization for each subsystem.

The most obvious examples of such connections in the "living environment" subsystem can be obtained by mathematical simulation of hazards propagation from sources. We obtain exposure levels at individual points or their fields foreseeable at given parameters of the source as a result of application of these models. The simulation results of such connections are often used in health risk assessment at the stage of chemical and physical factors exposure assessment.

When considering the subsystems "human health" and "population health", it is necessary to refer to the definition of "health". According to WHO Constitution, "health is a state of complete physical, mental, and social welfare in addition to the absence of disease or physical handicaps" [WHO Constitution (Charter),1946]. According to WHO, medical and sanitary statistics determines health at the individual level as the absence of identified disorders and diseases, and at the population level – the process of reduction of mortality, morbidity, and disability.

P.I. Kalju (1988) reviewed 79 definitions of health, formulated in different countries at different times, and by representatives of various scientific disciplines, and suggested that all possible health characteristics can be narrowed down to the following concepts:

- medical model – for definitions containing medical signs and characteristics; health as the absence of diseases and their symptoms;
- biomedical model is an absence of subjective feelings of ill health and organic disorders;
- biosocial model – includes medical and social features considered in the unity. At that the priority is given to social factors;
- value-social model – health as a value of a human; the WHO definition refers to this model.

According to the definition of the WHO it is reasonable to consider the following aspects with the allocation of corresponding elements in the "human health" subsystem: somatic, mental and reproductive.

At the same time, because health is considered as a normal function of the body at all levels of its organization, the normal course of the biological processes that contribute to individual survival and reproduction, it can be presented for simulation of internal connections as a multifunctional system, which in its turn includes a number of sub-systems responsible for a set of their functions.

Hierarchy is one of the main characteristics of the structure of the organization of self-regulatory mechanisms of biological systems. Hierarchy dynamically combines the principle of autonomy with the principles of subordination and centralized subordination [Bechtereva N.P., 1975]. Functional system is a classic example of hierarchically built mechanism with several levels (Fig. 2.2).

One of the purposes of a systemic approach to biology, medicine, and hygiene is to disclose the nature and mechanism of functional and structural integrity of hierarchical management systems.

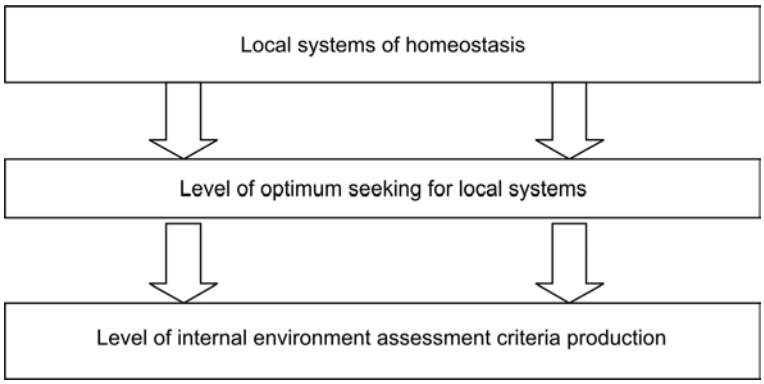


Fig. 2.2. Functional system as classical example
of hierarchically built multilevel mechanism
[Braynes S.N., Svechinskaya V.B., 1965]

The functional internal environment is composed of a set of physiology theories. These theories restrict the possible dynamics of the relationships between the elements of the body by some rules that do not allow those elements to be developed to damage the whole organism. Disorder of the functional environment causes disease. Elements of the system in this example are the cells of various organs and tissues of the body. System Components - various organs, composed of cells, which are based on the so-called specialized cells that ensure the functioning of these organs. The structure of the considered system - the body - is composed of a set of connections between organs and tissues. These connections are made in the functioning of respiratory, circulatory, nervous, excretory, and other body systems [Khomyakov P.M., 2008]. Such conceptual formulation allowed formulating provisions that formed the basis of health risk assessment based on the simulation of its evolution.

The assessment of the relationship in the "population health" subsystem has a number of features. In the first instance the statistical indicators characterizing the basic elements of population health, particularly morbidity and disability of the population, sufficiently depend not only on internal processes, but also on confounding factors. For example, morbidity rates (in fact, it is indicators of medical aid appealability) may depend on the availability of medical services, and disability rates – on the existing regulatory framework. Furthermore, the existing practice of morbidity and disability registering often does not provide information that fully reflects the relationship between these rates. Intensive morbidity and mortality rates reflect the frequency of the occurrences studied in the population, but do not allow correlating the occurrences between them [Gulitskaya N.I., Glinskaya T.N., 2007]. At the same time, the probability that the disease can cause death, is taken into account in the risk analysis at the assessment of the severity of health problems, which are seen as responses to the negative impact of living environment factors.

Response severity, except for immediate component of health risk assessment, is prominent in the validation of risk management measures, especially at the analysis of economic aspects. That particular indicator largely determines the reduction of the economically active period of the citizens' life that, in addition to direct costs, results in substantial losses. Costs and losses incurred by the society in this case include loss of profits, for example, in the form of underproduction of gross domestic product (GDP) due to premature mortality or full loss of ability to work [Revich B.A., Sidorenko V.N., 2007]. GDP reduction in its turn entails a reduction of the tax base and reduction of budgets and extra-budgetary funds saturation (Fig. 2.3). A distinctive feature of internal connections in this subsystem is that they are largely determined by the current legislation.

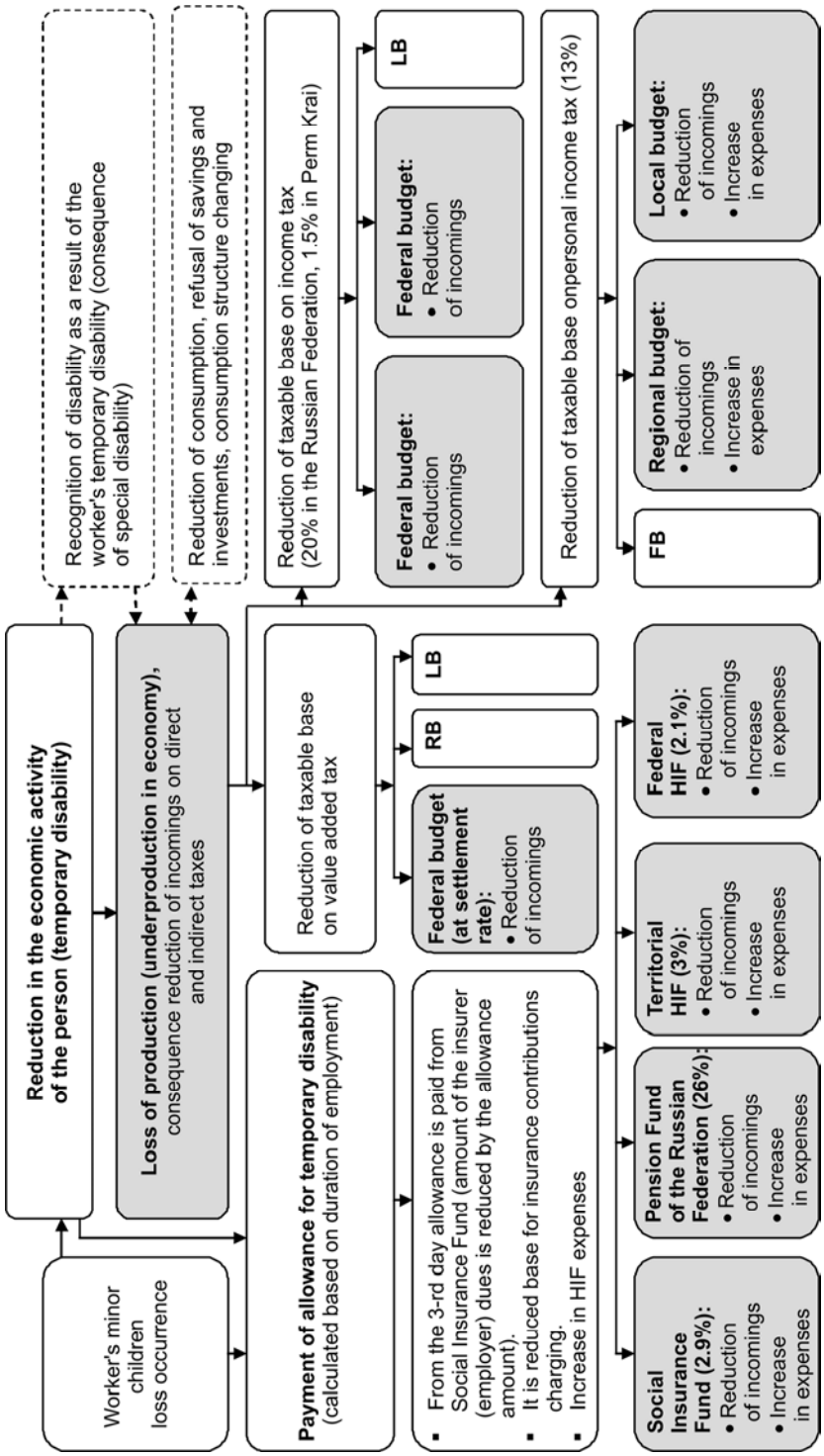


Fig. 2.3. Conceptual model of cost estimate of Reduction in the economic activity period associated with health risk as an element of systemic analysis

Intra-block connections in subsystem "management" could be vary by nature: from hierarchically-subordinated ones, for example, control and surveillance activities is determined by current legislative acts, to parallel connections - state and public control. In its turn, the intensity of control and supervisory activities at individual objects may vary based on the results of risk assessment [control and supervisory activities in the Russian Federation, 2014]. At that, management results can determine inverse intra-block connections. Thus, the results of social control can be the basis for adoption of legal regulations.

The models resulting from parameterization of interblock and intra-block connections could be used to optimize both the individual subsystems and the overall system. In the case of a systemic approach to the individual subsystems, models to solve a specific problem are developed. Thus, a system of algorithms to validate decision making in the system of Russian Federal Consumer Rights Protection and Human Health Control Service (Rospotrebnadzor) is formed.

The basic principles of the formation of the system of algorithms to validate decision making in the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance system are:

- use and development of the existing information base of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance, including the system of social-hygienic monitoring;
- implementation of cascade management model based on the nature and quantitative estimation of the relationship between the objects of management;
- application of indicators of immediate and eventual outcome of the authorities and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance;
- identification of quantitative parameters of health risks manageability in the system of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance;
- identification of priorities in surveillance activities based on risk criteria for public health;
- optimization of management decisions based on the criteria of minimal sufficiency of costs of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance authorities and organizations and the application of adequate sanitary and epidemiological situation of risk management methods.

Sequential cascade models are the most appropriate to describe such processes. The implementation of the principal scheme of the cascade model, shown in Fig. 2.4, is carried out by means of the algorithm, which involves the generation of the system of cascade elements that reflect the relationships between the elements. The establishment of quantitative parameters of the functional dependence of subordinate links from the higher ones characterizes the degree of subordinate links manageability.

Financing, logistics of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance authorities and organizations shall be defined within the framework of formation of the state task to perform public services (works) in accordance with the Regulation on the formation of the state task for federal and state budgetary institutions and the financial support of the state task performance, approved by the Government of the Russian Federation No.671 dated 02.09.2010 "On the order of formation of the state task in relation to the federal budget and state institutions and the financial support of the state task performance."

Management actions of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance authorities and organizations include activities of state control (supervision), and consumer protection, the establishment of conformity (non-conformity) of project and other documents, objects of economic and other activities, products, works and services provided by law, the requirements of technical regulations, government sanitary-epidemiological rules and norms of industrial, public facilities, buildings, equipment, vehicles, manufacturing equipment, processes, jobs in order to ensure state control (supervision) and consumer protection, for the establishment of the harmful effects of environment factors on human, determining the extent of this influence and prediction of

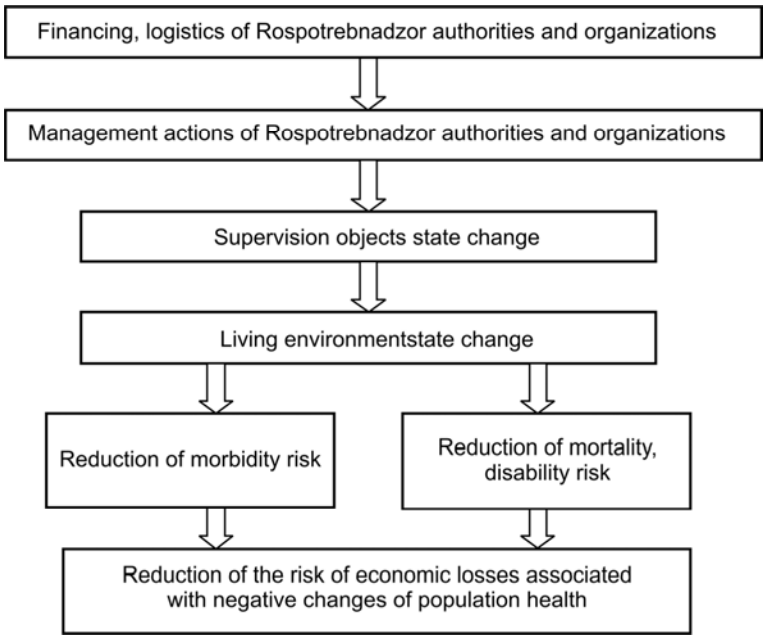


Fig. 2.4 Principal scheme of application of a systemic approach to health risk management (serial cascade model)

sanitary and epidemiological situation in order to ensure state control (supervision) and consumer protection, conduction of sanitary and epidemiological investigations aimed at establishing the causes and identification of conditions of incidence and distribution of infectious diseases, professional and mass noninfectious diseases (poisoning) of people associated with adverse living environment factors.

This activity should result in a change in the unfavorable condition of the objects of supervision (sources of risk factors) or stabilization of their condition to those relevant to applicable laws and guidelines. In its turn, the human living environment, which is recorded as a percentage of non-standard samples of living environment objects, should be improved as a result of improving of the supervision objects condition. These indicators are considered as indicators of direct result of the activities of authorities and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance.

It is reasonable to consider a reduction or stabilization of the individual risk to public health as indicative of final results of the authorities and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance. In the field of infectious diseases, where the cause-and-effect relationships of indicative of immediate and eventual outcome set, morbidity rates as indicatives of eventual outcome are used to the fullest.

Cascade management (implementation of such management is shown in Fig. 2.5) is the management of chain of sequential links. Two sequential links have a connection which can be described by a model with equation $A(t)\ F(x(t)) = y(t)$, where t – variable (e.g., time); $A(t)$ – dynamic coefficient matrix (matrix of mn dimension, characterizing the conditions of management); $F(x(t))$ – a function (a column vector of dimension n) from the controlling factors vector $x(t)$; $y(t)$ – output (response) which is a column vector with m elements. Moreover, the same model can describe the lower-level link management by any higher link. For example, you can consider management "actions of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance – mortality risk" or management "characteristics of objects of supervision – morbidity risk".

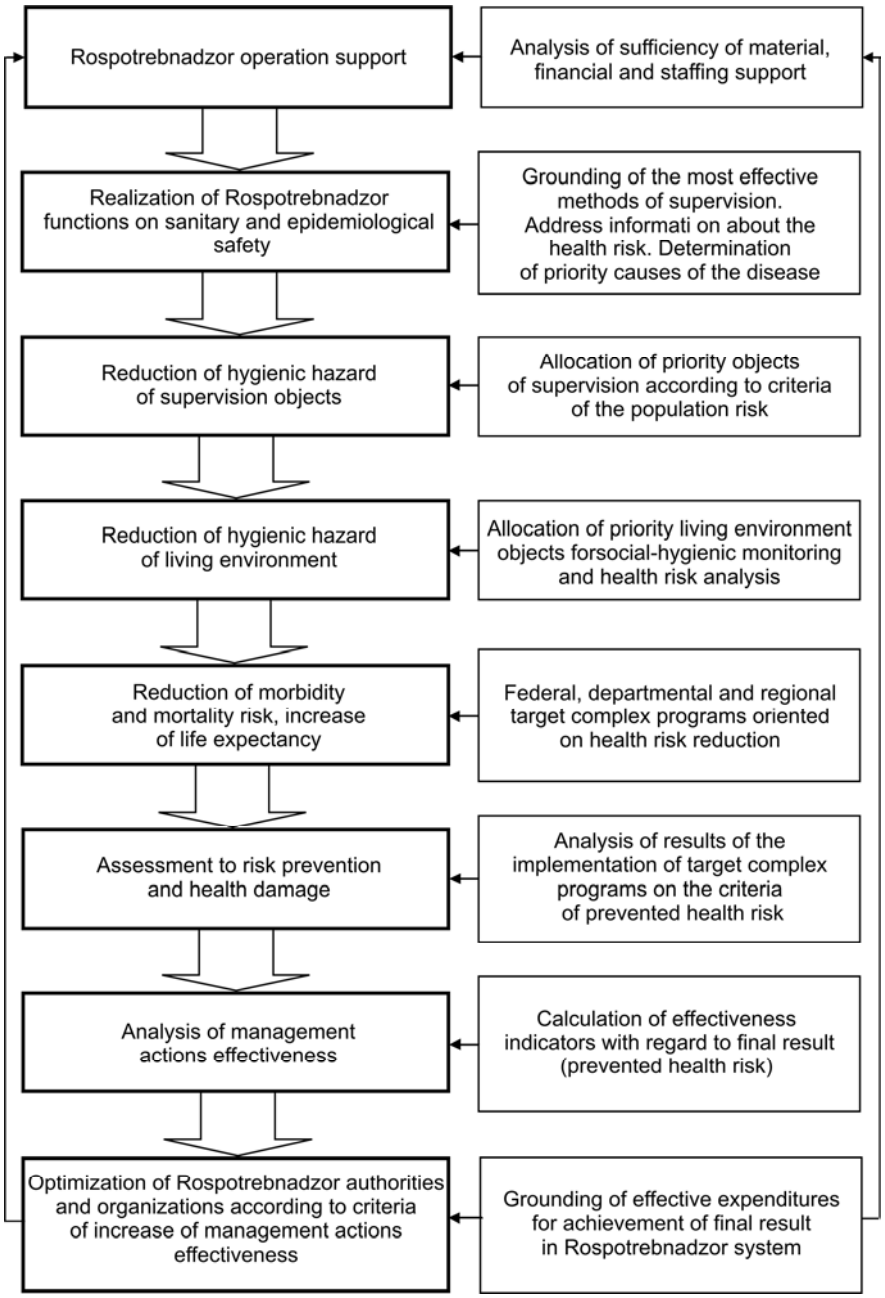


Fig. 2.5. Scheme of cascade risk management implementation

An important task is to select the function *F* (*x* (*t*)) from a parametric set of functions, which in the "best" way describes the dependence of *y* (*t*) from *x* (*t*) according to *N* observations of the vector *x (t).* Choosing the function *F(x (t))*, we actually determine the dynamic coefficient matrix A (t) according to *N* observations. Number of *N* observations, by which a matrix *A(t)* is made, may be equal to *(n + 1), (n + 2)*, etc. The model can be

constructed by a non-linear multivariate regression analysis or neural chain which has a set of matrices of dynamic factors (the number of matrices and their dimension is determined by the number of hidden layers of the neural network and the number of neurons in each level) [Yasnitsky L.N. et al., 2010; Zaitseva N.V. et al., 2011b; Yasnitsky L.N. et al., 2011].

Identification of functional relationships between the indicative figures of one link and different links can be produced using the method of matrix nonlinear prediction, which, along with new aspects and approaches (matrix stability, nonlinear functional correlation, etc.) uses the best aspects common to neural networks and traditional multivariate regression analysis [Zaitseva N.V. et al., 2010].

It is formulated the criteria of comparison of multivariate regression models of "controlling factors – responses" based on the information distance between the matrices of dynamic factors. This criteria allows selecting the most appropriate multi-factorial model of public health risk management [Gusev A.L., Khrushcheva E.V., 2010*a*, 2010*b*].

To conduct scheduled and unscheduled supervisory measures, the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance organizations need to solve the problem of determination of areas and facilities where it is the most reasonable to carry out supervisory activities. Such problems can be solved by applying the mathematical apparatus developed for continuous statistical monitoring of objects. Moreover, given the features of the collection of baseline data and factors management in the system of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance, it is proposed to perform continuous statistical control of facilities according to non-traditional scheme (after control termination it shall be resumed from scratch at classic plans of continuous control). In particular, it is reasonable to use a new type of continuous control – control with a memory in which the last control result is stored after control termination [Gusev A.L., 2010; 2013*a*; 2013*b*].

In general, the application of a systemic approach in the analysis of health risks is adequate and at the application of modern methodological approaches to the parametrization of intra-relations allows us to solve problems of situation and evolutionary simulation at the assessment and management of health risk.

2.2. Methodological bases for assessment of risk and its evolution at various factors impact on health

Risk assessment as a method of prediction of the state of the individual and population health has been developed from the theory of insurance, describing the regularities and methods of calculation of potential losses in the event of diseases, death or other adverse conditions of the human body. Modern methods of health risk assessment are based on the representation of the health of the individual and the population as a dynamic process, which describes a continuous course of negative (and positive) changes in the condition of the body from some initial level. At the mathematical description of this process, the term "evolution", which determines changes in health status as long-term and subtle is used when considering a particular point of time.

The evolution of health risk is a new idea in the systemic description of the regularities of formation of health problems not only due to natural causes, but also under the influence of various chemical, physical, biological, social, environmental factors and lifestyle.

Presentation of health in the form of the evolutionary process requires improvement of approaches to the simulation of relationships in the "living environment – health" system, taking into account not only the magnitude of the effective factors, but also the duration of exposure.

Conceptual bases of risk prediction using evolutionary models

The human body constantly interacts with living environment during the vital activity, receiving the necessary material from it and exposing to the harmful effects associated with chemical, physical, biological, and other factors. Over the years, the negative impact on human health increases with rise of emissions of industrial production and transport, noise pollution increase, introduction of new types of products, etc. The impact of socio-economic factors is also important, in particular, the character of distribution existing in the modern world is coupled with ever-increasing rise in the intensity of labor of large part of the population that has an impact on the mental state of a person, and through it – on health. It is well known that the health deterioration leads to economic losses due to premature mortality, disability, and morbidity with temporary disability.

Health status can be assessed using techniques of medical clinical laboratories and functional studies that provide the necessary information to solve a wide range of problems: from the clinical decision making to conduction of special examinations. Considered methods are well developed and allow conducting comprehensive examination of the human body, detecting functional disorders of organs and systems. At the same time, despite the rapid development of methods of laboratory diagnosis, many examinations are very time-consuming, costly, lengthy in time, have limited capacities both for the forecast of the expected adverse effects at exposure of diverse living environment factors and the effectiveness of risk management systems.

One of the most promising approaches to the prediction and assessment of the contributions by living environment risk factors to health disorder and establishment of cause-and-effect relationships is the use of mathematical simulation. Development of mathematical models is based on systemic analysis of consistency of internal and external functional relationships of organs and systems with living environment factors.

Thousands of factors affect human body. The air in a large industrial city alone contains about 400 different hazardous substances in various combinations. The carrying out of experiments, even with two dozen of substances requires considerable material costs. One of the major advantages of the mathematical simulation method is saving of time and resources. In addition, using mathematical simulation, you can change or completely exclude any influences, investigate the influence of individual factors, or various combinations thereof. In numerical experiments, it is possible to realize exposures, threatening to human life and health, that is unacceptable for field experiments conduction. The application of mathematical models can not only evaluate and compare disorders of human organs and systems, but also predict the development of their functional state under the influence of various living environment factors.

The basic and applied researches carried out under the leadership of N.F. Izmerov (1993–2012) highlights the importance and actuality of developments related to the creation of a coherent and clear system not only of assessment, but also prediction of health status of workers who are under the action of complex of heterogeneous and time-varying factors [National Guidelines 2011].

The diversity of theoretical approaches to the mathematical description of health disorders as events associated with the accumulation of deleterious effects of living environment factors, confronts the researchers with the choice of adequate approach to simulation, based on the principles of evidence based medicine. One of the main directions of studies which actively use simulation techniques related to risk management of occupational diseases is presented in the publications by E.I. Denisov, P.V. Chesalin, P.V. Stepanyan et al. [Izmerov N.F. et al., 2011; Denisov E.I. et al., 2011].

The development of a methodology to assess the health risks associated with exposure to living environment hazards, poses a number of problems the solution of which involves the application of the latest scientific and methodological approaches combining related field of knowledge such as medicine, biology, physics, mathematics. The present level of scientific researches in assessment of the impact of complex of chemical, physical,

biological and other factors on human health has identified promising approaches based on methods of mathematical simulation of evolutionary processes of accumulation of disorders of the body organs and systems [Zaitseva N.V. et al., 2011*c*].

The assigned tasks involve improving not only the quantitative risk assessment methods, but also the development of predictive models of health problems for assessment tasks and occupational hazard management.

The existing methods of risk assessment are focused on the implementation of direct analysis of changes of the probability of events that characterize health problems, due to the exposure of living environment factors. The mathematical models used for risk assessment, in most cases reflect the impact of exposure of factors (concentrations or doses) on frequency or probability of adverse health events in the form of individual diseases or death. It is considered that the dose enters in vivo instantaneously and acts for a long time. Such a hypothesis could be used when considering the permanent factor levels during a short time in relation to the human life. At the same time, it is sufficient to change the characteristics of factors intensity to compensate the harmful effects.

At the same time, the health risk assessment as a method of hygienic assessment is in demand at a variety of situations: in a short-term, but intensive exposures or exposure conditions, the effects of which become apparent in long term. Some types of ambient medium factors form a continuous long-term exposures, acting throughout a life. Furthermore, periodic exposures can lead to health problems, delayed in time. Additionally, the influence of the same exposures in different age groups can vary significantly. Significant time-varying exposures of factors, delay of negative effects lead to the need to develop a model for risk calculation based on the description of natural body functions involution and the one caused by exposure factors.

Another aspect that has not been adequately taken into consideration up to the present moment in a part of health risk assessment is the possible existence of a whole range of diverse factors that could cause adverse effects. The combined exposure of many diverse factors distributed over time requires the solution of multivariate problem of health risk assessment.

The statement of such a problem requires the use of the results of theoretical studies related to the description of the mechanisms of damage accumulation in vivo. The active development of theories in this area has led to the formation of two main approaches, which explain the process of loss of body functions over time: evolutionary theories and theories based on accident cell damages.

A hypothesis, which explains the loss of functions as a result of the process of evolution was proposed by the German scientist A. Weismann in 1891 [Weismann A., 1982]. The proponents of evolutionary theory conceive that the involution of function is a programmed process. The foundations of the theory are based on accident cell damages were established by P. Medawar [Medawar P.B., 1952]. In 1952, he proposed a theory of accumulation of mutations, considering the dysfunction as by-product of natural selection. Dysfunction theories suggest that the accumulation of dysfunctions is the result of a natural process of accumulation of dysfunctions with the course of time against which the body is trying to fight. The differences between these processes in different bodies are the result of varying efficacy of this fight. Currently, the latter approach is considered more reasonable.

Scientific works in the field of simulation of processes of accumulation of negative effects in vivo have existed since the formation of medicine as a science and application of mathematics as a tool for cognition. Works by Hippocrates and Aristotle devoted to the description of the phenomenon of aging due to loss of "natural heat" are well known in historical scientific instruments Recent researches in this field have been developed together with the advent of biophysics, biomechanics, mathematical biology as separate scientific fields.

In the late 1990s – early 2000s the works on simulation of the processes of human health changes in time had contradictions between the old principles of creation of conceptual gerontology models, reduced to absolutization of individual observed phenomena, and a number of purely mathematical approaches that were not interesting and did not take

acknowledgment among biologists [Krutko V.N., Dontsov V.I., 2008*b*]. According to some scientists (V.I. Dontsov, V.N. Krutko et al.), purely mathematical models have theoretical nature, not biologically established and in fact they are not correct due to incorrect initial assumptions.

At the same time, there is an urgent need to develop a clear overall view of the dynamic processes occurring in vivo, and its embodiment in models that allow interpreting body aging quantitatively and meaningfully. At that, V.N. Dontsov points out that many of the elements of such models already exist in various areas of biology. The presence of more than 200 theories of aging indicates not only and not so much the lack of a unified theory, common positions or lack of study of the causes and nature of aging, as often to methodological discrepancies with respect to the subject matter [Krutko V.N., Dontsov V.I., 2008*b*].

One of the first models, which meet the requirements to the essential theories of damage accumulation in vivo over time, is a well-known model of Gompertz-Meykem, which is coherent with the experimental data of human mortality in adulthood [Gompertz B., 1825; Makeham W.M., 1860]. Currently, there are many modifications of this model, which basically describe only natural processes of the human body "wear" [Weibull W., 1951; Gavrilov L.A., Gavrilova N.S., 1991]. Models of age-dependent mortality are used for the projections in demography and epidemiology [Korotaev A.V. et al., 2005; Medkov V.M., 2002; Zueva L.P., Yafaev R.Kh. 2005].

The so-called "stress" models describing the additional component of the intensity of mortality are used to consider the exposure of unfavorable chemical factors [Sakovich V.A. et al., 2004]. Models analyzed by authors are based on statistical data and do not take into account the mechanisms of formation and interaction of the processes and are not focused on the study of phenomenon character.

Recent approaches to the simulation of the processes of accumulation of damaging effects in vivo require obligatory account for the interaction of living organisms with the environment. In the studies, V.N. Krutko [Krutko V.N., 2002; Krutko V.N. et al., 2010] classifies the mechanisms of viability loss, where the most significant are:

1) systemic "pollution" of the body over time as a consequence of insufficient transparency to the environment and the low efficiency of the excretion process;

2) loss of non-renewable elements of the body - at all levels of its organization;

3) accumulation of damages and deformations due to the fundamental lack of forces for the selection of self-renewing structures to preserve essential elements of the system;

4) adverse changes in regulatory processes.

Most of the models describing the mechanisms of aging, are based on the formulation and solution of the systems of ordinary differential equations and reflect the evolution of human health problems.

Among the theories, which consider underlying mechanisms of accumulation of the body damages, we can identify homeostatic model developed by V.N. Novoseltsev (1992, 2008), in which physiological aging is associated with oxidative damages accumulation in vivo. The body is presented an integrated system capable to resist the action of various damaging and destructive factors. The model proposed by V.N. Novoseltsev is a tool of forecasting and analysis of death coming scenario. In the development of the concept proposed, E.A. Mashintsov and A.E. Yakovlev developed a mathematical model of the life cycle of the body, which key output parameters are life expectancy and the value of the lost years of potential life [Mashintsev E.A., A.E. Yakovlev, 2004; A.E. Yakovlev, 2005]. The authors consider only a few major organs and systems (kidney, liver, cardiovascular and respiratory system), at that the model does not contain components that reflect the interaction with living environment factors.

The effects of living environment exposure take into account the models proposed by L. Schlessinger and D.M. Eddy (2002), who describe changes of biological parameters of the person associated with diseases, taking into account external factors. Development of equations is based on statistical approaches, it being emphasized that although the model is based on data from the population level, it takes into account the health status of individuals in terms of anatomy, physiology, pathology and response to treatment. The authors described in

detail an algorithm for solving the problems of identification, verification and incompleteness of data. However, the lack of the model parameter values makes it difficult to use the submittals in further studies.

The diversity of theoretical mechanisms of the processes of damages accumulation in vivo leads to the advent of models, which are interest in the context of information and analytical methods of simulation, than in practical application in biological and medical problems. Information and entropy model proposed by A.Sh. Avshalumov could serve as an example. The model is based on the assumption of key role of information processes in human body vitality as an organic unity and its gradual loss due to reduction of information bond of the body stipulated by objectively flowing process of entropy augment in any closed system [Avshalumov A.Sh., 2009].

Recent studies in the field of development of mathematic models of accumulation of the body damages under the action of natural causes and living environment factors are characterized by essential amplification and application of large quantity of parameters. In this context the researchers are faced with the substantive problem connected with the identification of theoretical models. A.P. Parakhonskiy (2007) states that medicobiologic systems are characterized by very difficult dynamic of processes, which depend upon various factors that are hardly identifiable, analyzable and studied. Methods of functional and structural assessment are applied for handling the problem of parameters assessment in biotechnical models [Akulov S.A., Kalakutskiy L.I., 2007]. S.A. Akulov and L.I. Kalakutskiy showed in their works that in the first instance it is necessary to have experimental data on the system behavior under various input effects which is very difficult for the simulation of biological processes dynamic. On the other hand, structural identification enables determination of the interaction of individual components of the system in the process of reaction formation.

According to published scientific researches, it may be concluded that the application of structural identification followed by the planning of experiment for missing parameters identification (functional identification) is optimal. International project Physiome [Hunter P. et al., 2002], which contains works focused on mathematical simulation of physiologic processes acts as information resource for such works. The main purpose of the project is development of human body model using methods, which combine biochemistry, biophisics and anatomy of cells, tissues and organs. Application of such approaches allows describing underground processes of organs and systems physiology, but on this stage of the project development there is no task to describe processes of functional disorders accumulation in organs and analyze action of living environment factors. Even so some physiological models already consider individual exposure factors, e.i. cigarette smoke inhalation [Zhang Z. et al., 2012] or helicobacter infection of stomach mucous [Joseph I.M., Kirsher D., 2004].

The paucity or absence of references to other works in this area should be noted in most publications, which probably indicates a weak development of this area.

In connection with the above development of a mathematical model, which allow predicting the evolution of damage accumulation in vivo under the influence of living environment factors, is presented by the task required in the field of improvement and development of health risk assessment methodology. Due to the complexity of the objects under investigation and the broad spectrum of spatial (from 1 nm – ion channel size to 1–2 m – size of the human body) and time (from 1 mks – for molecular motion to 70–80 years (10^9 s) – human life) scales of physiological processes, a multilevel model of accumulation of disorders of the organs and systems of the human body is being developed [Trusov P.V. et al., 2012] as a basic model used at the assessment and analysis of health risk. The model focuses on three levels: the upper level (macro-level) – the organism as a whole, the average level (mesolevel) - processes in individual organs and systems, lower (micro level) – processes in cells. Multi-level representation of the processes occurring in the organism, is an approach that allows consistently detailing and clarifying assessments, moving from general notions of cause-and-effect relationships (usually based on statistical models) to private, which take into account physical, biological, chemical and other fundamental laws. Principal scheme of the interaction of levels of the model when deploying an in-depth risk analysis is shown in Fig. 2.6.

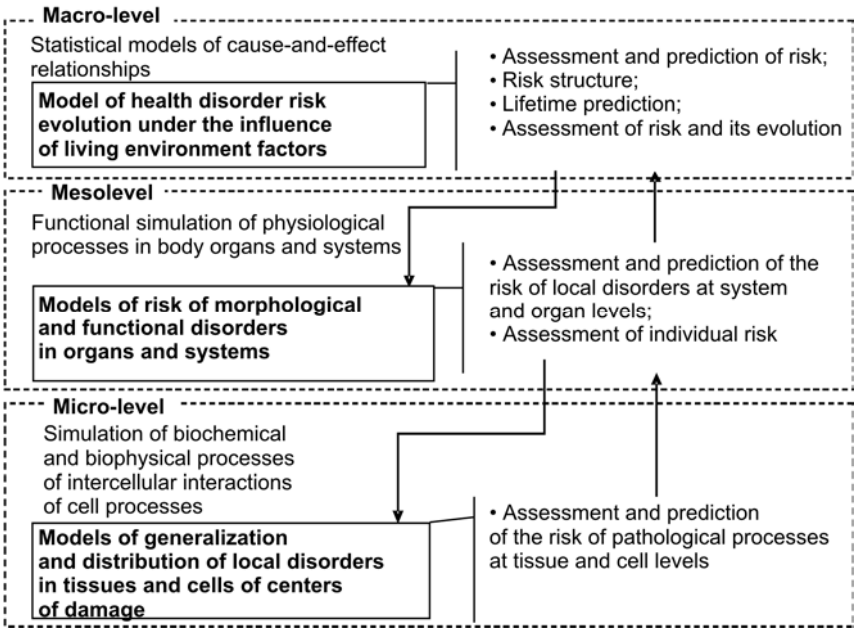


Fig. 2.6. Principal scheme of the assessment and prediction of risk and its evolution based on multi-level simulation

Simulation of the accumulation of health problems at the macro-level is focused on obtaining models that reflect the population patterns of influence of living environment factors on the population. Evolutionary models of the accumulation of risk of organs and body systems dysfunction obtained on the basis of statistical simulation of cause-and-effect relationships in the system "living environment – population health" allow performing structural and dynamic risk analysis and its assessment. The main results of the simulation of health risks at the macro-level are the critical parameters of the process of risk accumulation, which include:

- critical organs and systems of the body;
- critical parameters of factors exposure (level, time), corresponding to an unacceptable risk;
- the contributions of individual factors in the formation of unacceptable risk and related health disorders.

The results of health risks simulation at the macro-level are the input data for the simulation of the processes of development of the health risk disorders at the meso level, the purpose of which is to clarify the conditions of formation, localization of morphological and functional damages to certain organs. The development of such models is performed on the basis of functional simulation of physiological processes that occur in vivo at a negative impact of living environment factors. The areas of localization of disorders in certain organs and critical links of physiological processes are the results of risk estimation at the mesolevel.

The forecast of local risks realization in real pathologic process associated with damage of tissues of organs and cellular structures is performed on the basis of models of cell-cell interactions – micro level models.

In its turn, the problem of system analysis is solved at each level, that assumes the structuring of the processes of elements and subsystems interaction and requires the creation of sub-models describing the structural and functional relationships.

The proposed model takes into account the individual age characteristics of the body, the systemic interactions of organs, the accumulation of functional disorders due to natural physiological processes of the body and the effects of living environment factors, metabolic, regulatory and other processes most important for life.

Model of health risk evolution at macro-level

Statement of the problem of the macro-level simulation

At the statement of the problem of simulation of health risk caused by the variable exposures of diverse factors the homeostatic model developed by V.N. Novoseltsev was used as the basic theory (the Russian Academy of Sciences, A. Trapeznikov Institute of Control Problems). In this model physiologic aging is associated with the accumulation of oxidative damages in vivo, which cause dysfunction of organs and systems.

To construct a mathematical model the human body was presented as a finite set of organ systems that perform life support interrelated functions. In the general case, the model includes:

- respiratory function (respiratory system);
- digestive function (digestive system);
- circulatory function (cardiovascular system)
- excretive function (urinary system);
- integumentary function (skin and hypoderm);
- blood-forming function (hemic and hemopoietic organ system).
- regulatory function (immune, endocrine, nervous systems).

A parameter of *j*-th organ (system) damage $D_j(t)$, depending on time (age) t is introduced at development of an evolutionary model of accumulation of organs and systems dysfunctions: $D_j(t) \in [0,1]$. Value $D_j = 0$ corresponds to the normal (ideal) functioning, $D_j = 1 -$ the body's (system) impossibility to perform its functions [Trusov P.V. et al., 2012]. The associated functionality of the organ (system) $F_j(t)$ is determined according to the level of damage; it is defined as the organ ability to perform its functions: $F_j(t) = (1 - D_j(t))^{n_j}$, $n_j \in R \geq 1$. Organism as a biological system tends to accumulate over time functional disorders that occur in the form of diseases.

Essentially damage parameter when considering in prognostic sense can characterize the risk of organs and systems dysfunction due to natural causes and as a result of the influence of living environment factors is variable depending on time (age) t and taking values lying at a certain interval [0,1]:

$$D_j(t) \equiv R_j(t) \in [0,1]. \qquad (2.2.1)$$

At that the risk is a dimensionless value in the range [0; 1]. On the one hand, zero risk value (R = 0) corresponds to the absence of functional disorders in vivo and, consequently, the absence of cases of diseases and death. On the other hand, the risk values near unity ($R \to 1$) corresponds to an increase in the incidence of severe diseases and mortality.

Change of the risk value may be due to both natural causes related to the process of cellular aging and the impact of various factors.

Internal degradations – the processes of "self-degradation" that tend to occur on a cellular level and reflect the natural body aging are natural causes of the risk of organs and systems disorders. Organs and systems, as well as the whole body, have the property of self-regeneration (reparation) of lost functions.

Living environment factors that affect health, are classified as chemical, physical, biological, social, lifestyle factors and differ both in impact mechanisms and in critical organs and systems. Thus the consideration of the influence of various factors at macro-level simulation is identical, and is determined by a model based on statistical regularities.

At the same time, the chemical factors have a number of features associated with the ways of intake in vivo and mechanism of risk health effect. Effects associated with local irritants at direct contact (for example, at breathing or food consumption) and systemic effects at contact with the blood are pointed out when considering the chemical factors at macro-level simulation.

In the first case the factor exposure can be set either by daily dose or concentration in the medium (water, air). In the second case, it must be solved the problem of toxicokinetics. For this purpose it should be developed toxicokinetics submodel, which considers the mechanism of intake, excretion, metabolism and deposition of substances.

The development of a model of accumulation of functional disorders in the human body related to living environment factors, is focused on the study of negative effects on the part of critical organs and systems at the effect of chemical compounds at their entering into blood. This necessitates the establishment of relationships of substances intake in vivo from the ambient media taking into account the major routes of intake and excretion, changing the concentration of substances in blood: metabolism and deposition (accumulation) in organs.

The model of accumulation of risk of the body organs and systems disorders is based on the type of evolutionary model of damage accumulation, taking into account damages caused by constant and variable exposures of factors, processes, kinetics of substances, processes of functions self-regeneration.

The activation of the body's internal reserves for functional compensation, neutralization of harmful effects and their consequences is made through the information exchange between organs. Information exchange function is performed by regulatory mechanisms. Regulatory function in vivo is performed by three systems: endocrine, nervous and immune. These systems are intimately related, and their interaction generates neuroimmunoendocrine regulation. Functional disorders of human organs and systems can lead to failure of regulatory processes.

Formally, the rate of change of the $r_j(t)$ risk $R_j(t)$ of functional disorders of the *j*-th organ (system) is recorded as the sum of the rates of the risk change due to natural causes ($r_{1j}(t)$) and due to the impact of living environment factors ($r_{2j}(t)$):

$$\frac{dR_j(t)}{dt} \equiv r_j(t) = r_{1j}(t) + r_{2j}(t),\ j = \overline{1,\ J}. \tag{2.2.2}$$

In the first approximation the rate of natural damages can be described by the relation:

$$r_{1j}(t) = \alpha_j^0 + \alpha_j^1 R_j(t) - \alpha_j^2 (1 - R_j(t)), \tag{2.2.3}$$

where $\alpha_j^0 > 0$, $\alpha_j^1 > 0$ – coefficients, which characterize the risk increase rate due to natural processes of the *j*-th organ [1/s];

$\alpha_j^2 > 0$ – coefficient, which characterize the rate of decrease in the risk of disorders of the j-th organ due to reparation (regeneration) processes [1/s].

Relation (2.2.3) includes terms that implement three different processes. The first term describes the risk increase throughout life; in general, it is a non-decreasing function of time. The second term makes additional contribution to the risk due to the increase of the organ functional burden in the event of structural disorders. Increased burden reduces life time of cells and leads to an increased risk of functional disorders of the organ. Thus, this term must depend on the risk of the organ disorders $R_j(t)$ and the coefficient α_j^1, which characterizes the effect of the organ wear on the rate of risk increase. The third term describes the decrease in risk due to the processes of organs self-regeneration (reparation). Natural regeneration of the organ is constantly taking place throughout a human life (division and differentiation of cells), reduction of the recovery function in time is due to the accumulation of defects in the cells. In the general case, the coefficients α_j^0, α_j^1, α_j^2 are functions of time, at this stage of model development these parameters are constant.

The increased risk due to the impact of living environment factors in general can be described by the ratio

$$r_{2j}(t) = \sum_i \beta_{ji} f(F_{ji}, t), \tag{2.2.4}$$

where β_{ji} is empirical coefficient reflecting the impact force of the *i*-th factor to the risk of adverse effects from the *j*-th organ systems [1/c];

$f(F_{ji},t)$ – function, reflecting the submodel of impact of the current factor exposure F_{ji} on the *j*-th system derived from epidemiological studies or by adapting of known and published methods and models.

In the absence of these relationships it can be used the factor impact function in the form of

$$f(F_{ji},t) = \left\langle \frac{F_{ji}(t)}{F_{ji}^{N}(t)} - 1 \right\rangle, \tag{2.2.5}$$

where $F_{ji}^{N}(t)$ – the factor value, which does not make an impact at lifetime exposure;

$\langle x \rangle$ – McCauley brackets: $\langle x \rangle = \max(0,\ x)$.

Depending on the type of active factor and model function being considered the dimension F_{ji} can be various, particularly for chemical substances F_{ji} it has dimension of blood concentration or dose. In case of the standard value exceedance $F_{ji}^{N}(t)$ the factor contributes to the increase in the risk of disorders of *j*-th system.

In view of the above concepts and notations, taking the hypothesis of additivity of the rates of change of the risk of a variety of factors, the structure of the equations describing the evolution of the risk of human organs and systems disorders can be represented as follows:

$$\frac{dR_j(t)}{dt} = \alpha_j^0 - \alpha_j^2 + (\alpha_j^1 + \alpha_j^2)R_j(t) + \sum_i \beta_{ji} \left\langle \frac{F_{ji}(t)}{F_{ji}^{N}(t)} - 1 \right\rangle, j = \overline{1,\ J}. \tag{2.2.6}$$

To complete the formulation to the system of equations (2.2.6), it is necessary to add the initial conditions, i.e., determine the risk of disorders in the initial time. For these purposes, statistical data on morbidity and mortality in early childhood or developed diagnostic models with the assessment of risk indicators are used in sampling studies.

The relations (2.2.6) represent a system of ordinary differential equations, in general – with a nonlinear right side. At constant values of operative factors, the system (2.2.6) has a unique analytic solution, as the right side (2.2.6) in this case is continuous and differentiable on the whole range of definition. Depending on the values of the coefficients and initial conditions, graphics of system solutions are a family of exponential curves.

When considering the mechanisms of chemical factors impact, based on the receipt of substances in the blood from the environmental medium, the system (2.2.6) is added by mathematical models describing the toxicokinetics processes.

A mathematical model of chemical substances kinetics is based on physiological models. Structural basis of the physiological model is loculus (area) of the body with a uniform concentration of the substance. The loculus can be specific functional or anatomical part of the organ. Physiological models have several advantages: they can describe the distribution of substances in any real organ and tissue, allow establishing the influence of physiological parameters on the content of the substance in tissues, describe complex dosing regimens and processes of saturation at metabolism and complex formation. Kinetic constants in physiological models are empirically obtained in the studies of real biological or chemical processes, it is possible to extrapolate the obtained kinetic parameters to other external conditions and physiological states [Samura B.A., Dralkin A.V., 1996; Yakovlev V.A. 1965; Lakin K.M. Krylov Yu.F., 1981]. In this case it is necessary to carry out the verification of results obtained by extrapolation using careful empirical studies.

Changes in the concentration of substances in vivo are caused by several mechanisms, which involve transport across a number of biological membranes: intake from the ambient medium, accumulation, metabolism and excretion. Membrane systems of the body have the same structure, but different functional properties. They are mobile structures

formed by protein-phospholipid complexes and have limited permeability for various compounds. The mechanism of the passage of substances through membranes is rather difficult, because it is influenced not only by functional characteristics of the membranes, but certain features of the protoplasm and cellular proteins. Three routes of intake in vivo are pointed out in the study of the kinetics of substances: oral, inhalation and percutaneous. It should be noted that excretion of substances is also possible through these three routes.

The equation describing the absorption and excretion of harmful substances by lungs, skin and gastrointestinal tract are derived from Fick equation:

$$V_{ji}^{A-E}(t) = \lambda_{ji}^{A-E}(1-R_j(t))(\bar{C}_i^j(t) - h_{ji}^{A-E}C_i^b(t)), \tag{2.2.7}$$

where $C_i^b(t)$ – concentration of *i*-th substance in blood, kg/m^3;

$V_{ji}^{A-E}(t)$ – rate of change of the concentration of the *i*-th substance in the blood using *j*-th ($j = \overline{1,\mathrm{J}}$) absorption-excretion organs, kg/(m^{3}s) (conventionally substance flow entering the blood has the positive rate of concentration change, and negative one at outgoing flow);

$\lambda_{ji}^{A-E} \geq 0$ – constant of intake (excretion) rate of *i*-th substance through *j*-th intake (excretion) organ, 1/s;

h_{ji}^{A-E} – dimensionless coefficient of equilibrium in *i*-th substance between blood and intake medium;

$\bar{C}_i^j(t)$ – concentration of *i*-th substance in *j*-th medium (air, water, food, etc., depending on the route of intake), kg/m^3.

Basing on the principles of development of loculus physiological models, the equation of substances excretion by kidneys and liver can be written as:

$$V_{ji}^{E}(t) = -\lambda_{ji}^{E}(1-R_j(t))C_i^b(t), \tag{2.2.8}$$

where $V_{ji}^{E}(t)$ is the rate of change of the concentration of the *i*-th substance in blood using *j*-th excretion organs, kg/(m^{3}s);

$\lambda_{ji}^{E} \geq 0$ – constant of the rate of excretion of *i-th* substance through *j*-th excretion organ, 1/s.

The basic enzyme kinetics equation of Michaelis-Menten is used to describe the mechanism of substances metabolism by enzymes. Considered relation describes the dependence of the reaction rate, catalyzed by the enzyme from the enzyme and substrate concentration:

$$\mathrm{a}V_{ik}^{M}(t) = \frac{\lambda_{ik}^{cat}\sum_j((1-R_j(t))E_{ikj}^{N}(t))C_i^b(t)}{K^{ik} + C_i^b(t)}, \tag{2.2.9}$$

where $V_{ik}^{M}(t)$ is rate of change of the concentration of *i*-th substance in the blood during the formation of *k*-th substance with an enzyme, kg/(m^{3}s) (substances quantity depends on the specific conditions and may vary in different variants of the model application);

$\lambda_{ik}^{cat} \geq 0$ – coefficient characterizing the metabolic rate, s^{-1};

$E_{ikj}^{N}(t)$ – normal concentration of enzyme that converts *i*-th substance to *k*-th substance, generated by *j*-th organ, kg/m^3;

K^{ik} – Michaelis constant characterizing the affinity of the enzyme to the substrate, kg/m^3.

The reaction with a single enzyme is described at this stage. In the case where the reaction requires several enzymes or the reaction takes place in several stages, the equation (2.2.9) shall be complicated, e.g. for a multistage reaction Michaelis constant shall be calculated with regard to the rate constants for each stage.

The flow of substances from deposition organs to blood is made by diffusion in the presence of a concentration gradient between the organ and blood:

$$V_{ji}^{Sb}(t) = \lambda_{ji}^{S}(1-R_j(t))(C_i^j(t) - h_{ji}^{S}C_i^b(t)), \tag{2.2.10}$$

where $V_{ji}^{Sb}(t)$ is the rate of change of the concentration of *i*-th substance in blood due to intake from *j*-th organ, kg/(m^{3}s);

$\lambda_{ji}^{S} \geq 0$ – constant of intake rate of *i*-th substance from *j*-th organ to blood, [1/s];

h_{ji}^{S} – dimensionless coefficient of equilibrium in *i*-th substance between blood and deposition organ;

$C_i^j(t)$ – concentration of *i*-th substance in *j*-th organ [kg/m^3];

$R_j(t)$ – risk of disorders of *j*-th deposition organ.

Rate of change of the concentration $V_{ji}^{Sd}(t)$ of *i*-th substance in *j*-th organ due to receipt from blood is determined using the formula:

$$V_{ji}^{Sd}(t) = -\frac{U^b}{U_j^d}V_{ji}^{Sb}(t), \tag{2.2.11}$$

where U^b, U_j^d is volume of blood and biological media of accumulation organ, respectively.

On the basis of the balance equations (mass conservation) change of the concentration of *i*-th substance in blood and accumulation in organs can be represented as:

$$\begin{cases} \dfrac{dC_i^b(t)}{dt} = \sum\limits_j V_{ji}^{A\text{-}E}(t) + \sum\limits_j V_{ji}^{E}(t) + \sum\limits_j V_{ji}^{Sb}(t) - \sum\limits_k V_{ik}^{M}(t) + \sum\limits_k V_{ki}^{M}(t), \\ \dfrac{dC_i^j(t)}{dt} = V_{ji}^{Sd}(t). \end{cases} \tag{2.2.12}$$

The coefficients of equations (2.2.7) – (2.2.12) are generally dependent on the physical parameters of organs: size, weight, membranes capacity. To solve the system, it is necessary to set the initial conditions for the concentration of substances in the blood and organs of accumulation. The relations (2.2.12) are related to the evolutionary model through the concentrations of substances in the blood and the risk of organs and systems disorders.

Combining relations (2.2.6) – (2.2.12), we can write the general system of equations of mathematical model of the evolution of the risk of functional disorders (2.2.13):

$$\begin{cases} \dfrac{dR_j(t)}{dt} = \alpha_j^0 - \alpha_j^2 + (\alpha_j^1 + \alpha_j^2)R_j(t) + \sum\limits_i \beta_{ji}\left\langle \dfrac{F_{ji}(t)}{F_{ji}^N(t)} - 1 \right\rangle, j = \overline{1,\ J}; \\ \dfrac{dC_i^b(t)}{dt} = \sum\limits_j \lambda_{ji}^{A-E}\left(1-R_j(t)\right)(\bar{C}_i^j(t) - h_{ji}^{A-E}C_i^b(t)) - \\ -\sum\limits_j \lambda_{ji}^{E}\left(1-R_j(t)\right)C_i^b(t) + \sum\limits_j \lambda_{ji}^{S}\left(1-R_j(t)\right)(C_i^j(t) - h_{ji}^{S}C_i^b(t)) - \\ -\sum\limits_k \dfrac{\lambda_{ik}^{cat}\sum\limits_j (\left(1-R_j(t)\right)E_{ikj}^{N}(t))C_i^b(t)}{K^{ik} + C_i^b(t)} + \\ +\sum\limits_k \dfrac{\lambda_{ki}^{cat}\sum\limits_j (\left(1-R_j(t)\right)E_{ikj}^{N}(t))C_k^b(t)}{K^{ki} + C_k^b(t)}; \\ \dfrac{dC_i^j(t)}{dt} = -\dfrac{U^b}{U_j^d}\lambda_{ji}^{S}\left(1-R_j(t)\right)(C_i^j(t) - h_i C_i^b(t)). \end{cases} \tag{2.2.13}$$

For practical applications, it is advisable to introduce some simplifying hypothesis. In first approximation parameters α_j^0, α_j^2 are taken to be equal to zero, the kinetics of chemicals in vivo is considered without regard to metabolism. In this case, the numerical solution of the system of equations (2.2.13) using mesh schemes (mesh schemes are used for approximation of the first time derivatives) leads to the recurrence relations:

$$\begin{cases} R_j(t+1) = R_j(t) + [\alpha_j^1 R_j(t) + \sum_i \beta_{ji} \left\langle \frac{F_{ji}(t)}{F_{ji}^N(t)} - 1 \right\rangle] K, j = \overline{1, J}; \\ C_i^b(t+1) = C_i^b(t) + [\sum_j \lambda_{ji}^{A-E} \left(1 - R_j(t)\right)(\bar{C}_i^j(t) - h_{ji}^{A-E} C_i^b(t)) - \\ - \sum_j \lambda_{ji}^E \left(1 - R_j(t)\right) C_i^b(t) + \sum_j \lambda_{ji}^S \left(1 - R_j(t)\right)(C_i^j(t) - h_{ji}^S C_i^b(t))] K; \\ C_i^j(t+1) = C_i^j(t) + [\lambda_{ji}^S \left(1 - R_j(t)\right)(C_i^j(t) - h_i C_i^b(t))] K, \end{cases} \quad (2.2.14)$$

where $R_j(t+1)$ is the risk of disorders of *j*-th body at a time *t*+1;

$R_j(t)$ – the risk of disorders of *j*-th body at a time *t*;

K – temporary empirical coefficient taken according to Table 2.1.

Table 2.1

The *K* value for the calculation of risk for the period *t*

Parameter	Period of time, *t*				
	hour	day	week	month	year
K	0.000114	0.00274	0.019231	0.083333	1

To start the calculation procedure using recurrence equations the system (2.2.14) is supplemented by the initial conditions – values of risk $R_j(t_0)$ and concentrations in blood and organs of accumulation $C_i^b(t_0)$, $C_i^j(t_0)$ in the reference time t_0.

It should be noted that an equality $F_{ji}(t) = C_i^b(t)$ is true for *i*-th chemical which affects negative impact through blood, for systems (2.2.13), (2.2.14).

The proposed method, which uses evolutionary simulation of health risk, essentially develops a methodology based on the classical approach, by taking into account the time factor and expansion of time scale for long periods. Complexity of the method structure is compensated by new analytical capabilities, in addition, the current development of information technologies makes the task of the model implementation feasible for experts in the field of risk assessment.

Substantial simplification of the mathematical model (2.2.13) and its numerical analogue (2.2.14) is achieved by eliminating the kinetic submodel and the assumption of a stable cause-and-effect relationships between exposure of living environment factors and the risk of dysfunctions of body organs and systems. In this case, the basic relation for evolutionary simulation can be written as the following system of recurrence relations ($\alpha_j^1 = \alpha_j$):

$$R_j(t+1) = R_j(t) + [\alpha_j R_j(t) + \sum_i \beta_{ji} f(F_{ji}, t)] K, j = \overline{1, J}, \quad (2.2.15)$$

where $f(F_{ji}, t)$ is function that reflects the influence of *i*-th factor in the risk of dysfunctions of *j*-th organ or system.

The solution of the system of equations (2.2.15) allows defining the evolutionary curve of the risk of dysfunctions of each considered organ or system individually. The formula of integration, similar to the formula for calculation of the total probability of related events is used at simulation of the risk of dysfunctions of the body:

$$R = 1 - \prod_{j=1}^{J} (1 - R_j), \tag{2.2.16}$$

A general view of the solutions of equations (2.2.15) - functions which are based on the exponential dependence. Fig. 2.7 shows a general view of evolutionary models obtained by solution of recurrence equations and integration using the relation (2.2.16).

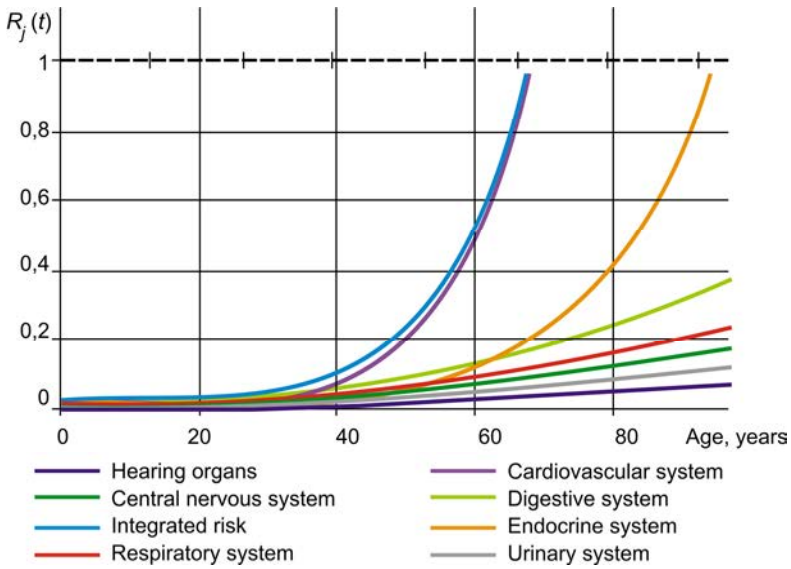


Рис. 2.7. A general view of evolutionary models of accumulation of organs and systems dysfunctions at macro-level

One of the limitations of the method application is a lack of published models and those accepted by the scientific community that reflects the influence of individual factors on health. The development of such models requires special epidemiological studies and the procedure of meta-analysis. At the same time currently we have a number of scientific developments, appear new data on harmful effects, new risk factors. their combinations and modifications of impacts. All this allows us to pose the problems, not only in a part of its risk assessment methodology, but also in identification of new areas of special epidemiological studies.

The application of evolutionary models is accompanied by an assessment of uncertainties to be described and accounted. Uncertainties arising from the implementation of the calculations are connected with several factors:

- firstly, the exposure assessment used the averaged parameters of living environment factors that may cause a dispersion of input and output values at individual calculations;
- secondly, the methods and models of determination of the levels of factors exposure are based on approximate calculations;
- thirdly, at the simulation we use relationships obtained in epidemiological studies based on sample data, which does not fully reflect the population segments, and the ranges of operating factors;

- fourthly, the evolutionary model describes the general regularities of accumulation of the risk of body dysfunctions, designed for the average person, and may not fully reflect the characteristics of these processes in specific population groups.

Thus, the concept of the model of the evolution of health risk at macro-level contains two main groups of parameters, which require identification, namely the parameters describing the accumulation of risk due to natural processes and due to the impact of living environment factors. In addition, the model provides for possible use of toxicokinetic relationships, reflecting systemic impact of toxicants if ingested.

An approximate solution of the basic equations of the model using mesh scheme in the form of the recursion relations makes it possible to program implementation, thus simplifying the calculation process.

The development of classical risk assessment methodology in the direction of the priority implementation of the results of evolutionary simulation allows us to select a number of advantages. Firstly, considering the time factor makes it possible to consider the risk as a dynamic process, thereby clarifying the calculation results and their assessment. Secondly, the mathematical formulation presupposes multifactor impacts, which automatically gives the effect of impacts integration. Thirdly, the possibility of use of voluntary scenarios of exposure change with time, both retrospectively and in perspective, allows the use of the model as a tool of simulation. In general, it should be noted that the use of evolutionary simulation significantly improves the predictive value of health risk assessment methodology at complex impact of heterogeneous living environment factors.

Identification of parameters of macro-level evolutionary model

Recent studies in the development of mathematical models of body damages accumulation are characterized by the use of a large number of parameters, which poses a complex problem associated with the identification of theoretical models, one of the most important stages of mathematical simulation [Parakhonsky A.P., 2007]. Identification of the model parameters consists in calculation of numerical values of coefficients.

Methods of functional and structural identification are applied for handling the problem of parameters assessment in biotechnical models [Akulov S.A., Kalakutskiy L.I., 2007]. In the first case, it is necessary the presence of the experimental data on the behavior of the system at different inputs that is not always possible for biological processes simulation. On the other hand, structural identification enables determination of the interaction of individual components of the system in the process of reaction formation, i.e. on the basis of observations.

The functional identification of parameters for the complete system of equations involves organization of the individual long-term monitoring studies during the entire period of human life, including clinical and laboratory, and functional examination with measurement of the level of contamination of biological media, as well as the exposure of operating factors. In reality, the constant monitoring of factors of living environment and health problems of the population is replaced by adequate selected studies according to the structure of the population (gender, age, social and others.).

Structural identification is applied to solve the problem of identification of the parameters of the health risk evolution model at macro-level. Structural identification requires much less organizational efforts and allows combining the results of studies carried out by different research groups.

Quantitative determination of the values of the model parameters is most commonly performed on the basis of mathematical statistics methods with the use of the system of population health and living environment factors surveillance.

On identification of the macro-level evolutionary model, it is necessary to develop a method to determine the risk of organs and body systems disorders. Both morbidity and mortality rates in the case of calculations at the level of populations, and clinical and laboratory parameters at individual assessments can serve as the initial data for such calculations. The application of statistical models of population level can be used to

determine the parameters that characterize the process of accumulation of risk due to natural causes.

In this regard, there are two approaches to calculate the risk of the body organs and systems dysfunctions in individual populations. The first approach involves the use of statistical information on morbidity and mortality, the second supposes a decision of "diagnostic problem" (the definition of functional disorders of organs system according to the marker indicators of clinical and laboratory, and functional diagnostics) for individuals [Kamaltdinov M.R., 2010; Kamaltdinov M.R. et al., 2013]. Both approaches allow calculating the same value - the risk of the organs and systems dysfunctions, based on different sources of information, and use it for identification of the model parameters.

Table 2.2 lists the methodological approaches used to identify macro-level model.

Table 2.2

List of the methodological approaches used to identify macro-level model

Model parameters	Identification method	Data source
The rate of risk accumulation due to natural causes	Methods of mathematical statistics	Population morbidity and mortality rates
Parameters of impact of living environment factors on the risk of organs and systems disorders	Methods of mathematical statistics	The results of epidemiological studies, the solution of "diagnostic problem" at the individual level
	Adaptation of existing relationships	Published materials of scientific researches, scientific articles, monographs

It should be noted that the problem of identification of model parameters is the subject of special scientific researches, in which not only calculation of the coefficients, but also proposed development of methodological approaches is performed. In this regard, materials presented in this section are not the only option for solving the problem of identification and they can be extended.

Application of statistical data for identification of macro-level model parameters

The system of observation for two groups of indicators is used to perform parameter identification of evolutionary model: on the one hand, the values of living environment factors, on the other hand, population health indicators associated with it. Risk of body organs and systems dysfunctions is used as the main indicator of health in the simulation of relationships, which is characterized by population morbidity and mortality at the use of the statistical approach.

The application of statistical approach is based on the value of the risk of organs and systems dysfunctions in the form of a severity weighted sum of population morbidity and mortality rates in the context of individual age groups:

$$\overline{R}_t^j = \frac{\sum_j \overline{z}_t^{ji} g^i + \overline{s}_t^j}{1000}, \qquad (2.2.17)$$

where t is the age group with a five-year interval;

$\overline{R}_t^j$ – indicator that corresponds to the average population risk of j-th system or organ dysfunction at the age t;

$\overline{z}_t^{ji}$ – average population i-th disease morbidity of j-th system or organ at the age t (sl./1000);

$\bar{s}_t^j$ – average population mortality from diseases of *j*-th system or organ at the age *t* (sl. / 1000);

g^i – value of *i*-th disease severity.

The severity of disease is measured as non-dimensional coefficient in the range from 0 to 1. At that minor diseases, which slightly worsen functional state of organs, are characterized by the value of the severity coefficient is close to 0, on the other hand, in cases of severe diseases severity coefficient is close to 1. Severity coefficient equal to 1 corresponds to cases of death.

The severity coefficient is determined based on expert estimates using the method of median values. For this purpose, all diseases registered during the year, shall be broken down into sub-classes according to the International Classification of Diseases-10. The most common disease called representative, the severity of which is estimated by experts is selected in each subclass.

Determination of remaining diseases severity is based on a comparison with a representative disease according to treatment duration:

$$g_i = 1 - e^{T_i \frac{\ln(1-g_M)}{T_M}}, \qquad (2.2.18)$$

where g_M and T_M – the value of severity and the average duration of representative disease;

g_i and T_i – calculated value of severity and the average duration of *i*-th disease.

The function corresponding to expression (2.2.18), looks like shown in Fig. 2.8.

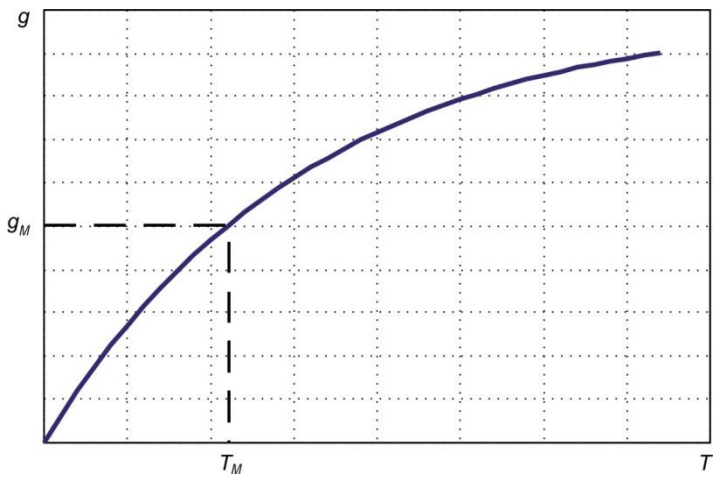


Fig. 2.8. Form of the function to assess the disease severity

The severity rate is determined for 208 representative diseases derived from special studies with the assistance of experts. The list of representative nosologies includes representatives of all classes and subclasses of diseases that provides complete coverage of possible health problems at the population-based studies in accordance with ICD-10.

The calculations show that individual nosologies severity within a class varies within wide limits, taking a value from 0.1 to 0.9. The average weighted severity of population diseases in terms of main classes of diseases is presented in Table 2.3.

The methodology of the determination of the risk of organs and systems dysfunctions, based on population morbidity and mortality rates with regard to severity, requires data on the duration of each type of disease. The sources of such information: electronic databases containing registers of diseases of the population, for example, in the territorial mandatory health insurance funds.

Table 2.3

The average weighted severity per disease classes

ICD-10 code	Class	Children	Adults	All population
A00-B99	Some communicable and parasitic diseases	0.257	0.288	0.275
C00-D48	Neoplasms	0.375	0.554	0.547
D50-D89	Blood, hemopoietic organ diseases and certain disorders involving the immune mechanism	0.282	0.273	0.277
E00-E90	Endocrine system diseases, eating disorders and metabolism disorders	0.293	0.270	0.274
F00-F99	Psychiatric disorders and behavioral disorders	0.325	0.388	0.357
G00-G99	Nervous system disorders	0.372	0.419	0.402
H00-H59	Diseases of the eye and adnexa	0.212	0.393	0.353
H60-H95	Diseases of the ear and mastoid process	0.241	0.336	0.308
I00-I99	Circulatory diseases	0.515	0.578	0.576
J00-J99	Diseases of the respiratory system	0.120	0.214	0.163
K00-K93	Diseases of the digestive system	0.138	0.162	0.156
L00-L99	Diseases of the skin and subcutaneous tissue	0.324	0.309	0.314
M00-M99	Diseases of the osteomuscular system and connective tissue	0.254	0.414	0.397
N00-N99	Diseases of the genitourinary system	0.375	0.294	0.302
O00-O99	Pregnancy, childbirth and the puerperium	0.435	0.430	0.430
P00-P96	Certain conditions originating in the perinatal period	0.540	–	0.540
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities	0.563	0.615	0.569
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0.304	0.274	0.290
S00-T98	Injuries, poisonings and certain other consequences of external causes	0.372	0.442	0.427
A00-T98	Totals	0.223	0.363	0.327

The values of the risk of organs and systems dysfunctions obtained according to statistics of morbidity and mortality rates are most often used to determine the regularities of change in public health at the population level. At solving the problem of evolutionary model parameter identification average population risk values are used to calculate the rate of increase of the risk of organs and systems dysfunctions due to natural causes α_j.

The identification of parameters of evolutionary model of health risks accumulation due to natural processes involves a series of calculations for different areas and determines the 5th percentile in each age group. Determination of the coefficients is performed by solving the optimization problem by least square method with objective function:

$$\sum_t \left(\overline{R}_t - R_t\right)^2 \to \min, \qquad (2.2.19)$$

where $R_t = R_{t-1} + \alpha R_{t-1}$ – the risk value as determined by the recurrence relation.

The method uses a values $\overline{R}_t$, corresponding to the 5th percentile, in individual subjects of the Russian Federation in each age group over the last few years.

Table 2.4 shows the parameters α_j, obtained by statistical data on the Russian Federation for 2009–2013.

Risk values at the initial time (t = 0) are given in Table 2.5.

Table 2.4

Model parameters α_j

Critical system	α_j
Cardiovascular	0.0835
Respiratory	0.0245
Central nervous	0.0106
Endocrine	0.0578
Organs of hearing	0.0303
Urinary	0.0046
Digestive	0.0178

Table 2.5

Risk values at the initial time

Critical system	$R_j(t_0)$
Cardiovascular	0.001359
Respiratory	0.014177
Central nervous	0.003560
Endocrine	0.000945
Organs of hearing	0.001247
Urinary	0.013102
Digestive	0.022168

The values of body organs and systems dysfunction risk accumulation rates are presented in Table 2.4, and initial risk levels shown in Table 2.5, are the basic parameters of the evolutionary model, characterizing the risk accumulation due to natural causes. Mentioned data reflect all-Russian trends, which can be updated at introduction of new statistical information.

While solving the problems of simulation for specific conditions peculiar to certain regions, the procedure of identification of these parameters should be based on regional statistics.

Diagnosis of organs and systems dysfunctions according to clinical, laboratory and functional examinations

The performance of structural identification of the evolutionary model parameters based on sample studies involves development of relationships between exposure of living environment factors and body organs and systems damage parameter (dysfunction), which is determined from the "diagnostic problem" solution.

The "diagnostic problem" is to determine the extent of individual body organs and systems dysfunctions on the basis of individual clinical, laboratory and functional tests.

The initial stage of the diagnostic problem solution is the choice of laboratory and functional marker indicators that most accurately reflect the state of individual organs and systems. The degree of damage (dysfunctions) is determined according to bias of marker indicators from the norm. Denoting $D_i \in [0,1]$ the disruption degree of *i*-th marker indicator, the damage of organ or system is determined by a weighted sum of functional disorders:

$$D = \sum_i a_i D_i \ , \qquad (2.2.20)$$

where a_i – weight coefficients.

In this case $D_i = 0$, if the value of the marker indicator is in the normal range, $D_i = 1$, if the marker indicator reaches extreme possible values that characterize the states, close to

total loss of functionality. At intermediate values of the marker indicator in the range between the limit of normal and extreme possible value D_i it ranges from 0 to 1.

In general terms, the marker indicator disruption degree is described by a piecewise linear function:

$$D_i = \begin{cases} -\dfrac{x_i - K_i^{\min}}{N_i^{\min} - K_i^{\min}} + 1, x_i < N_i^{\min}, i = \overline{1;n}, \\ 0, x_i \in [N_i^{\min}; N_i^{\max}], i = \overline{1;n}, \\ 1, x_i \in [-\infty; K_i^{\min}] \cup [K_i^{\max}, +\infty], i = \overline{1;n}, \\ \dfrac{x_i - N_i^{\max}}{K_i^{\max} - N_i^{\max}}, x_i > N_i^{\max}, i = \overline{1;n}, \end{cases} \quad (2.2.21)$$

where x_i – the value of *i*-th marker indicator;

$N_i^{\min}$ – lower limit of normal *i*-th marker indicator;

$N_i^{\max}$ – upper limit of normal *i*-th marker indicator;

$K_i^{\min}$ – minimum extreme value of *i*-th marker indicator;

$K_i^{\max}$ – maximum extreme value of *i*-th marker indicator;

The function (2.2.21) is shown graphically in Fig. 2.9.

Formalization of marker indicators disruption degree, using the relation (2.2.21) is universal, but in some cases it is advisable to use a tabular method of functions setting, based on expert opinion.

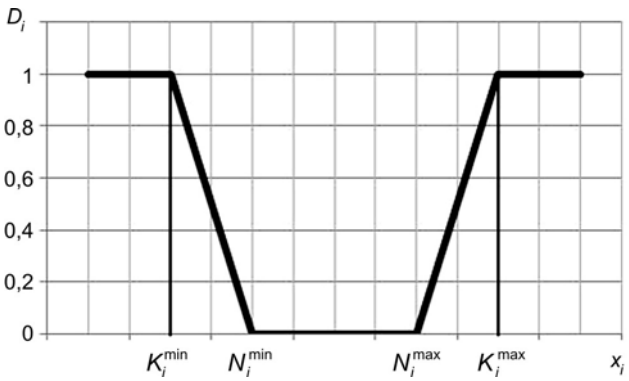


Fig. 2.9. Setting the degree of marker indicator bias from the norm using a piecewise linear function

It should be noted that a particular type of damage formula for each organ or system is defined by special studies with the assistance of experts. Below is a description of the results of diagnostic problem solving in in terms of four major systems: digestive, respiratory, urinary, circulatory.

Diagnosis of functional disorders of the digestive system

The damage of the digestive system is evaluated by functional disorders on the example of three organs: stomach, liver, pancreas. Functional state of each organ is determined by a set of clinical, laboratory, and functional parameters. Due to the studies presented in the works of M.R. Kamaltdinov et al. (2013), damage to the digestive system is described using 12 indicators listed in Table 2.6.

Table 2.6

The list of indicators used to describe the damage to the digestive system

Organ	Indicator	Designation	Function/function condition
Stomach	The average pH of the stomach fundic	x_1	Acid forming function
	Difference of minimum pH in stomach fundic and maximal pH in antral segment	x_2	Neutralizing function
	Rugae condition	x_3	Morphological condition
	Mucosa and antral segment condition	x_4	
	Erosions	x_5	
	Ulcers	x_6	
Pancreas	α-amylase	x_7	Secretory
Liver	Total bilirubin	x_8	Detoxication function
	Conjugated bilirubin	x_9	
	Albumins	x_{10}	Synthetic ability
	Total protein	x_{11}	
	Dextrose	x_{12}	Regulatory function

The indicators presented in Table 2.6 describe the state of the main functions of the digestive system and the morphological condition of the stomach. Since the indicators refer to different scales of measurement (x_1–x_2 – interval scale, x_3–x_6 – nominal scale, x_7–x_{12} – ratio scale), a way to specify the marker indicators disruption degree may differ from the relation (2.2.21). Tabular method of setting the disruption degree of D_1–D_6 is used for indicators x_1–x_5 (Table 2.7–2.9).

Table 2.7

x_1 indicator disruption degree

Parameter	pH (x_1)						
	<0.5	0.5–1.0	1.0–1.7	1.7–2.2	2.2–3.0	3.0–5.0	>5,0
D_1	0.6	0.4	0.2	0.0	0.2	0.4	0.6

Table 2.8

x_2 indicator disruption degree

Parameter	Δ_{pH} (x_2)		
	<2	2.0–4.0	>4,0
D_2	0.8	0.4	0

Table 2.9

x_3–x_6 indicators disruption degree

Indicator	Value	Disruption function
Stomach rugae (x_3)	Significant	$D_3 = 0$
	Other conditions	$D_3 = 0.2$
Stomach mucous (x_4)	Pink and smooth	$D_4 = 0$
	Hyperemic	$D_4 = 0,2$
	Other conditions	$D_4 = 0,4$
Erosion (x_5)	Absent	$D_5 = 0$
	Singular	$D_5 = 0.2$
	Multiple	$D_5 = 0.4$
Ulcer (x_6)	Absent	$D_6 = 0$
	Singular	$D_6 = 0,2$
	Multiple	$D_6 = 0,4$

The parameters for x_7–x_{12} disruption degree calculation using formula 2.2.21 are given in Table 2.10.

Table 2.10

Threshold values of x_7–x_{12} indicators

Indicator	Age group	N_i^{min}	N_i^{max}	K_i^{min}	K_i^{max}	Units of measurement
x_7	All	0	100		1000	unit/l
x_8	All	0	19	–	210	mcmole/l
x_9	All	0	4.3	–	60	mcmole/l
x_{10}	All	38	51	0	–	g/l
x_{11}	Children (0–14 years)	60	80	40	–	g/l
	Adults	66	87	45	–	g/l
x_{12}	Children (0–18 years)	4.1	5.9	1.3	–	mmol/l
	Adults	4.0	6.1	1.3	–	mmol/l

To use the formula (2.2.20) in the calculation of the degree of damage of the functional state of the digestive system the Table 2.11 shows weight coefficients.

Table 2.11

Weight coefficients of functional disorders on *i*-th marker indicator

a_1	a_2	a_3	a_4	a_5	a_6
0.111	0.111	0.027	0.027	0.027	0.027
a_7	a_8	a_9	a_{10}	a_{11}	a_{12}
0.333	0.082	0.082	0.058	0.058	0.049

These parameter values allow calculating for each individual in the sample the degree of disorders of the digestive system, which is a component of the data system used in the parameterization of cause-and-effect relationships.

Essentially damage, defined by the formula (2.2.20) is the indicator of the risk of digestive system dysfunctions.

Diagnosis of functional disorders of the respiratory system

Assessment of the respiratory system damage is based on spirogram data. 4 uncorrelated indicators for functional assessment, which can more fully characterize the respiratory function are used among the parameters obtained from the use of this diagnostic method [Tsinker M.Yu., 2010]:

- lung capacity;
- peak expiratory flow rate;
- maximum expiratory flow at 50%FVC (forced vital capacity) (MEF50);
- maximum expiratory flow at 25%FVC (MEF25).

For each indicator, there are standard values that depend on gender, age and height [Spirovit SP-10 Lung Function Recorder, 1996]. Based on the percentage of bias from the standard we can judge the respiratory system functions damage. Table of damage for each indicator it is formed based on the works of St. Petersburg State Medical Academy [Starshov A.M., Smirnov I.V., 2003] present gradations of values of the indicators in relation to the norm for 10 categories (Table 2.12, 2.13).

Calculation of total damage of the respiratory system is performed by the formula

$$D = 1 - \prod_{i=1}^{4} (1 - D_i) . \qquad (2.2.22)$$

Table 2.12

The values of disruption degree for graduations of indicators with respect to the standard for women

Indicator	*D*	lung capacity	peak expiratory flow rate	MEF25	MEF50
Above the norm	0	>111.4	>117.2	>120	>123.9
Norm	0	88.6	82.8	80	76.1
Conventional norm	0	81.3	71.8	67.2	60.8
Very slight reduction of norm	0.1	75.0	63.3	58.7	50.8
Slight reduction	0.2	68.8	54.8	50.2	40.8
Moderate reduction	0.3	62.6	46.3	41.8	30.8
Significant reduction	0.4	56.4	37.8	33.3	20.8
Quite considerable reduction	0.5	–	29.3	24.8	10.8
Sharp reduction	0.6	–	20.8	16.3	<
Extremly sharp reduction	0.7	<	<	<	<

Table 2.13

The values of disruption degree for graduations of indicators with respect to the standard for men

Indicator	*D*	lung capacity	peak expiratory flow rate	MEF25	MEF50
Above the norm	0	>113.3	>117.2	>120	>123.9
Norm	0	86.2	82.8	80	76.1
Conventional norm	0	78.2	71.8	67.2	60.8
Very slight reduction of norm	0.1	72.0	63.3	58.7	50.8
Slight reduction	0.2	65.8	54.8	50.2	40.8
Moderate reduction	0.3	59.6	46.3	41.8	30.8
Significant reduction	0.4	53.4	37.8	33.3	20.8
Quite considerable reduction	0.5	47.1	29.3	24.8	10.8
Sharp reduction	0.6	40.9	20.8	16.3	<
Extremly sharp reduction	0.7	<	<	<	<

Application of the formula (2.2.22) allows summarizing the parameters of individual indicators disruption degree at unknown weight coefficients.

Verification of methodology for the respiratory system damage calculation with real data showed that the majority of the child population has normal or slightly deviated indicators (about 60% of children), and the average population damage of the respiratory system is at the level of D = 0,1.

Diagnosis of functional disorders of the urinary system

Diagnosis of the urinary system dysfunctions is based on the analysis of 12 marker laboratory indicators obtained as a result of urinalysis, biochemical analysis of blood and urine [Sukhareva T.N., 2010], namely: urine specific gravity ((x_1), the presence of protein in the urine (x_2), the level of sugar in the urine (x_3), the level of creatinin in serum (x_4), glomerular filtration rate (x_5), the percentage of water reabsorption (x_6) and the concentration index (sample by Rehberg) (x_7), white blood count (x_8) and red blood cell count (x_9) in the urine, the content of salt in the urine – urate (x_{10}), phosphates (x_{11}), oxalate (x_{12}).

Thresholds of marker indicators are shown in Table 2.14.

Table 2.14

Thresholds of marker indicators of the urinary system

Functional marker	$K_i^{\min}$	$N_i^{\min}$	$N_i^{\max}$	$K_i^{\max}$	Units of measurement
x_1	1000	1006–1018*	1010–1030*	1040	g/l
x_2	0	0	0	3	‰
x_3	0	0	0	4	mlmol/l
x_4	0	0	80–97	450	mcmole/l
x_5	8**	80	–	–	ml/min
x_6	50	98.5	99	100	%
x_7	10	35	100	130	–
x_8	0	0	6	99	units per field
x_9	0	0	3	200	
x_{11}	0	0	0	4	crosses
x_{10}, x_{12}	0	0	1	4	

Note: "–" – standard values of urine specific gravity for different age groups.

Algorithm which reflects the relationships between the selected marker indicators is used to calculate the damage of urinary function. Since the urinary system dysfunctions are accompanied by changes in several indicators at the same time, there were made 4 uncorrelated complexes ($\tilde{D}_i, i = \overline{1,4}$).

- Complex, which considers the urine specific gravity ($\tilde{D}_1$):

$$\tilde{D}_1 = \begin{cases} 0, x_1 \in \left[N_1^{\min}; N_1^{\max}\right]; \\ \frac{1}{2}\sum_{i-1}^{2} D_i, x_1 \in \left[K_1^{\min}; N_1^{\min}\right), x_2 \neq 0; \\ \frac{1}{3}\sum_{i=1}^{3} D_i, x_1 \in \left(N_1^{\max}; K_1^{\max}\right], x_2 \neq 0, x_3 \neq 0; \\ c_1 D_1, x_1 \in \left[K_1^{\min}; N_1^{\min}\right), x_2 = 0, x_3 \neq 0; \\ c_2 D_1, x_1 \in \left(N_1^{\max}; K_1^{\max}\right], x_2 = 0, x_3 = 0; \\ 1, x_1 \in \left(0; K_1^{\min}\right) \bigcup \left(K_1^{\max}; \infty\right). \end{cases} \quad (2.2.23)$$

- The complex characterizing the presence of protein ($\tilde{D}_2$):

$$\tilde{D}_2 = \begin{cases} 0, x_2 \le N_2^{\max}; \\ \frac{1}{7}\sum_{i=1}^{7} D_i, x_2 \in \left(N_2^{\max}; K_2^{\max}\right] \\ 1, x_2 > K_2^{\max}. \end{cases} \quad (2.2.24)$$

- The complex, which include the content of red blood cells in the urine ($\tilde{D}_3$):

$$\tilde{D}_3 = \begin{cases} 0, x_9 \le N_9^{\max}; \\ \frac{1}{4}\sum_{i=9}^{12} D_i, x_9 \in \left(N_9^{\max}; K_9^{\max}\right] \\ 1, x_9 > K_9^{\max}. \end{cases} \quad (2.2.25)$$

- The complex, which include the content of white blood in the urine ($\tilde{D}_4$):

$$\tilde{D}_4 = c_3 D_8. \tag{2.2.26}$$

The relations use constants c_1, c_2, c_3, resulting from caculation data verification: $c_1 = c_2 = 0{,}3$; $c_3 = 0{,}71$.

Calculation of the urinary system function damage is made by relation similar to (2.2.22):

$$D = 1 - \prod_{i=1}^{4} \left(1 - \tilde{D}_i\right). \tag{2.2.27}$$

The calculation of the damage of the urinary system is based on the use of data of common laboratory tests, so it is available at the organization of any epidemiological studies.

Diagnosis of functional disorders of the cardiovascular system

The indicators of functional and laboratory tests (measurement of blood pressure, electrocardiogram (ECG), ultrasound (US), blood chemistry) available during the screening studies are used as markers that characterize the state of the cardiovascular system [Chigvintsev V.M., Nosov A.E., 2012]. Diagnosis of the disruption degree of the cardiovascular system functions uses 20 marker indicators, threshold values of which are given in the Table 2.15.

Application of relations (2.2.20), (2.2.21) with weight coefficients given in Table 2.16, allows calculation of the cardiovascular system function damage parameter.

The proposed approach was tested on data from sampling studies of the adult population aged from 30 to 60 years living in the urban environment, with the release of the group that is exposed to a complex of factors of production (Fig. 2.10).

Table 2.15

Threshold values of marker indicators of the cardiovascular system state

Functional marker	$K_i^{\min}$	$N_i^{\min}$	$N_i^{\max}$	$K_i^{\max}$	Units of measurement
Heart rate (x_1)	24	60	80	126	beats per minute
PQ (x_2)	0.07	0.12	0.2	0.24	s
QRS (x_3)	0.03	0.06	0.1	0.146	s
QTc (x_4)	–	–	0.44	0.62	s
P (x_5)	0.02	0.06	0.11	0.15	s
The Sokolow-Lyon index (x_6)	–	–	0.35	0.62	–
Dextrose (x_7)	1.8	4	6.1	8.3	mmol/l
Uric acid (x_8)	–	–	380	566	mcmole/l
Triglycerides (x_9)	–	–	1.7	3.75	mmol/l
HDL cholesterol (x_{10})	0.43	1.1	–	–	mmol/l
LDL cholesterol (x_{11})	–	–	3	5.3	mmol/l
Total cholesterol (x_{12})	–	–	5	8.4	mmol/l
Ejection fraction (x_{13})	27	50	–	–	%
End-systolic volume (x_{14})	–	–	45	68	ml
End-diastolic volume (x_{15})	37	59	157	186	ml
Left atrial dimension (x_{16})	–	–	40	63	ml
Pulmonary artery pressure (x_{17})	–	–	25	48	mmhg
Left ventricular mass index (x_{18})	–	–	117	147	–
Arterial blood pressure (diastolic) (x_{19})	27	60	90	113	mmhg
Arterial blood pressure (systolic) (x_{20})	68	100	140	186	mmhg

Table 2.16

Weight parameters of marker indicators

a_1	a_2	a_3	a_4	a_5	a_6
0.0229	0.0076	0.0115	0.1145	0.0076	0.1527
a_7	a_8	a_9	a_{10}	a_{11}	a_{12}
0.0763	0.0229	0.0076	0.0153	0.0153	0.1145
a_{13}	a_{14}	a_{15}	a_{16}	a_{17}	a_{18}
0.1527	0.0076	0.0076	0.0076	0.0076	0.0191
a_{19}	a_{20}	–	–	–	–
0.1145	0.1145	–	–	–	–

The calculations have shown the existence of different extent of the cardiovascular system function damage depending on age and exposure of operating factors (Fig. 2.10).

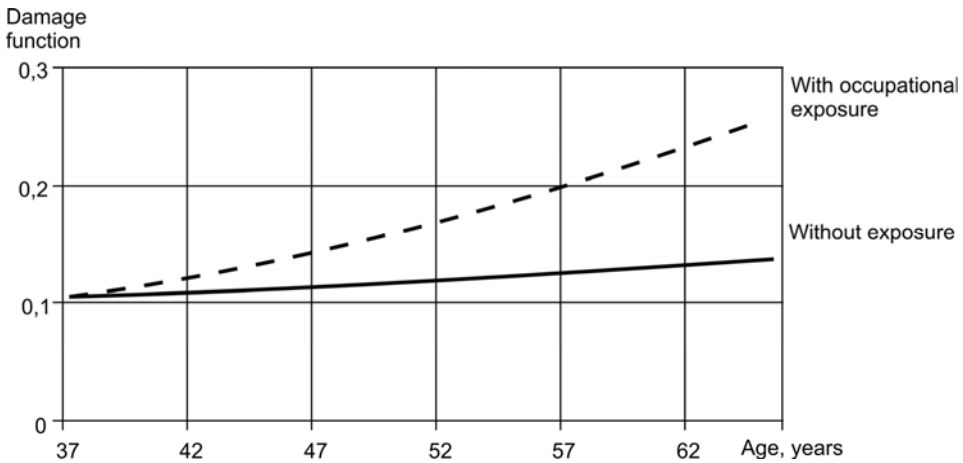


Fig. 2.10. Charts of age dynamics of cardiovascular system dysfunction value

The results indicate that dysfunction of the cardiovascular system gradually increase with age, starting with the values of D = 0,1. In this case, the rate of increase depends strongly on the degree of living environment factors exposure.

Presented in this section methodological approaches to determining the extent of damage of certain body system functions allow using the data from sampling epidemiological studies to parameterize the relationships between the exposure of living environment factors and the risk of health problems. Thus, the indicator of individual damage is used for characterization of the functional status of each individual, but in the case of studies of cause-and-effect relationships, relationships parameterization and prediction it is changed by the risk of body organs and systems dysfunctions, according to (2.2.1).

The procedure of development of paired models of relationship between risk (damage) and exposure of living environment factors is performed for the identification of evolutionary model parameters at the use of solution of the tasks of organ and system functions state diagnostic. Most often, simulation is performed using mathematical statistics methods (regression analysis). At the same time, it is necessary to consider the probabilistic nature of this indicator at the simulation of consistencies of health risk formation.

Defining the parameters of the relationships of the risk of organs and systems dysfunctions from the exposure of living environment factors

The development of paired mathematical model reflecting the effects of exposure of living environment factors on the risk of body dysfunctions, involves the use of epidemiologic studies data, containing both clinical and laboratory and functional test values, and information about the presence of diseases of individuals included in observation and control (comparison) groups. The task of development of paired models reduces to determining the parameters of relationships between factors exposure and the probability of indicators deviations.

The method of determining the parameters of such relationships is based on the transformation of initial system of indicator values to probabilistic and the determination of the parameters of the logistic function. The method of development of models of paired relationships requires consistent fulfillment of the following steps:

Step 1. Formation of a data table of consistent values "exposure marker – response marker".

Step 2. Calculation of the probability of the marker index deviation from the norm for each observation in the data table.

Step 3. Assessment of the parameters of the mathematical model that reflects the relationships of the probability of the marker index deviation from the norm with the level of exposure.

Formation of the data table is made according to the pattern shown in Table 2.17.

Table 2.17

Pattern of the data table of paired models formation

Observation number	Exposure value (F)	Response value (y)
1		
2		
3		

The calculation of the probability of the marker index deviation from the norm for each observation in the data table is made using "sliding window" technology.

To do this, each observation in the data table (each exposure marker value F_i) receives an appropriate assessment of the probability of response marker deviation from the norm (p_i), calculated for the range ("sliding window"): $F_i - \delta < F \le F_i + \delta$. Here δ is width of the "sliding window", which is defined by the relation:

$$2\delta = 10\frac{F_{\max} - F_{\min}}{N}, \qquad (2.2.28)$$

where N – total number of studies for the entire set.

The assessment of the probability of the marker index deviation from the norm is made by the classical formula of probability:

$$p_i = \frac{m_i}{n_i}, \qquad (2.2.29)$$

where m_i – the number of studies that deviate from the norm for the range $F_i - \delta < F \le F_i + \delta$;

n_i – total number of studies for the range $F_i - \delta < F \le F_i + \delta$.

The graphic illustration of the process of assessment of the probability of the marker index deviation from the norm using "sliding window" is shown in Fig. 2.11.

The assessment of parameters of paired model reflecting the dependence "exposure – response probability" is made by the method of logistic regression model development:

$$p = \frac{1}{1+e^{-(b_0+b_1F)}}, \qquad (2.2.30)$$

where p – the probability of response deviation from the norm;

F – exposure level;

b_0, b_1 – mathematical model parameters.

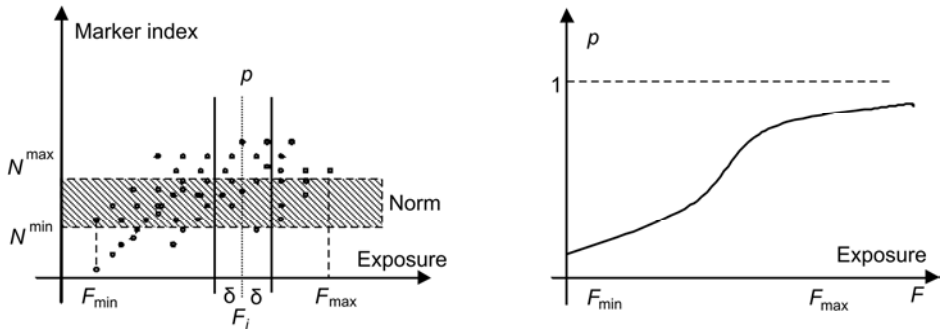


Fig. 2.11. Graphic illustration of technology of assessment of the probability of response deviation from the norm using "sliding window"

The exposure marker values from the data table and probabilities corresponding to them is used to develop the model.

The definition of the parameters of the mathematical model (b_0, b_1) is performed by least squares method using software packages for statistical analysis of data (Statistica, SPSS, SAS, etc.).

The assessment of the reliability of parameters and model adequacy is carried out based on one-way analysis of variance on the basis of Fisher's ratio. The determination of 95% confidence limits is carried out at a calculation of mathematical models.

In the process of models development in addition to statistical hypothesis, it is necessary to carry out expertise of obtained dependences for their biological relevance assessment.

The concept of increment of the risk of body system disorders due to the action of a chemical in the time specified by the study objectives is used at the simulation of the risk of noncarcinogenic effects from analytic factors using evolutionary models of risk accumulation:

$$\Delta R = g\left\langle p(F) - p(F_0)\right\rangle, \qquad (2.2.31)$$

where ΔR – increment of the risk of body critical system disorders, caused by the action of chemical in the time specified by the study objectives;

g – coefficient characterizing the severity of critical system disorders in relation to the performance of the body functions, assessed by the ratio of mortality and morbidity for the same reason of a separate organ/system dysfunction;

F_0 – reference level for exposure marker;

$\langle\ \rangle$ – Kelly's brackets, taking the values $\langle F\rangle = 0$ at $F < 0$ and $\langle F\rangle = F$ at $F \geq 0$.

The algorithm for F_0 calculation is based on the development of regression models, reflecting the impact of the level of exposure on "odds ratio" indicator (OR), which characterizes the strength of the relationship between the values of the level of exposure and response. $OR \geq 1$ is taken as a criteria of relationship presence.

For each observation the data table presents a calculation of the odds ratio index, which is held by conventional sample dividing into two parts: below and above the current level of exposure marker ($[F_{min}, F_i]$ and $[F_i, F_{max}]$, respectively, where F_i – the current level of exposure marker). Value that characterizes the probability of response marker deviation

from the norm p_i^- and p_i^+, respectively, is calculated for both intervals as the relation of number of observations with deviation from the norm to the total number of observations. Schematically technology of sampling division in two parts is shown in Fig. 2.12.

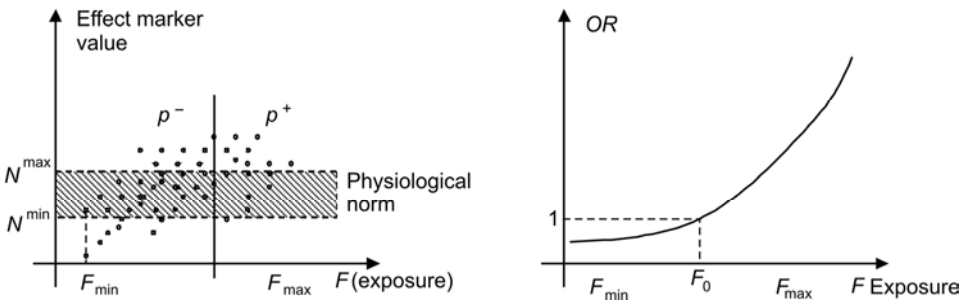


Fig. 2.12. Sample data representation scheme

The odds ratio for each observation in the data table is determined from the ratio:

$$OR_i = \frac{p_i^+}{1-p_i^+} \Big/ \frac{p_i^-}{1-p_i^-}, \tag{2.2.32}$$

where i – index, which reflects the number of observations.

Assessment of parameters of the odds ratio dependence from the exposure value is carried out by development of a regression model in the form of an exponential function:

$$OR = e^{a_0 - a_1 F}, \tag{2.2.33}$$

where a_0, a_1 – model parameters determined by regression analysis.

The information from the data table and odds ratio values corresponding to them is usedto develop the model.

Definition of the parameters of the mathematical model (a_0, a_1) is performed by least squares method using software packages for statistical analysis of data (Statistica, SPSS, SAS, etc.).

Calculation of the reference level of exposure factor (F_0) with respect to the form of the response is performed based on OR = 1, by the formula:

$$F_0 = \frac{a_0}{a_1}. \tag{2.2.34}$$

The assessment of model adequacy is carried out based on one-way analysis of variance on the basis of Fisher's ratio. Determination of 95% confidence limits of point estimates of acceptable levels of exposure markers is carried out at mathematical models developing.

Determination of the parameters of the evolutionary model based on adaptation of the results of epidemiological studies

The adaptation of the results of studies of living environment factors influence on the population health on the basis of evolutionary simulation is a necessary step in the development of health risk assessment methodology. The initial information for assessment of the equation parameters (2.2.15), which describes the risk evolution are data from scientific publications containing the results of epidemiological studies, proceedings of international and national forums, congresses, conferences, monographs, analytical materials, patents of the Russian Federation and other countries, regulatory and procedural documents of the Russian Federation, international guidelines, data of environment and

health monitoring for characterization of quality of living environment objects and health of the population, including sensitive groups.

In solving the problem of adaptation of the epidemiological studies results to identify the parameters of a multifactor evolutionary model (2.2.15), a simplification in the form of the recurrence relation with one operating factor is considered:

$$R_{t+1} = R_t + \left(\alpha R_t + \beta f\left(F\right)\right)K, \tag{2.2.35}$$

where R_{t+1} – the risk of health problems at time t + 1;

R_t – the risk of health problems at time t;

α – coefficient of background accumulation of risk;

β – coefficient reflecting the power of the factor influence on the rate of risk accumulation;

K – empirical conversion coefficient for different periods of averaging (for average annual exposure K = 1, for monthly average K = 0.083, for daily average K = 0.0027).

Algorithm for calculating the unknown coefficient β, which reflects the power of the influence of living environment factors on the rate of risk accumulation, is based on the statement: increment of the risk of health problems among the population under the impact of the level factor F, is determined by the function $f\left(F\right)$. Factor impact occurs in a period of time $\left[t_1, t_2\right]$. Then the expression that specifies the factor impact coefficient can be written as follows:

$$\beta = \frac{\left(\frac{f\left(F\right)}{f\left(F_0\right)} - 1\right) R\left(t_0\right)\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{f\left(F\right)\left(\frac{\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{e^{\alpha \cdot t_0}\alpha} - \left(t_2 - t_1\right)\right)}, \tag{2.2.36}$$

where $R\left(t_0\right)$ – the risk at the initial time;

α – coefficient of background accumulation of risk;

t_0 – the initial time;

t_1 – the start time of factor impact;

t_2 – the end time of factor impact;

$f(F)$ – function reflecting the law of the factor impact x on the rate of risk accumulation;

F_0 – The background or standard level of factor with respect to whichthe risk increment in the basic data is calculated;

F – the level of the factor for which we know the value of the risk increment.

Method of assessment of the evolutionary model parameters has features for different types of relationships. Most often in the publications relationship assessment is performed based on the application of linear models, which emanates threshold and non-threshold models. Let's consider the examples of the calculation of parameters in each of these cases.

Linear non-threshold model

In the case of application of the linear non-threshold model, the basic differential equation (2.2.6) takes the form of a linear function of factor impact:

$$\frac{dR\left(t\right)}{dt} = \alpha R\left(t\right) + \beta F. \tag{2.2.37}$$

The solution of this equation subject to the initial condition has the form:

$$R(t) = \frac{(\alpha R(t_0) + \beta F) e^{a(t-t_0)} - \beta F}{\alpha}, \quad (2.2.38)$$

where t_0 – the initial time;

$R(t_0)$ – the risk at the initial time;

If according to the original information, it is known that the risk of health problems in conditions of impact of level factor F more in *RR* times (*RR*-risk ratio), in this case a factor impact coefficient can be written in the following relationship:

$$\beta = \frac{\frac{(RR-1)R(t_0)\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{e^{a \cdot t_0}}}{F\left(\frac{\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{e^{\alpha \cdot t_0}\alpha} - (t_2 - t_1)\right)}. \quad (2.2.39)$$

As an example, let us consider the evolution of the risk of gastric cancer under the influence of active smoking factor. The following information is used as background information to determine the coefficient β: risk of gastric cancer in smokers is greater than the risk of its genesis in never-smokers is 2.6 times [Smoking and Health, 1989].

The parameters of the equation for determining the coefficient β are defined as follows. Risk $R(t_0)$ at the initial time $t_0 = 1$ is10^{-7}. Smoking starting time $t_1 = 18$ years, the time of expiration of the harmful factor $t_2 = 60$ years. The coefficient α for the background risk of gastric cancer is 0.139. The average level of influencing factor throughout the entire period of time is $[t_1, t_2]$ equal to 5 mg of nicotine Risk of gastric cancer in $N = 2,6$ times greater in the case of influencing factor. If we substitute these values in the ratio, we can calculate the value of the coefficient β:

$$\beta = \frac{\frac{(2,6-1)10^{-7}\left(e^{0,139 \cdot 60} - e^{0,139 \cdot 18}\right)}{e^{0,139 \cdot 1}}}{5 \cdot \left(\frac{\left(e^{0,139 \cdot 60} - e^{0,139 \cdot 18}\right)}{e^{0,139 \cdot 1} \cdot 0,139} - (60-18)\right)} = 4,46 \cdot 10^{-9}.$$

Linear threshold model

If a negative factor has a threshold nature, i.e. there is a level at which factor affects, the differential equation for the evolution of risk (2.2.6) is defined as follows:

$$\frac{dR(t)}{dt} = \alpha R(t) + \beta \left\langle \frac{F}{F^N} - 1 \right\rangle, \quad (2.2.40)$$

where F^N – threshold level of factor influence;

$\langle F \rangle$ – McCauley brackets: $\langle F \rangle = \max(0, F)$.

If it is known that the risk in people who are under the influence of level factor F (assuming $F > F^N$), in comparison with people who never were exposed, more in *RR* times, then the equation (2.2.36) that specifies the factor influence can be written as follows:

$$\beta = \frac{\dfrac{(RR-1)R(t_0)\left(e^{\alpha t_2}-e^{\alpha t_1}\right)}{e^{a\cdot t_0}}}{\left\langle \dfrac{F}{F^N}-1\right\rangle\left(\dfrac{\left(e^{\alpha t_2}-e^{\alpha t_1}\right)}{e^{\alpha t_0}\cdot\alpha}-(t_2-t_1)\right)}. \qquad (2.2.41)$$

As an example, let us consider the evolution of the risk of breast cancer under the influence of alcohol overindulgence factor. The following information is used as background information for finding the coefficient β: The risk of breast cancer in people daily using 40 g of alcohol, compared with people who do not exceed the rate of 30 g, is more in 1.4 times.

The parameters of the equation for determining the coefficient β are defined as follows. Risk $R(t_0)$ at the initial time $t_0 = 1$ is10^{-7}. Alcohol consumption starting time $t_1 = 18$ years, the time of expiration of the harmful factor $t_2 = 60$ years. The coefficient α for the background risk of breast cancer is 0.184. The average level of influencing factor throughout the entire period of time is $[t_1, t_2]$ equal to 40 g of absolute alcohol. Risk of breast cancer in $N = 1{,}4$ times greater in the case of factor influencing. If we substitute these values in the ratio, we can calculate the value of the coefficient β:

$$\beta = \frac{\dfrac{(1{,}4-1)10^{-7}\left(e^{0{,}184\cdot 60}-e^{0{,}184\cdot 18}\right)}{e^{0{,}184\cdot 1}}}{\dfrac{1}{3}\cdot\left(\dfrac{\left(e^{0{,}184\cdot 60}-e^{0{,}184\cdot 18}\right)}{e^{0{,}184\cdot 1}\cdot 0{,}139}-(60-18)\right)} = 2{,}21\cdot 10^{-8}.$$

Exponential threshold model

If a negative factor has a threshold nature, i.e. there is a level at which factor affects and factor influence function is given in exponential form, the differential equation for the evolution of risk (2.2.6) is defined as follows:

$$\frac{dR(t)}{dt} = \alpha R(t) + \beta\left\langle \gamma\left(1-e^{-\delta\left(F-F^N\right)}\right)\right\rangle, \qquad (2.2.42)$$

where F^N – threshold level of factor influence;

δ, γ – equation parameter;

$\langle F\rangle$ – McCauley brackets: $\langle F\rangle = \max(0,\ F)$.

If it is known that the increase of people morbidity under the influence of the level factor F (assuming $F > F^N$), is determined by the exponential equation of the following form:

$$\Delta p = -\left[\gamma\left(e^{-\delta\left(F-F^N\right)}-1\right)\right], \qquad (2.2.43)$$

where γ – the background level of incidence rate per person of the population being analyzed;

δ – equation parameter;

F^N – threshold level of factor influence;

Then the risk of people morbidity under the influence of the level factor F (assuming $F > F^N$), is determined by the equation of the following form:

$$p = \gamma - \left[\gamma\left(e^{-\delta\left(F-F^N\right)}-1\right)\right], \qquad (2.2.44)$$

where γ – the background level of incidence rate per person of the population being analyzed;

δ – equation parameter;

F^N – threshold level of factor influence;

Considering the relationship type, the equation (2.2.36) that specifies the factor influence coefficient can be written as follows:

$$\beta = \frac{\left(\frac{\gamma - \left[\gamma\left(e^{-\delta\left(F-F^N\right)}-1\right)\right]}{\gamma} - 1\right) R\left(t_0\right)\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{e^{a \cdot t_0}} \Bigg/ \left(\gamma - \left[\gamma\left(e^{-\delta\left(F-F^N\right)}-1\right)\right]\right)\left(\frac{\left(e^{\alpha t_2} - e^{\alpha t_1}\right)}{e^{\alpha t_0}\alpha} - \left(t_2 - t_1\right)\right). \quad (2.2.45)$$

The presented method allows transfering relationships between indicators of risk to human health and the values of living environment factors in relation suitable for use in the evolutionary models of health risk accumulation. The methodology takes into account the limitations of various kinds: associated with the range of definition and range of existing relationships, and limitations on the method of their description.

Work performed on the adaptation of existing relationships between living environment factors and health risk values are the basis of development of the information system "Models Library" containing parameters of relationships of the risk values from living environment factors used to develop multiple evolutionary models.

Models Library

Evolutionary model of accumulation of body organs and systems dysfunctions at macro-level is a universal tool of assessment of health risk of the population living in conditions of exposure of an arbitrary number of diverse factors. Complex of living environment factors, which have health effect, and consequently forming the risk of organs and systems dysfunctions varies greatly, differing in composition and values. In general, the number of operational factors may reach several hundred, which greatly complicates the process of simulation of the risk evolution in view of the need to perform the identification procedure for each factor.

The solution to this problem is achieved by creating and accumulation of specialized information of the system designed for rapid formation of multi-factor model of health risk evolution. The information system "Models Library" is based on the results of the identification procedures for the various living environment factors, performed according to studies materials, published in the scientific literature.

Table 2.18 shows the initial filling of the "Models library" containing parameters of about thirty paired relationships.

The technical implementation of the "Models library" developed a special structure of the database containing the attributes and linkages of tables containing data on the characteristics of living environment factors, critical organs and systems, as well as the values of relationship parameters.

The logical structure of the data of the "Models Library" block is shown in Fig. 2.13.

The structure of "Models Library" data is a collection of related tables containing parameters of relationships of factors (chemical, biological, physical, and others) influence on health risk values. The structure details tables, containing various kinds of models defined by the formula used in the computational procedures, probable responses to the factors influence with indication of relationship parameters, initial levels of probable responses. Relations between tables are set by key fields system.

Table 2.18

Example of "Models library" filling

Model name	Initial models	Source	Relationship model for recurrent relations
1	2	3	4
Noncarcinogenic risk of cardiovascular system disorders – noise	Genesis of non-specific effects: $R = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{P} e^{\frac{y}{2}} dy$, where $P = -4,551 + 0,0853x$	Instruction 2.1.8.10-12-3-2005	$\Delta R = 0,015 \left\langle \frac{F}{58,5} - 1 \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the concentration of carbon monoxide in the air	$\Delta\text{incedences} = -\left[9,33\text{E-}6\left(e^{-0,0340 \cdot \Delta CO} - 1\right)\right]$	Burnett R.T. et al., 1999	$\Delta R = 0,00065 \left\langle e^{-0,102} - e^{-0,034 \cdot F} \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the concentration of nitrogen dioxide in the air	The average content of nitrogen dioxide in ambient air 0.0735 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[2,58\text{E-}5\left(e^{-0,0378 \cdot \Delta NO_2} - 1\right)\right]$	Burnett R.T. et al., 1999	$\Delta R = 0,44 \left\langle e^{-0,000106} - e^{-0,00264 \cdot F} \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the concentration of ozone in the air	The average content of ozone in ambient air 0.0824 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[3,81\text{E-}5\left(e^{-0,00531 \cdot \Delta O_3} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0,32 \left\langle e^{-0,000159} - e^{-0,00531 \cdot F} \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the concentration of suspended substances in the air	The average content of suspended substances in ambient air 0.0168 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[3,81\text{E-}5\left(e^{-0,00704 \cdot \Delta PM_{2,5\text{-}10}} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0,105 \left\langle e^{-0,000528} - e^{-0,00704 \cdot F} \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the concentration of plumbum in foods	$\left[1/\left(1 - e^{2,744 - 0,793 \cdot \ln(Pb)}\right) - 1/\left(1 - e^{2,744 - 0,793 \cdot \ln(0,03)}\right)\right]$	CalEPA, 2003; Sherlock J.C. et al., 1982	$\Delta R = 0,004367 \left(\frac{1}{1 + exp^{2,744 - 0,793 \cdot \ln\left(5,6 + 2,62 \cdot \sqrt[3]{F}\right)}} - \frac{1}{1 + exp^{2,744 - 0,793 \cdot \ln\left(5,6 + 2,62 \cdot \sqrt[3]{0,03}\right)}} \right)$

1	2	3	4
Noncarcinogenic risk of the cardiovascular system disorders – the dose of arsenic by the oral route	Risk of disease increases by 2.51 times at 0.025 mg/l arsenic concentration in water	Hung-Yi Chiou et al., 1997	$\Delta R = 0{,}00037334\left\langle \frac{F}{0{,}0003} - 1 \right\rangle$
Noncarcinogenic risk of the cardiovascular system disorders – the dose of ractopamine by the oral route	Application of evolutionary models for health risk assessment at ractopamine admission with foods	Onishchenko G.G. et al., 2013	$\Delta R = 0{,}3352F$
Noncarcinogenic risk of the nervous system disorders – noise	Complaints from the public about noise: $R = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{P} e^{\frac{y}{2}} dy$, where $P = -6{,}5027 + 0{,}0889x$	Instruction 2.1.8.10-12-3-2005	$\Delta R = 0{,}0016\left\langle \frac{F}{43} - 1 \right\rangle$
Noncarcinogenic risk of the nervous system disorders – the concentration of formic aldehyde in the air	Regional investigations	Research report, 2009	$\Delta R = 0{,}0018\left\langle \frac{1}{1+e^{-(-5{,}18+1{,}72 \cdot F)}} - \frac{1}{1+e^{-(-5{,}18+1{,}72 \cdot 36{,}5)}} \right\rangle$
Noncarcinogenic risk of organs of hearing disorders – noise	Genesis of specific effects: $R = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{P} e^{\frac{y}{2}} dy$, where $P = -6{,}6771 + 0{,}07041x$	Instruction 2.1.8.10-12-3-2005	$\Delta R = 0{,}001\left\langle \frac{F}{50} - 1 \right\rangle$
Noncarcinogenic risk of the respiratory system disorders – the concentration of suspended substances in the air	$\Delta\text{incedences} = -\left[4{,}75\text{E-}6\left(e^{-0{,}0332 \cdot \Delta CO} - 1\right)\right]$	Burnett R.T. et al., 1999	$\Delta R = 0{,}00065\left\langle e^{-0{,}0996} - e^{-0{,}0332F} \right\rangle$
Noncarcinogenic risk of the respiratory system disorders – the concentration of sulfur dioxide in the air	The average content of nitrogen dioxide in ambient air 0.0735 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[9{,}33\text{E-}6\left(e^{-0{,}00318 \cdot \Delta NO_2} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0{,}36\left\langle e^{-0{,}000151} - e^{-0{,}00378F} \right\rangle$

Continuation of Table 2.18

1	2	3	4
Noncarcinogenic risk of the respiratory system disorders – the concentration of ozone in the air	The average content of ozone in ambient air 0.0824 mg/m^3, study group: all population $\Delta\text{случаев} = -\left[2{,}58E - 5 \cdot \left(e^{-0{,}00498 \cdot \Delta O_3} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0{,}36\left\langle e^{-0{,}000149} - e^{-0{,}00498F}\right\rangle$
Noncarcinogenic risk of the respiratory system disorders – the concentration of sulfur dioxide in the air	The average content of sulfur dioxide in ambient air 0.0210 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[2{,}58E - 5 \cdot \left(e^{-0{,}00446 \cdot \Delta SO_2} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0{,}26\left\langle e^{-0{,}000233} - e^{-0{,}00466F}\right\rangle$
Noncarcinogenic risk of the respiratory system disorders – the concentration of suspended substances in the air	The average content of suspended substances in ambient air 0.0168 mg/m^3, study group: all population $\Delta\text{incedences} = -\left[2{,}58E - 5 \cdot \left(e^{-0{,}00147 \cdot \Delta PM_{2{,}5-10}} - 1\right)\right]$	Burnett R.T. et al., 1997	$\Delta R = 0{,}33\left\langle e^{-0{,}00011} - e^{-0{,}00147F}\right\rangle$
Noncarcinogenic risk of the nervous system disorders – the concentration of phenol in the air	Regional investigations. Rated concentrations – 0.0000081 to 0.0027 to 0.00369 mg/m^3. Approximation results – 0.00042 to 0.2304 mg/m^3, study group: child population at the age of 4 to 7 years, 249 persons	Research report, 2011	$\Delta R = 0{,}0014 \times \times\left\langle \frac{1}{1+e^{-(-0{,}406+360{,}5F)}} - \frac{1}{1+e^{-(-0{,}406+360{,}5 \cdot 0{,}0033)}}\right\rangle$
Noncarcinogenic risk of the nervous system disorders – the concentration of formic aldehyde in the air	Regional investigations. Rated concentrations – 0.0003 to 0.002 mg/m^3. Approximation results – 0.0011 to 0.0618 mg/m^3, study group: child population at the age of 4 to 7 years, 249 persons	Research report, 2011	$\Delta R = 0{,}0043 \times \times\left\langle \frac{1}{1+e^{-(-0{,}072+150{,}6F)}} - \frac{1}{1+e^{-(-0{,}072+150{,}6 \cdot 0{,}013)}}\right\rangle$
Noncarcinogenic risk of the urinary system disorders – the dose of chloroform by the oral route	Regional investigations	Research report, 2009	$\Delta R = 0{,}00057 \times \times\left\langle \frac{1}{1+e^{-(-5{,}88+1{,}68F)}} - \frac{1}{1+e^{-(-5{,}88+1{,}68 \cdot 0{,}01)}}\right\rangle$

Continuation of Table 2.18

1	2	3	4
Noncarcinogenic risk of the urinary system disorders – the concentration of plumbum in foods	Risk of disease increases by 1.08 times at 0.013 mg/l plumbum concentration in blood	CalEPA, 2003; Sherlock J.C. et al., 1982	$\Delta R = 8,83 \cdot 10^{-5} \left\langle \frac{\left(5,6 + 2,62 \sqrt[3]{F}\right)}{\left(5,6 + 2,62 \sqrt[3]{0,03}\right)} - 1 \right\rangle$
Noncarcinogenic risk of the urinary system disorders – the dose of cadmium by the oral route	Change in renal incidence rate 1% causes dose of Cadmium of 0.018 mg/kg-day	Nogawa, K. an T. Kido, 1993	$\Delta R = 9,8 \cdot 10^{-5} \left\langle \frac{F}{0,0005} - 1 \right\rangle$
Noncarcinogenic risk of organs of vision disorders – the concentration of total ferrum in foods	Regional investigations The average content of ferrum – 0.035 mg/l. Study group: child population, 198 persons	Research report, 2009	$\Delta R = 0,00035 \times \left\langle \frac{1}{1+e^{-(-4,12+0,31F)}} - \frac{1}{1+e^{-(-4,12+0,31 \cdot 0,3)}} \right\rangle$
Noncarcinogenic risk of blood, hemopoietic organ disorders – the concentration of total ferrum in foods	Regional investigations. The average content of ferrum – 0.035 mg/l. Study group: child population, 198 persons	Research report, 2009	$\Delta R = 0,00052 \times \left\langle \frac{1}{1+e^{-(-5,64+1,22x)}} - \frac{1}{1+e^{-(-5,64+1,22 \cdot 0,3)}} \right\rangle$
Noncarcinogenic risk of blood, hemopoietic organ disorders – the concentration of nitrates in foods	Regional investigations	Research report, 2009	$\Delta R = 0,00052 \times \left\langle \frac{1}{1+e^{-(-6,89+0,04F)}} - \frac{1}{1+e^{-(-6,89+0,04 \cdot 1,6)}} \right\rangle$
Noncarcinogenic risk of skin disorders – the concentration of total ferrum in foods	Regional investigations. The average content of ferrum – 0.035 mg/l. Study group: child population, 198 persons	Research report, 2009	$\Delta R = 0,00035 \times + \left\langle \frac{1}{1+e^{-(-4,93+1,03F)}} - \frac{1}{1+e^{-(-4,93+1,03 \cdot 10,95)}} \right\rangle$
Noncarcinogenic risk of the digestive disorders – the concentration of chloroform in foods	Regional investigations	Research report, 2009	$\Delta R = 0,0048 \times \left\langle \frac{1}{1+e^{-(-9,01+8,82F)}} - \frac{1}{1+e^{-(-9,01+8,82 \cdot 0,01)}} \right\rangle$

Continuation of Table 2.18

1	2	3	4
The risk of gastric cancer – specific activity of strontium-90 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 81 additional case of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 2{,}8 \cdot 10^{-8} \cdot 0{,}71 \cdot 10^{-4} F$
The risk of gastric cancer – specific activity of cesium-137 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 81 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 1{,}3 \cdot 10^{-8} \cdot 0{,}71 \cdot 10^{-4} F$
The risk of esophageal cancer – specific activity of strontium-90 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 23 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 2{,}8 \cdot 10^{-8} \cdot 2{,}32 \cdot 10^{-4} F$
The risk of esophageal cancer – specific activity of cesium-137 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 23 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 1{,}3 \cdot 10^{-8} \cdot 2{,}32 \cdot 10^{-4} F$
The risk of lung cancer – specific activity of strontium-90 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 198 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 2{,}8 \cdot 10^{-8} \cdot 4{,}12 \cdot 10^{-4} F$
The risk of lung cancer – specific activity of cesium-137 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 198 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 1{,}3 \cdot 10^{-8} \cdot 4{,}12 \cdot 10^{-4} F$
The risk of bladder cancer – specific activity of strontium-90 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 48 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 2{,}8 \cdot 10^{-8} \cdot 0{,}55 \cdot 10^{-4} F$
The risk of bladder cancer – specific activity of cesium-137 (oral exposure route)	At single exposure of dose of 0.1 Sv – lifetime risk is 48 additional cases of gastric cancer (per 100 thousand).	UNSCEAR, 2008	$\Delta R = 1{,}3 \cdot 10^{-8} \cdot 0{,}55 \cdot 10^{-4} F$
Risk of shigellosis – dose of *Shigella spp*, coming with foods	Equation – model of Poisson beta-distribution $P = 1 - \left(1 + \frac{x\left(2^{\frac{1}{b_1}} - 1\right)}{b_2}\right)^{-b_1}$,	Strachan N.J. et al., 2005	No accumulation of risk, the risk at daily consumption: $R = 1 - \left(1 + \frac{F\left(2^{\frac{1}{0{,}266}} - 1\right)}{1479{,}1}\right)^{-0{,}266}$

1	2	3	4
	where P – disease probability; x – obtained bacterium dose; Equation parameters: $\log_{10} b_2 = 3{,}17$; $b_1 = 0{,}266$		
Risk of salmonellosis – dose of *Salmonella Typhi*, coming with foods	Equation - model of Poisson beta-distribution $P = 1 - \left(1 + \frac{x\left(2^{\frac{1}{b_1}} - 1\right)}{b_2}\right)^{-b_1}$, where P – disease probability; x – obtained bacterium dose; Equation parameters: $b_2 = 1110000$; $b_1 = 0{,}175$	Hornick R.B. et al., 1966; Hornick R.B. et al., 1970	No accumulation of risk, the risk at daily consumption: $R = 1 - \left(1 + \frac{F\left(2^{\frac{1}{0{,}175}} - 1\right)}{1110000}\right)^{-0{,}175}$
Risk of listeriosis – dose of *Listeria monocytogenes*, coming with foods	Equation – exponential model $P = 1 - e^{-b_1 x}$, where P – disease probability; x – obtained bacterium dose. Equation parameters: $b_1 = 5{,}6 \cdot 10^{-10}$	FDA/FSIS, 2003	No accumulation of risk, the risk at daily consumption: $R = 1 - e^{-5{,}6 \cdot 10^{-10} F}$
The risk of renal lithiasis – melamine dose by the oral route	Risk increases by 10% at melamine dose of 0.74 mg/kg per unit weight	Scientific Opinion on Melamine in Food and Feed, 2010	$\Delta R = 6{,}19 \cdot 10^{-8} \left\langle \frac{F}{0{,}2} - 1 \right\rangle$

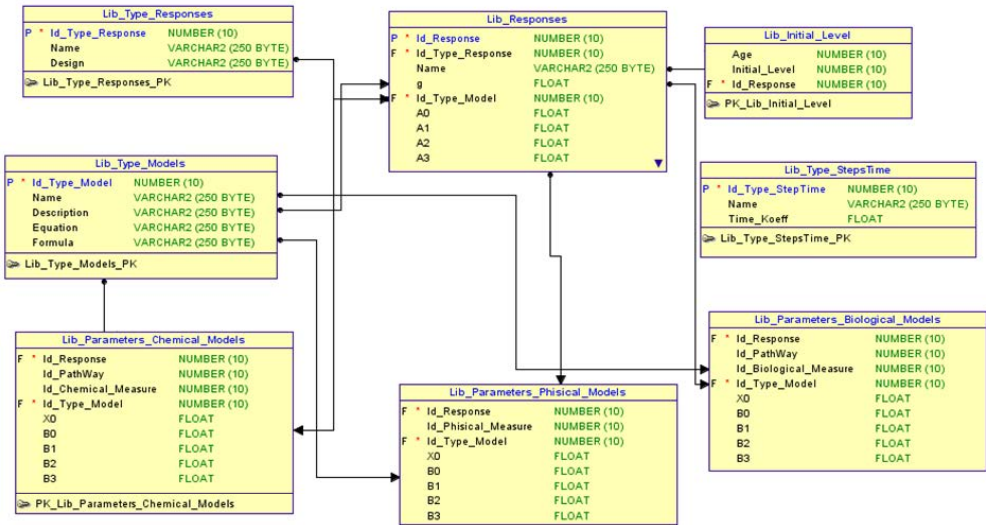


Fig. 2.13. Basic structure of the database of information system "Models Library"

Filling of the "Models Library" is a continuous process involving the interaction of research groups, exchange of research results at scientific conferences, monitoring of scientific publications in national and international publications.

Risk assessment and risk structure analysis using evolutionary macro models

The numerical implementation of evolutionary model in the form of the recurrence relations (2.2.15) with the identified parameters recorded in the "Models Library" allows calculations to be performed with regard to the risk of body organs and systems dysfunctions for arbitrary conditions on the composition and level of operating factors. Moreover, the model allows taking into account the variables of factors exposure associated with changes in the socio-economic living conditions, working conditions, schedules of work and rest At that the method of evolutionary simulation allows prediction and assessment of the consequences of health impact factors both in the aggregate and separately. The following is allocated as a part of the calculation procedures used for health risk analysis:

– calculation of additional risk;
– calculation of indicators to analyze the risk structure;
– calculation of indicators for risk assessment.

Additional risk indicator

An additional risk is the main indicator of the impact of factors on health. To calculate the additional risk, it is necessary to define at least two exposure scenarios, one of which reflects the actual factor levels, the second - the background factor levels. Most often scenario of accumulation of the risk of organs and systems dysfunctions only due to natural causes, i.e., in the absence of relevant factors is used as background.

Additional risk at each time point is calculated as the risk difference in the actual and background exposure of factors:

$$\Delta R_j(t) = R_j(t) - R_j^{\Phi}(t)\,, \qquad (2.2.46)$$

where $\Delta R_j(t)$ – additional risk of *j*-th system disorder at the age of *t*;

$R_j(t)$ – the risk of *j*-th organ system disorder under the influence of a combination of factors, in accordance with the actual exposure scenario;

$R_j^{\Phi}(t)$ – the risk of *j*-th organ system disorder without the influence of factors (in accordance with the background scenario).

Illustration of the additional risk calculation based on evolutionary models is shown in Fig. 2.14.

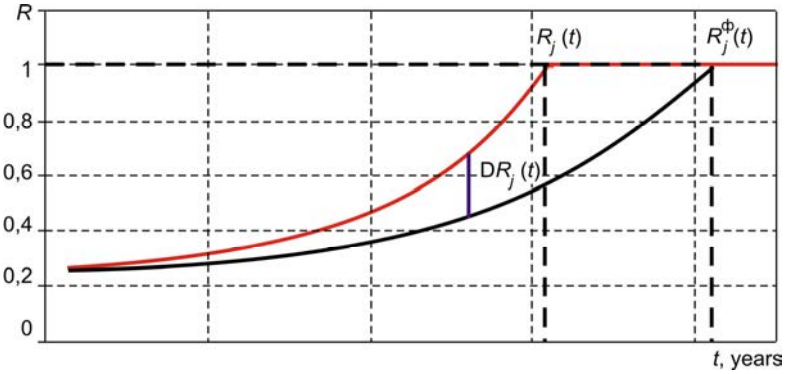


Fig. 2.14. Simulation of the evolution of risk and additional risk of health problems

Estimated risk values

Calculations of risk values make it possible to analyze the contributions of the individual factors in the formation of health problems during the exposure time. Special estimation scale based on the calculation of the given index of health risk associated with factors exposure is used at the same time to perform the categorization of risk:

$$\tilde{R}(t) = \frac{\Delta R(t)}{1 - R^{\Phi}(t)}. \qquad (2.2.47)$$

Mentioned risk index indicates the probability of health problems at impact of factors with regard to the increase of the overall health risk in proportion to increase of the exposure duration.

Recommendations for the management of the health disorders risk associated with the effect of factors can be developed based on the following assessment scale of index $\tilde{R}$ (Fig. 2.15):

- value $\tilde{R}$ is less than 0.05, which can be assessed as *negligible risk*, which is no different from ordinary, everyday risks; there is no necessity in measures to reduce the health risk;
- value $\tilde{R}$ is in the range of 0.05–0.35, which can be assessed as *moderate risk*. It is recommended to inform the public about the presence of risk. It is recommended to perform planned reassessment at a frequency of at least once every three years;
- value $\tilde{R}$ is in the range of 0.35–0.6, which can be assessed as *high risk*. It is recommended to inform the public about the presence of risk. Development of special measures is recommended to reduce risk. It is recommended a further review of risk during the year;
- value $\tilde{R}$ exceeds the level of 0.6, which is assessed as very high risk. It is recommended to inform the public about the presence of risk.

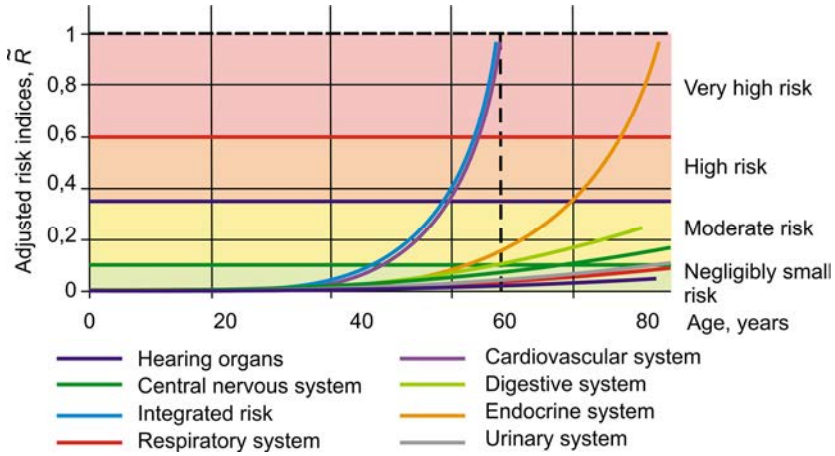


Fig. 2.15. Scale of mentioned risk index assessment $\tilde{R}$

The model of risk evolution enables estimative risk calculations for any age groups of the population, exposed to prolonged and irregular factors exposures. In addition, the risk assessment methodology based on evolutionary simulation, provides an analysis of risk category change time. In accordance with the scale of assessments it is determined the time at which the boundary values of mentioned risk index:

$$T_{0,05} = t\big|_{\hat{R}_t=0,05},$$

$$T_{0,35} = t\big|_{\hat{R}_t=0,35},$$

$$T_{0,6} = t\big|_{\hat{R}_t=0,6},$$

$$T_1 = t\big|_{\hat{R}_t=1}.$$

The time of risk transfer from one category to another allows determining the critical parameters of factors exposure and predicting the losses associated with reduction in life expectancy.

The critical parameters of factors exposure are dynamic characteristics of influencing factors at which the risk is acceptable (negligible or moderate) during the time corresponding to the life expectancy, i.e. $T_{0..05}$ = LE.

Life expectancy is a calculated value at which the risk reaches 1 (T_1).

Indicators to analyze the risk structure

The following indicators are used to analyze the structure of risk characterizing:

– the contributions of the risk of the individual organs and systems disorders to the overall risk of functional disorders of the whole organism;

– the contributions of individual factors to the additional risk of health problems;

– the contribution of individual factors to the change in the projected life expectancy.

Analysis of the structure of the organs and systems disorders risk provides the integration procedure implementation according to the relation (2.2.16). The following designations should be adopted to emphasize the importance of the integration procedure:

– $R^{Int}(t) = 1 - \prod_{j=1}^{r}\left(1 - R_j(t)\right)$ – integrated risk of body disorders under the influence of factors;

– $R^{Int/\Phi}(t) = 1 - \prod_{j=1}^{r}\left(1 - R_j^{\Phi}(t)\right)$ – integrated risk of body disorders without the influence of factors;

– $\Delta R^{Int}(t) = R^{Int}(t) - R^{Int/\Phi}(t)$ – additional integrated risk of body functions disorders.

The following contributions are calculated to analyze the structure of risk according to the disorders of individual organs and systems:

– the absolute contributions of risk of the disorders of individual organs to an integrated additional risk according to the relation (2.2.46);

– a relative contribution:

$$\delta\left(\Delta R_j(t)\right) = \frac{\Delta R_j(t)}{\Delta R^{Int}(t)} 100\ \%. \qquad (2.2.48)$$

The calculation of the following contributions is performed to analyze the structure of contributions of the individual factors to the additional risk of body organs and systems disorders:

– an absolute contribution due to the influence of individual factors:

$$\Delta R_j^i(t) = R_j^i(t) - R_j^{\Phi}(t)\ , \qquad (2.2.49)$$

where $\Delta R_j^{\ i}(t)$ – is an additional risk of the *j*-th organ systems disorders associated with exposure to a single *i*-th factor,

$R_j^i(t)$ – the risk of the *j*-th organ systems disorders under the influence of individual *i*-th factor;

$R_j^{\Phi}(t)$ – the relative contribution of individual factors:

$$\delta(\Delta R_j^{\ i}) = \frac{\Delta R_j^{\ i}(t)}{\sum_i \Delta R_j^{\ i}(t)} 100\ \%, \qquad (2.2.50)$$

where $\delta(\Delta R_j^{\ i})$ – is the proportion of the *i*-th factor contribution to the additional risk of the *j*-th organ systems disorders.

The analysis of the structure of individual factors' contributions to the change in the projected life expectancy is performed based on calculation of the exposure time at which the risk value reaches a unity. The time point t is a predicted age of death or projected life expectancy, when the value of the integral risk is equal to a unity. Change in the projected life expectancy under the conditions of environmental factors exposure is determined by the following formula

$$\Delta T = T^{\Phi} - T\ , \qquad (2.2.51)$$

where T – the projected life expectancy in terms of exposure factors;

T^{Φ} – projected lifetime without factors exposure;

ΔT – change in the projected life expectancy in terms of exposure factors.

Changes the projected life expectancy under the impact of a single factor is determined by the following formula

$$\Delta T^i = T^{\Phi} - T^i\ , \qquad (2.2.52)$$

where T^i – the projected life expectancy in terms of exposure of the *i*-th environmental factor;

ΔT^i – change in the projected life expectancy in terms of exposure of the *i*-th environmental factor.

The following formula is used to determine the proportion of the individual factor's contribution to the change in the projected life expectancy in terms of exposure to the combination of factors

$$I^i = \frac{\Delta T^i}{\sum_i \Delta T^i} 100\ \%\ , \qquad (2.2.53)$$

where I^i – the proportion of the *i*-th factor contribution to the change in the projected life expectancy.

The absolute value of each factor's contribution to the change in the projected life expectancy in terms of factors exposure is determined by the following formula

$$L^i = I^i \Delta T\ , \qquad (2.2.54)$$

where L^i – the *i*-th factor's contribution to the change in the projected life expectancy.

The risk values under the impact reflect mainly the long-term trend of health indicators change emerging subject to all the initial conditions (for example, a certain duration and intensity of exposure, the exposure immutability through time, the specific values of the exposure factors, etc.) accepted in the calculations.

Thus, the developed system of risk indicators allows the evaluation and structural analysis in three areas. The first area involves the study of the major health disorders' structure (differentiation by organs and systems), the second area is analysis of the factors' contribution to the formation of the health risk disorders (differentiation by factors), the third area involves the analysis of the factors' contributions to the change in the projected life expectancy. However, the methodology of evolutionary simulation suggests the possibility of analytical calculations at any specific time.

It should be noted that the estimated risk scale is universal and allows to perform estimative calculations both for generalized (integrated) additional risk indicators taking into account the effect of all factors combination on all body systems, and for all of their structural elements.

Calculation of an additional morbidity and mortality based on the evolutionary simulation of population health risk

The general algorithm of a quantity assessment of additional morbidity and mortality incidence associated with the risk of body organs' and systems' disorders is based on an analysis of the age distribution of health indicators [Kirjanov D.A., Kamaltdinov M.R., 2014], and involve consistent fulfillment of several steps (Fig. 2.16):

Stage 1. The calculation of the risk of body organs' and systems' disorders with and without the exposure of environmental factors (R_t^j, $R_t^{j/\Phi}$).

Stage 2. The assessment of the average population disease severity index g_i in terms of the body organs' and systems' disorders. Assessment of disease severity is based on a comparison of the data obtained with the use of expert estimates and data provided by territorial fund of compulsory health insurance.

Stage 3. The calculation of the average population risk of body organs' and systems' disorders ($\bar{R}_t^j$) based on the population mortality and morbidity data, taking into account the severity of disease.

Stage 4. The construction of a system of reduced population morbidity $\tilde{z}_t^{ji}$ and mortality $\tilde{s}_t^{ji}$ rates corresponding to the evolutionary curve of health risk accumulation without the influence of environmental factors.

Stage 5. The construction of a system of estimated population morbidity z_t^{ji} and mortality s_t^{ji} rates corresponding to the evolutionary curve of health risk accumulation under the influence of environmental and lifestyle factors.

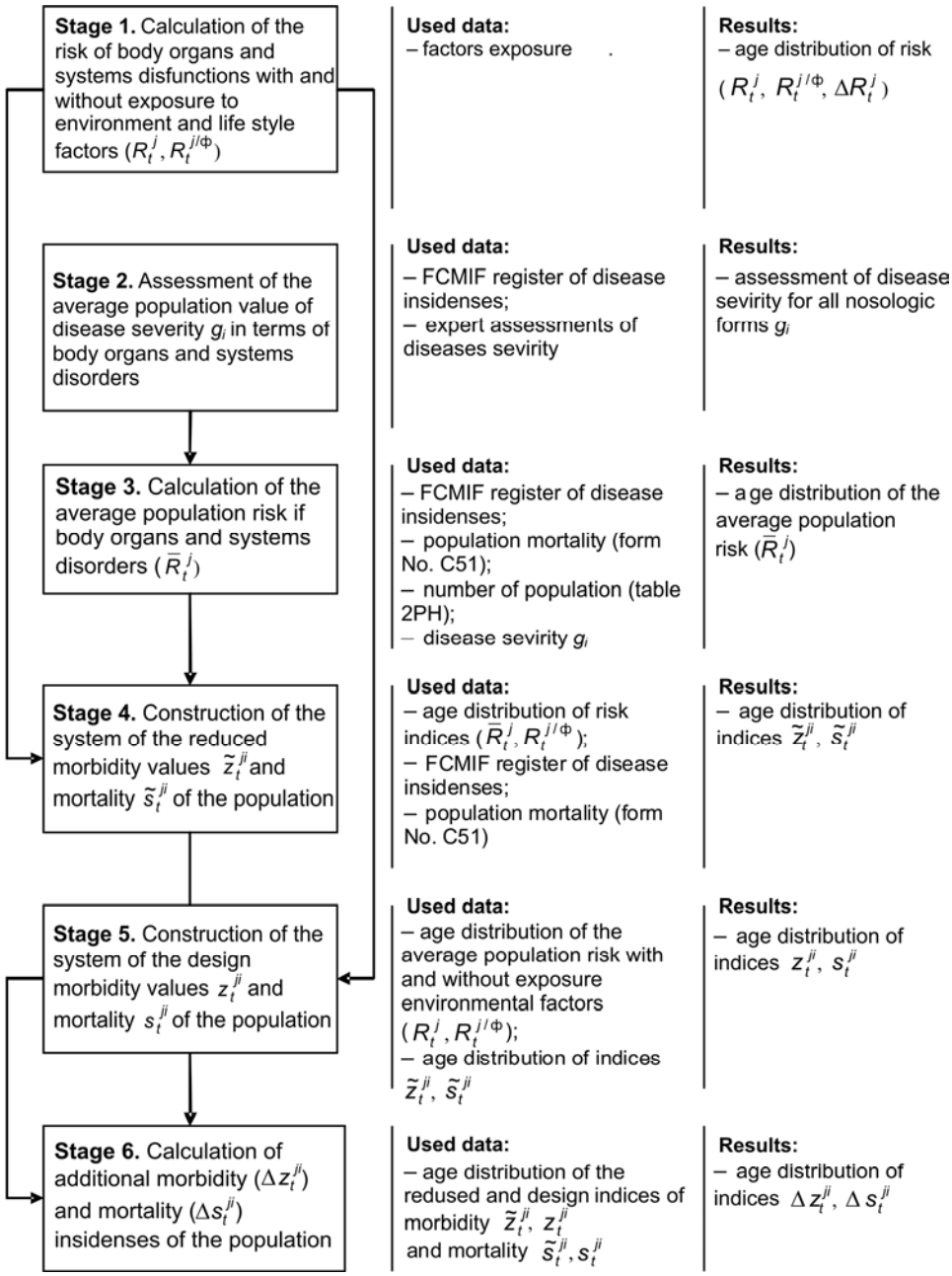


Fig. 2.16. The general algorithm of a quantitative assessment of additional morbidity and mortality incidences associated with the risk of organs' and body systems' disorders

Stage 6. The calculation of additional population morbidity (Δz_t^{ji}) and mortality (Δs_t^{ji}) incidences associated with the risk of accumulation of body organs' and systems' disorders.

Reduction factors are calculated according to the ratio between the values corresponding to the average population risk of body organs' and systems' disorders, the estimated level of risk when exposed to the studied factors and background evolutionary risk curve:

$$k_t^j = \frac{R_t^{j/\Phi}}{\bar{R}_t^j}, \quad I_t^j = \frac{R_t^j}{R_t^{j/\Phi}}. \tag{2.2.55}$$

The reduced and estimated system of population morbidity and mortality rates is defined by the relations:

$$\begin{array}{ll} \tilde{z}_t^{ji} = \bar{z}_t^{ji} k_t^j & z_t^{ji} = \tilde{z}_t^{ji} I_t^j \\ \tilde{s}_t^{ji} = \bar{s}_t^{ji} k_t^j, & s_t^{ji} = \tilde{s}_t^{ji} I_t^j, \end{array} \tag{2.2.56}$$

where $\tilde{z}_t^{ji}$, z_t^{ji} – the estimated and reduced *i*-th disease morbidity of the *j*-th system at the *t* age;

$\tilde{s}_t^{ji}$, s_t^{ji} – the estimated and reduced mortality due to *i*-th disease of *j*-th systems at the *t* age.

Additional morbidity and mortality is defined as the difference between the calculated and reduced values:

$$\begin{array}{l} \Delta z_t^{ji} = z_t^{ji} - \tilde{z}_t^{ji} \\ \Delta s_t^{ji} = s_t^{ji} - \tilde{s}_t^{ji}, \end{array} \tag{2.2.57}$$

where Δz_t^{ji} – an additional *i*-th disease morbidity of the *j*-th system at the *t* age;

Δs_t^{ji} – an additional mortality due to *i*-th disease of *j*-th systems at the *t* age.

Algorithm for a quantitative assessment of population health risk indices allows supplementing the individual risk assessment using evolutionary models with a forecast of the number of additional incidences of illness and death associated with exposure to environmental factors. The proposed algorithm can be used in the evaluation and analysis of the population health risk based on evolutionary simulation. In addition, the obtained results can serve as a basis for the organization of in-depth studies of the environmental factors effect on the health, and for medical preventive measures.

Thus, simulation of the macro-level risk evolution is a fully formed section of the risk assessment concept focused on the use of evolutionary models. In this case, the basic provisions of this section are published in scientific publications of various levels are discussed at national and international conferences, implemented in the form of guidance documents, and tested in practice.

Suggested approaches include all simulation stages starting with conceptual positions and finishing with the implementation in the form of software. It should be noted that the methodology includes both theoretical foundations and positions, and approaches suitable to understand and use in solving practical problems of risk assessment and analysis.

The consideration of the health risk as an evolutionary process associated with constant exposure to a complex of heterogeneous environmental factors on human, essentially develops classical approaches. Moreover, the technology of models parameters identification and their adaptation to the evolution implies the absence of conflicting results in comparison with classical approaches.

The vector of the further development of evolutionary simulation involves the expansion and refinement of the possibilities of the method by interfacing with meso-level models considering the deeper and more detailed processes of health disorders formation.

Construction of meso-level mathematical models

The development of health risk accumulation model at the meso-level provides for the submission of functioning of individual body organs and systems as a complex dynamic process combining morphological, functional and geometric features. Moreover, meso-models involve the allocation of the entire set of biomechanical, biochemical and bioelectrical processes occurring in the bodies or parts thereof. At that, the organ and the system are considered in a close relationship with other organs and systems of the body, and this connection is determined taking into account the parameters of injury (risk of functional disorders) obtained as a result of the macro level simulation.

Geometry of organs, their morphological and functional structure becomes essential when considering the meso-level processes. Consideration of the processes occurring in the body, from the perspective of the systematic analysis provides a detailed and in-depth understanding of the laws governing the formation of functional disorders, their localization, the possible consequences for the body as a whole.

Taking into account the complexity and diversity of the processes occurring in the body (mechanical, gas- and hydrodynamic, biochemical, bioelectric etc.), there is no typical approach to the construction of meso-level models.

In this regard, the solution of simulation tasks at the meso-level requires the development of original mathematical and technical solutions. The following two examples of mathematical description of meso-level processes illustrate the diversity of methodological approaches to simulation, and opportunities for the in-depth analysis of health risk.

The submodel of digestive system [Trusov P.V. et al., 2012]

The simulation of processes occurring in the digestive system is focused on the development of tools for integrated forecasting of the risk of pathological conditions in different parts of the gastrointestinal tract, based on the damage of absorption, motility, and secretion functions in different areas. Statement of the simulation problem involves the interaction with other organs and systems of the body, especially the circulatory, nervous, and endocrine ones.

The simulation of physiological processes occurring in the digestive system was traditionally based on experimental approaches, but mathematical models developed within the *Physiome* project have appeared in the last 5–10 years [Schulze K., 2006; Woda A. et al., 2006; Kong F., Singh R.P., 2008; Liao D. et al., 2008].

The existing models of the digestive system include the allocation of three main processes: bolus formation in the oral cavity, food mixing and absorption in the intestine. Most researchers consider each process separately describing the special submodels.

The interactions of digestion subsystems and also relations with the state of other organs are considered for the problem of simulation of the digestive system disorders accumulation.

The model of the "meso-level" of digestion in the cavity of the gastrointestinal tract combines modern concepts of the description of the digestive processes in various tract sections with the addition of body organs and systems functionality taking into account the impact factors (Fig. 2.17).

The conceptual formulation assumes that digestive system consists of the gastrointestinal tract (oral cavity, esophagus, stomach, intestine), pancreas, and liver. The implementation of the digestive process is ensured by the three physiological functions – secretory, motor, and absorptive, which are necessary for the conversion of complex nutrients to simpler ones able to be absorbed by the human body [Korotko G.F., 2004]. Secretion is the process of formation of the substances incoming from blood into the secretory cells, liquids with biologically active substances followed by their emission to the cavity of the gastrointestinal tract. Motor function performing the mixing and movement of food through the gastrointestinal tract is provided by the contractile activity of the gastrointestinal walls caused by the transmission of nerve impulses. The suction process is a transport of food components from the digestive tract cavity into the blood system of the

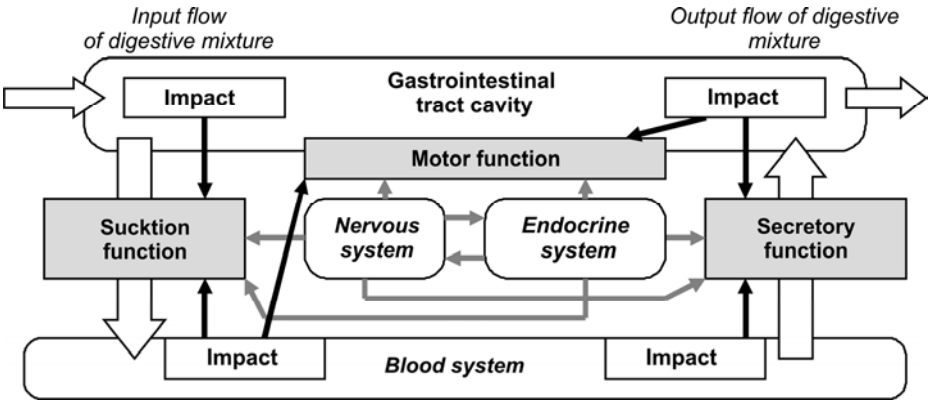


Fig. 2.17. The functions of the digestive system

human body [Human Physiology, 1997*a*, 1997*b*]. The control over the digestive process is carried out through the nervous and endocrine systems. Depending on the particular gastrointestinal tract section, general scheme is concretized, specified, detailed by additional structural elements, parameters, and relations.

The proposed model has a streaming nature, according to which all interactions between the organs and external environment are carried out by the flow of matter and energy [Trusov PV et al., 2012] resulting from metabolic processes. The digestive system is one of the major sources of substances (both useful and harmful) entering the body. The digestive system damage occurs due to metabolic imbalance. Furthermore, the flow of harmful substances located in the gastrointestinal tract cavity may have a damaging effect directly on the tract wall. Substances received by the blood system during the suction through the wall of the gastrointestinal tract, are distributed throughout the body and can have noci-influence on other organs and systems. The macro-level model shows the relationship for substances that have a systemic impact through the blood system. An equation binding the flow and concentration in the gastrointestinal tract can be used for substances that have an impact by the intake of food into the body:

$$p_{ji}(t) = \overline{\gamma}_{ji}\overline{C}_i(t), \tag{2.2.58}$$

where $p_{ji}(t)$ – the flow of the *i*-th substance to the *j*-th body, kg/s;

$\overline{C}_i(t)$ – the concentration of the *i*-th substance in the near-wall layer of the gastrointestinal tract cavity, kg/m^3;

$\overline{\gamma}_{ji} \geq 0$ – proportionality factor characterizing the intake rate of the *i*-th substance to the *j*-th body, m^3/s.

The associated organ (system) functionality $F_j(t)$ can be determined according to the level of damage. The functionality is the ability of the *j*-th body to perform its motor, secretory, and absorptive functions in relation to the digestive system.

The meso-level model considers the movement of multiphase mixture (suspension) in the complex channel with moving boundaries, in the first approximation, we can consider the two-phase system. The first phase is a liquid with chemicals dissolved at the molecular level, the second phase is the solid food particles. Digestive processes at the initial stage - in the oral cavity and stomach – are discussed more detailed at this stage of the simulation. The size of the second phase particles at the beginning of the digestive process is determined using the Rosin-Rammler equation [Olthoff LW et al., 1984] and depends on the functional state of the dento-facial system and the number of masticatory cycles. The

construction of a two-dimensional model of the stomach with moving boundaries is performed taking into account the parameters of the contraction waves in the antral segment based on the results of ultrasound examination performed by qualified personnel. The elements of the neuroendocrine regulation model are used in the simulation of acid secretion through the wall of the gastrointestinal tract [Joseph I.M. et al., 2003; Marino S. et al., 2003]. The process of chemicals' suction through the stomach wall is described by the diffusion equation (the main mechanism of the absorption of substances in the gastrointestinal tract).

It is assumed that the decrease in the secretory functionality is expressed by the reduction of the rate of secretions emission by glands, for example, the production of acid in the stomach, saliva in the oral cavity. Recession of motor functionality generally can be represented by changing the characteristics of peristaltic waves running through the digestive tract, for example, by reduction in their amplitude. Reduced absorption functionality can be described through the decrease of the diffusion coefficient in equation of substance transport from the gastrointestinal tract into the blood system. The disorder of the functionality of control systems is taken into account in relation describing the regulation of gastric acid secretion in general – in the body parts responsible for the neurohumoral elements production rate.

In mastication, the food is grinded, which leads to an increase in the surface area available for further digestion. The particle size distribution after grinding is described by Rosin-Rammler equation:

$$Q(r) = 100\{1 - exp[-(r / r_{50})^b \ln 2]\}, \quad (2.2.59)$$

where $Q(r)$ – the relative mass of particles with a diameter less than r;

median r_{50} – the size of a square lattice of a theoretical sieve sifting 50% of the particles mass;

$b > 0$ – the parameter characterizing the distribution width; the increase of the value b leads to an increase of the curve slope and a decrease of the distribution width.

Experimental data show that the dependence r_{50} on the number of masticatory cycles (*N*) can be described by the relation [Kawashima K. et al., 2009]:

$$r_{50}(N) = (R - K)e^{-aN} + K, \quad (2.2.60)$$

where a, K – parameters describing the rate of decrease in the median value r_{50};

R – median value of the particle size distribution prior to mastication.

The damage of dento-facial system is determined based on the number of healthy and prosthetic teeth:

$$D_1 = 1 - M_z / M_{max} - \eta M_{zp} / M_{max}, \quad (2.2.61)$$

where M_{max} – is the normal number of teeth of a healthy human (28–32 teeth);

M_z – is the number of healthy teeth of the studied individual;

M_{zp} – is the number of prosthetic teeth in the studied individual;

η – is the factor determining the ratio of contributions M_z, M_{zp} to the damage. Since an average particle size is 1.7 times larger after mastication in people with full dentures compared to the size of the particles in people without dento-facial system disorders [Mishellany A. et al., 2008], the coefficient η is equal to 0.59.

The increase of the relation complexity (2.2.59) by adding the functionality of dento-facial system $F_1 = 1 - D_1$ results in the relation

$$Q(r) = 100\{1 - exp[-(r / ((R - K)e^{-aNF_1} + K))^b \ln 2]\}. \quad (2.2.62)$$

The results of calculations according to the equation (2.2.62) at twenty masticatory cycles show significant difference in the size of food particles depending on the functionality of dento-facial system. The resulting particle size distributions are used in the simulation of the digestive mixture movement in the subsequent sections of the gastrointestinal tract. It is subsequently assumed to take into account the secretory function of the oral cavity.

The simulation of digestion in the stomach focuses on the development of the model of food mixing with the wave reduction propagation in the antral segment, as there are the effects of contractile motor activity ensuring the homogenization and mixing of digestive mixture that are most pronounced in this part of the gastrointestinal tract.

The mixing process of the digestive mixture occurs due to the propagation of the stomach wall contraction waves - a compression of areas (bands) of the circular muscle layer over the entire circumference of the stomach. The main parameters of the waves are the amplitude of contraction d_c, the width of the wave λ, and the wave velocity v (Fig. 2.18). In published studies [Pal A. et al., 2004] there are indicated the average values: the average velocity along the axis X – $v_x^{cp} = -2{,}5 \cdot 10^{-3}$ m/s, the wave width – λ = 0.018 m, the contraction amplitude is given using the ratio of the distance between the walls in the contracted and uncontracted state, which has a value from 1 to 0.1 as the wave moves to the pyloric opening.

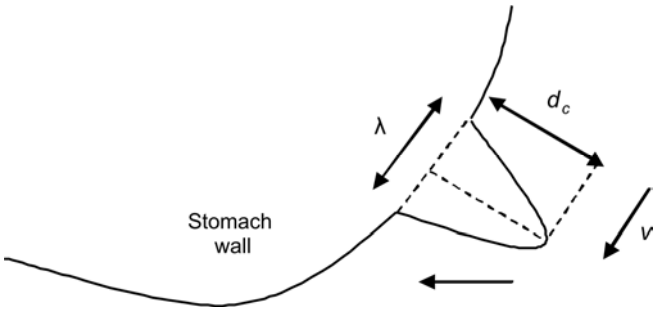


Fig. 2.18. Parameters of the contraction wave in the antrum

In the model the flow of a viscous incompressible fluid is considered, the equation of motion can be written as:

$$\frac{\partial v}{\partial t} + (v\nabla)v = \frac{-\nabla P}{\rho} + \nu \Delta v \,, \tag{2.2.63}$$

where v – velocity;

P – pressure;

ρ – density of the medium;

ν – kinematic viscosity factor.

Functional disorders in gastric motility are taken into account when setting the parameters of the wave amplitude of antral contractions in the following form: $d_c F_2$, where F_2 – gastric functionality ($F_2 = 1 - D_2$).

Most toxicants and nutrients are absorbed by the digestive tract through diffusion, the rate of absorption V_a through the stomach wall in terms of functionality may be calculated using the relation

$$V_a = F_2 SB\left\langle \bar{C} - hC^b \right\rangle, \tag{2.2.64}$$

where S – the surface area of absorption, m^2;

B – diffusion coefficient, m/s;

$\bar{C}$ – the concentration of the *i*-th substance in the near-wall layer of the gastrointestinal tract cavity, kg/m^3;

C^b – the concentration of the substance in blood, kg/m^3;

h – the non-dimensional coefficient of substance solubility in blood.

It should be noted that in most cases the inverse substance intake (at $C^b > \bar{C}$) from blood into the lumen of the gastrointestinal tract does not occur (other excretion mechanisms predominate), so (2.2.64) uses McCauley brackets: $\langle x \rangle = max(0,\ x)$.

The stomach images (the vertical position of the body) in planes parallel to the two main anatomical planes are obtained as a result of ultrasound investigation: horizontal (parallel to the ground level) and middle one (dividing the human body into two symmetrical halves). At a first approximation, stomach size is estimated and two-dimensional form antral segment is restored in the third main (front) anatomical cross-section perpendicular to the first two (Fig. 2.19).

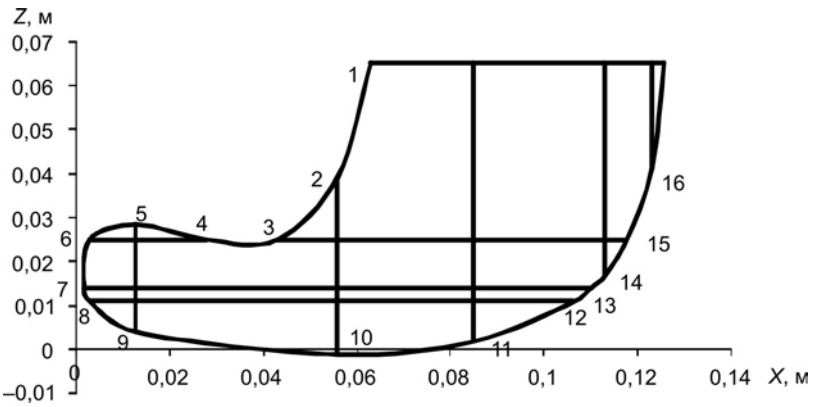


Fig. 2.19. The contours of the antrum in the front section obtained using ultrasound

The circuit 1–16 is exported in *Ansys DesignModeler* taking into account the approximation; the initial configuration of the grid consisting of 51,727 design triangular elements (linear dimension of elements is about $4 \cdot 10^{-4}$ m) is built in *Ansys Meshing*. A significant change in the geometry of the cavity requires periodic re-meshing, which is carried out using the tools of the *Dynamic Mesh* in the Fluent solver using a script (*User-Defined Function*) written in *C*-language. This script is a software implementation of a two-dimensional algorithm for estimating the bias of the computational grid nodes in wave movement. The algorithm is based on the application of sinusoidal function for the description of the waveform.

There are two calculation scenarios (Fig. 2.20): without disorders of the gastric functionality ($F_2 = 0$) and in the presence of functional disorders ($F_2 = 0{,}5$). Both scenarios use the parameters of waves obtained based on the results of ultrasonic examination. Water (ρ = 1000 kg/m^3; $\nu = 10^{-6}$ m^2/s) is considered as media material. Change in the volume of the computational domain occurs during the deformation of the wall, so the condition of an outlet flow – zero relative pressure – is set at the right upper boundary. The condition of impermeability and the absence of friction (*no slip*) are set at all other boundaries of the computational domain. Time step remains constant during the whole calculation time and equals 0.01.

The calculation results indicate the formation of fluid flow in the direction reverse to the *X* axis with the largest module velocity in the convergent section of the stomach of 0.0262 m/s (Fig. 2.20, *а*, *в*), which is consistent with the above literature data. In addition,

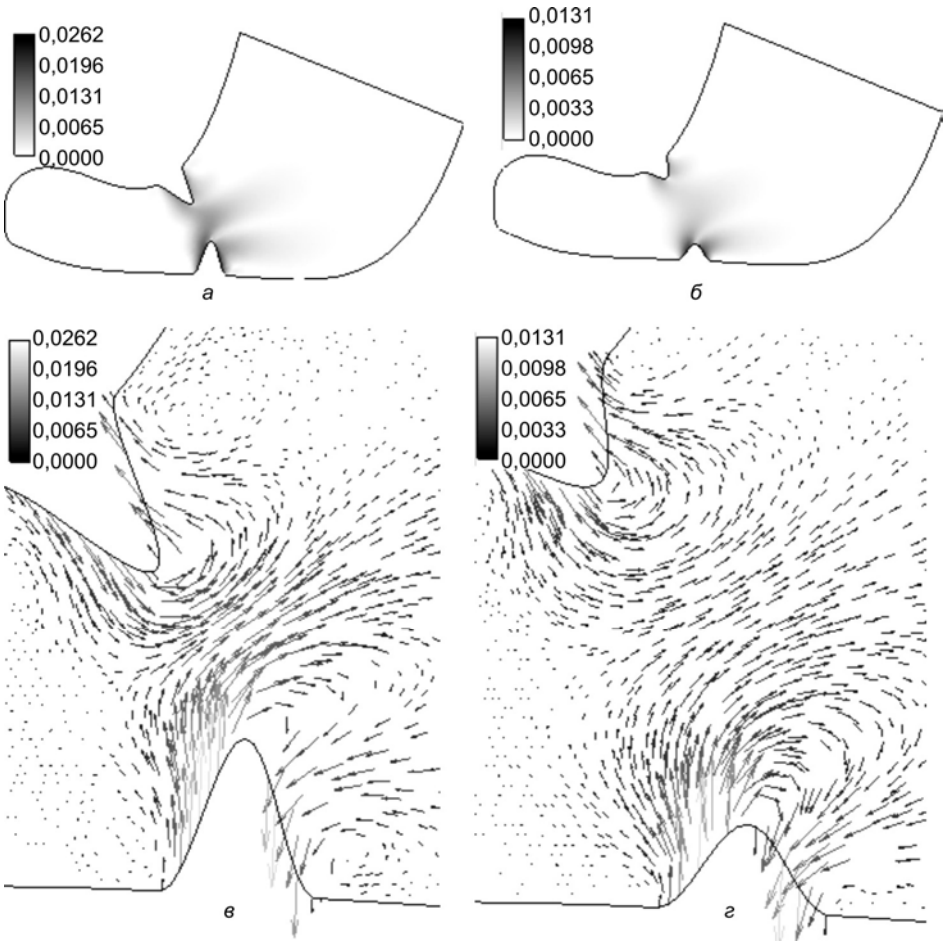


Fig. 2.20. The flow rate in the stomach at t = 5.5: *а* – in the absence of functional disorders of the stomach, $F_2 = 1$; *б* – at the functionality of the stomach $F_2 = 0{,}5$; *в*, *г* – enlarged illustration of the contracted area of the stomach corresponding to figures *а*, *б*, with presentation of the velocity vectors

the flow areas with vortex structures are found behind the contractive area. In the gastric functionality $F_2 = 0{,}5$, the maximum amplitude of contractions is d_c = 0.0045 m, the maximum velocity – 0.0131 m/s (Fig. 2.20 *б*, *г*). Reduction of the flow velocity results in poor food mixing, entrapment of the mixture in the cavity of the gastrointestinal tract. Further development of the flow simulation in the stomach provides complication towards three-dimensional geometry, adding of biochemical processes and multiphase to the model, measurement of the wave process frequency, secretory and absorptive gastric functions.

Mathematical model of the meso-level of the digestive system is designed in accordance with modern visions of the digestive processes in the human body. At this stage of simulation, most attention is paid to the digestion in the oral cavity and the stomach, in particular, food particles crushing during food mastication, and the influence of wave contraction propagation on the flow in the antrum. The measurement of the interaction of organs and systems of the human body is proposed to be implemented

through the introduction of neurohumoral elements regulating the secretion of acid in the stomach. Subsequently, the control system must be also taken into account in the description of motor function of the gastrointestinal tract. In addition, the processes of intestinal digestion require a detailed review; during the description of these processes other organs of the digestive system – liver, pancreas, and gallbladder should be taken into account.

The development of the digestive system submodels developed an algorithm for the reconstruction of the three-dimensional form of antrum area of the gastrointestinal tract and evaluation of the computational grid nodes shifts in the propagation of the contraction wave in the antral segment and motor activity of the pyloric sphincter.

Algorithm for the reconstruction of three-dimensional shape of antrum area of the gastrointestinal tract according to the results of ultrasound investigation is based on the construction of the ellipses of varying sizes, which are the basis for the approximation of three-dimensional surface of the stomach. The centers of the ellipses lie on the center line, and the ellipses are arranged in the normal plane in relation to the center line.

The approximation of three-dimensional surface is performed on the basis of the reference ellipses coordinates using the tools of *Ansys Design Modeler* (Fig. 2.21).

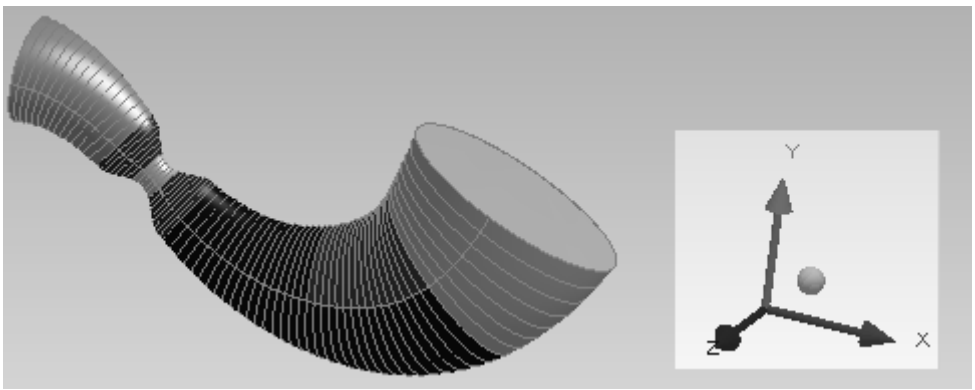


Fig. 2.21. Construction of the three-dimensional surface of the stomach in *Ansys Design Modeler* (contracted segment – an area of pyloric outlet, segment to the left of contraction area – is the intestine, to the right – antrum)

Ansys Meshing built a grid consisting of 717,953 tetragonal elements. The size of the surface elements edge varies from 0.6 mm (in the areas of the incurvateportion of the antrum and in the area near pyloric outlet) to 1.5 mm (the area of the convex portion of the antrum).

Wave propagation and interaction with the motility of the pyloric sphincter is simulated on the basis of published data [Pal A. et al., 2007] and the results of the ultrasound investigation. The wave of the antral contractions is initiated by an ellipse with the center at the beginning of antral segment and moves to pyloric outlet with speed $v = 2.2 \cdot 10^{-3}$ m/s tangential to the center line for 38 seconds. The parameter values of the wave (Fig. 2.22) in the baseline scenario: wave width value does not depend on the time $\lambda_c = 0{,}01$ m (one-half of the wave width), contraction amplitude increases linearly within the first 12 seconds up to a value of 0.011 m ($d_c^t = (t/12) \cdot 0{,}011$ m) at time $t \in [12{,}34]$ s, the amplitude remains unchanged, at $t \in [34{,}38]$ s decreases linearly to 0. Waves are initiated with a period of 18 seconds. The opening of the sphincter is carried out at $t \in [26{,}28]$ s, the closing at $t \in [30{,}32]$ s (Fig. 2.23).

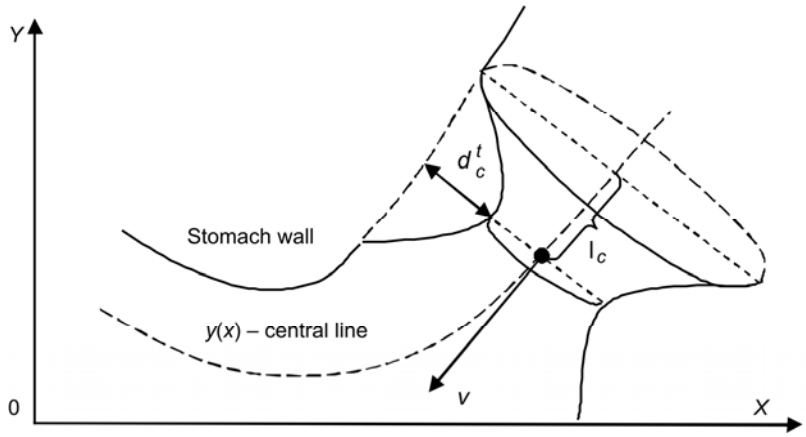
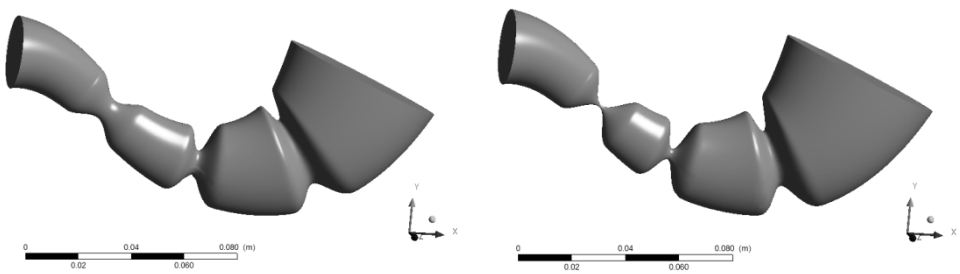


Fig. 2.22. Parameters of the contraction wave in the antrum



a *b*

Fig. 2.23. Wave position in antral segment
a – with an open pyloric sphincter; *b* – with the closed pyloric sphincter

The main stage of the algorithm is to determine the position of the node in the design time through the displacement of the non-deformed state along the perpendicular to the center line using the sinusoidal function:

$$d_{node}^{t+1} = (r_{node} / r_{1node}) d_c^{t+1} (1 + \sin(\pi \frac{\lambda_c - \rho_c}{2\lambda_c}))^2 / 2, \quad \text{at } \rho_c \le \lambda_c, \tag{2.2.65}$$

where d_{node}^{t+1} – the displacement amount;

ρ_c – the distance between the center of the ellipse and the position of the wave center;

r_{1node} – a large radius of the ellipse in the initial configuration;

r_{node} – a radius of the ellipse in the initial configuration corresponding to the grid point.

Exponentiation of a multiplier and sinus (in this case – the squaring) enables smoothing in the wave peak.

Thus, the formulation of the simulation problem of the digestive processes at the meso-level, followed by damage assessment and risk of dysfunctions requires the development of specific technical solutions in the field of mathematical simulation. The spatial approximation of organs is particularly costly in the formulation and calculation. Despite this, the simulation of the "meso-level" of the digestive system can solve a number of critical tasks of the individual level involving the analysis of the spatial distribution of damage parameters. These calculations

allow taking into account the individual characteristics of organs geometry and functionality which are the basis for prediction of pathological processes development not only in the digestive organs, but also in other body systems.

The presented results of simulation of the digestion processes are the basic technical solutions used in the study of patterns of spatial and temporal risk distribution in the meso-level tasks, and the model itself is a tool to perform calculations.

Submodel of neuroimmunoendocrine regulation [Zaitseva NV et al., 2014]

Regulatory processes in the body perform one of the most important functions aimed at maintaining the balance in the work of the organs, tissues, and cells. The concept of the "triune" regulatory "metasystem" [Poletaev AB et al., 2002], which includes the neuroendocrine and immune regulation circuits is currently universally recognized. Moreover, different regulatory systems (neuroendocrine and immune one) have a mutual regulatory influence and are "subordinated" to each other to some extent [Heijnen C.J., 2007; Chapman C.R. et al., 2008; Smith A.M., 2011; Lanin D.V. et al., 2011]. The work of the individual circuits (immune, nervous, endocrine) and the "neuroendocrine and immune" regulation in general can be interfered with the technogenic chemical factors [Holsapple et al., 1996; Janosek J. et al., 2006; Pabello N.G. et al., 2006; Onishchenko G.G. et al., 2011]. The control of foreign genetic material including microorganisms, in particular bacteria, is considered as one of the major functions of the immune system since the inception of immunology science. Change in the interaction of microorganism (bacteria) and macroorganism (human), the so-called indirect effect related to the change in the functions of the host organism and especially the influence of chemical factors on the immune system, occurs in terms of the human body contamination with technogenic chemical factors [Sattar S.A. et al., 2007].

There is a well-documented epidemiological evidence of an increased frequency and severity of infectious diseases in different population groups exposed to technogenic chemical factors [Hu G., Ran P., 2009; Zaitseva N.V. et al., 2011*a*]. Epidemiological studies are confirmed with the experimental data, the authors of which associate the decrease in the body's resistance to infectious agents with the impact of chemical compounds on the immune mechanisms [Ehrlich R., 1980; Siegel P.D. et al., 2004, Yin X.J. et al., 2005]. However, it should be noted that, the immune system is in a complex relationship with the neuroendocrine system as indicated above and therefore indirect effects associated with the interaction of the host organism and the microorganism may be mediated not only through the change of the immune system, but also through modulation of other regulatory mechanisms affecting the immune defense of the body.

It is well known that starting from a certain age the body starts the processes of "natural aging", which occur irregularly in different organs and tissues, but, in general, there is an accumulation of various pathophysiological disorders, deviations from the standard indicators that impair the performance of the organism as a whole and the systems under consideration in particular [Roberts-Thomson I.C. et al., 1974; Zaitseva N.V. et al., 2011*c*]. The accelerated accumulation of disorders data and the reduced efficiency of the regulatory functioning of organs and systems occur under the influence of technogenic chemical factors [Zaitseva N.V. et al., 2011c]. These processes, which can be defined as "the evolution of functional disorders of organs and systems", must be considered when examining issues related to the influence of chemical factors on the interaction of the immune and neuroendocrine systems.

Complexity, branching, and poor study of different regulation mechanisms should be noted in the simulation of the processes occurring in the neuroendocrine and immune systems. It certainly leads to problems in the conceptual and mathematical formulation, as well as the identification and verification of parameters. Most of the work in this area is devoted to biological and mathematical description of the individual units of regulatory mechanisms [Zabel P. et al., 1990; Savic D., Jelic S., 2005; Bairagi N. et al., 2008], which greatly facilitates the understanding of the studied phenomena, though it does not give a complete and systematic understanding of the internal relations and current processes.

The mathematical description of the regulation mechanism based on the interaction axis of the elements of the neuroendocrine and immune systems is the task of meso-level simulation and takes into account the evolution of functional disorders at the negative impact of chemicals entering the body from the environment.

The block diagram of the model shown in Fig. 2.24 consists of several interrelated elements of the neuroendocrine and immune systems of the human body involved in the case of bacterial invasion, each of which can be effected by chemicals entering the body from the environment by disrupting their functions, resulting in the failure of regulation and efficiency reduction.

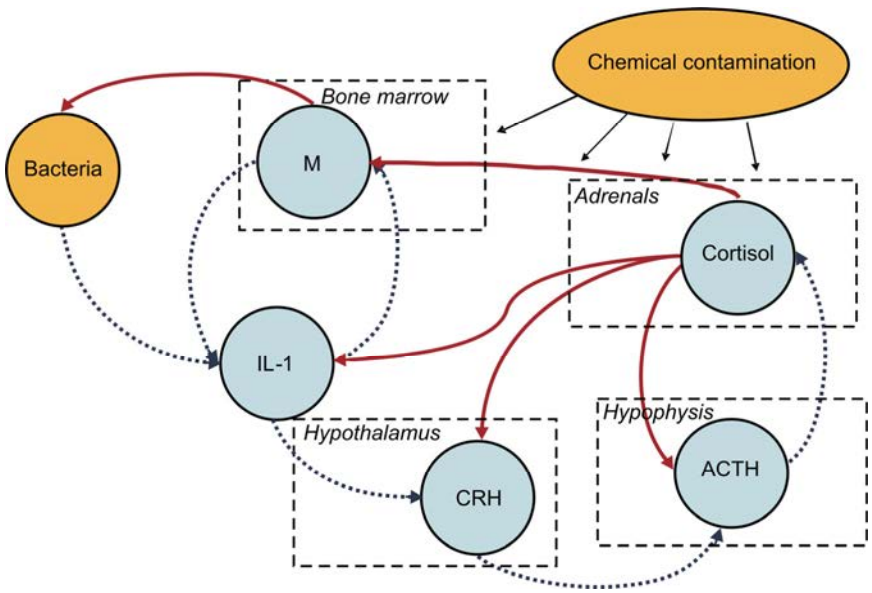


Fig. 2.24. The scheme of interaction between the elements of the neuroendocrine and immune systems of the body in response to bacterial invasion (infection) (M – monocytes – macrophages, CRH – corticotropin releasing hormone (corticotropin), ACTH – adrenocorticotropic hormone. The boxes indicates bodies of origin (organs-producers)

The mechanism of bacterial invasion (bacterial contamination) control is based on the ability of monocytes and their mature macrophage forms to perform phagocytosis (engulfing, absorption, and destruction) of foreign material, including pathogenic bacteria. Since the quantitative determination of macrophages content in the body is hindered, the estimation of their content in this study is performed based on monocyte concentration in blood, which is produced by the bone marrow. The absorption of infectious agents by a "monocyte – macrophage" complex (M) is accompanied by synthesis and release of a number of cytokines, which include the proinflammatory interleukin-1 (IL-1) [Zabel P. et al., 1990]. In its turn, the appearance of the increased content of IL-1 in the blood, in addition to numerous regulatory effects, leads to the mobilization of monocytes in the focus of inflammation and specific receptors in the hypothalamus stimulates the production of corticotropin-releasing hormone (*CRH*), which causes the secretion of adrenocorticotropic hormone (ACTH) when effect in the anterior pituitary. When getting into the blood, ACTH stimulates the adrenal glands to develop cortisol, increasing concentration of which according to the mechanism of negative feedback inhibits the secretion of ACTH and CRH, stimulates apoptosis of "monocyte – macrophage", and blocks the production of IL-1 [Savic D. and Jelic S., 2005; Bairagi N. et al., 2008]. At the same time, the stated effects of cortisol appear from some normative level, and have a non-linear nature. Due to the negative feedback caused by increased concentration of cortisol, the system is in equilibrium (homeostasis).

The proposed mechanism describes the self-regulating system, the operation of which depends on the functional state of organs (bone marrow, pituitary, hypothalamus, adrenal glands). The disorder of the function of the neuroendocrine and immune systems organs can lead to faulty regulation and imbalance of indicators. These disorders can be accumulated over the life of the individual both in natural aging of the studied bodies and under the influence of external technological chemical factors. When entering the body from the environment, the complexes of chemical agents interfere in almost any interaction chains enhancing pathological processes [Onishchenko G.G. et al., 2011] and modifying the response to bacterial infection [Sattar S.A. et al., 2007].

The changes in the number of macrophages depend on the content of monocytes in the blood, so "monocytes – macrophages" system is considered when writing constraint equations. A special feature of the macrophages existence is the programmed death (apoptosis) at high levels of cortisol [Smith A.M. et al., 2011]. Based on the existing concepts of the mechanism of monocytes production by bone marrow, their maturation into macrophages and subsequent death, the equation describing the change in the number of "monocyte - macrophage" is presented as follows:

$$\frac{dM}{dt} = \beta_1 (1 - D_1) + \beta_2 IL\text{-}1 \left(1 - \frac{M}{M_{\max}} \right) - \beta_3 M \left(1 + \beta_4 \frac{K (t - \tau)^n}{c^n + K (t - \tau)^n} \right), \qquad (2.2.66)$$

where M – the number of "monocyte – macrophage", $cell$;

D_1 – the parameter of bone marrow hematopoietic function disorder ($D_1 \in [0;1]$);

IL-1 – the concentration of IL-1 in the blood, pg/ml;

$M_{\max}$ – the maximum possible number of "monocyte – macrophage", $cell$;

K – the concentration of cortisol, pg/ml;

β_1 – the rate of "monocyte – macrophages" intake, $cell/hour$;

β_2 – parameter characterizing the rate of monocytes attraction in the inflammatory focus, $cell \cdot ml/(hour \cdot pg)$;

β_3 – the clearance of "monocyte – macrophage", $hour^{-1}$;

β_4 – parameter characterizing the effect of cortisol on "monocyte – macrophage" apoptosis;

c – the average standard level of cortisol concentration, pg/ml;

n – the parameter of model non-linearity;

τ – temporary effect delay, $hour$.

The first summand of equation (2.2.66) describes the process of "monocyte – macrophage" production in terms of reduction of intensity in the disorder of hematopoietic function of bone marrow. The second summand takes into account the effect of additional monocytes attraction to the inflammatory focus associated with the activity of IL-1. The third summand describes the mechanism of macrophages destruction in terms of the launch of the apoptotic process at high cortisol levels.

Change in the number of bacteria is caused by three processes, the first of which is the intake of bacteria from the external environment, the second is the process of propagation in the body, the third is the destruction of bacteria with a "monocyte – macrophag" complex. Similar phenomena are described by the "predator – prey" equations proposed by Lotka-Volterra [Brauer F., Castillo-Chavez C., 2000]:

$$\frac{dP}{dt} = \alpha_1 + \alpha_2 P \left(1 - \frac{P}{P_{max}} \right) - \alpha_3 M \left(\frac{\alpha_4 P}{1 + \alpha_4 P} \right), \qquad (2.2.67)$$

where P – the number of pathogenic bacteria, CFU/ml;

P_{max} – the maximum possible bacteria concentration, CFU/ml;

α_1 – the parameter of bacteria intake, $CFU/ml \cdot hour$;

α_2 – the parameter of bacteria growth, $hour^{-1}$;

α_3 – the parameter of the bacteria absorption by the "monocytes – macrophages" complex, $CFU/ml \cdot cell \cdot hour$;

α_4 – the parameter characterizing the probability of bacteria contact with "monocytes – macrophages", ml/CFU .

Equation (2.2.67) indicates that the more bacteria and macrophages are present in the body, the more frequently their interaction occurs resulting in the decrease in the number of bacteria.

The contact of the "monocyte – macrophage" complex and bacteria produces IL-1, which increases cortisol level being a marker of inflammation. In its turn, the increased levels of cortisol inhibits IL-1 synthesis. Equation of the rate of change in the amount of IL-1 in blood is as follows:

$$\frac{dIL\text{-}1}{dt} = \gamma_1 M \left(\frac{\alpha_3 P}{1+\alpha_3 P} \right) \left(1 - \gamma_2 \frac{K\left(t-\tau\right)^n}{c^n + K\left(t-\tau\right)^n} \right) - \gamma_3 IL\text{-}1, \qquad (2.2.68)$$

where IL-1 – concentration of interleukin-1, pg/ml ;

γ_1 – parameter characterizing the intensity of interleukin-1 production, $pg/ml \cdot cell \cdot hour$;

γ_2 – the parameter of the cortisol effect on the production of IL-1;

γ_3 – the clearance of IL-1, $hour^{-1}$.

The first summand of equation (2.2.68) characterizes the rate of IL-1 synthesis in the interaction of "monocyte - macrophage" with bacteria taking into account the suppression of this process at high concentrations of cortisol. The second summand is responsible for the natural elimination of IL-1 from the body.

The appearance of interleukin-1 in the blood increases the rate of CRH production by hypothalamic. In this case, the rate of CRH change is affected by five processes: synthesis due to the IL-1 hypothalamus stimulation, the reduction of synthetic hypothalamic function, the suppression of the synthesis with high cortisol content, the oscillation of hypothalamic activity in accordance with circadian rhythms, natural CRH elimination from the body. Equations published in papers on the simulation of the hypothalamic-pituitary-adrenal axis [Savic D., Jelic S., 2005; Bairagi N. et al., 2008] and modified to measure for the impact of the hypothalamus synthetic function disorders were used when describing the processes of CRH change:

$$\frac{dCRH}{dt} = \lambda_1 \left(1 - D_2\right) G\left(t\right) \left(1 - \lambda_2 \frac{K\left(t-\tau\right)^n}{c^n + K\left(t-\tau\right)^n} \right) + \lambda_3 IL\text{-}1 - \lambda_4 CRH , \qquad (2.2.69)$$

where CRH – the concentration of CRH, pg/ml ;

D_2 – the parameter of hypothalamus synthetic function disorder ($D_2 \in [0;1]$);

$G\left(t\right)$ – harmonic function that simulates the circadian rhythms;

λ_1 – the parameter of CRH production, $pg/ml \cdot hour$;

λ_2 – the parameter of the cortisol effect on the CRH production;

λ_3 – the parameter of the IL-1 effect on the CRH production, $hour^{-1}$;

λ_4 – CRH clearance, $hour^{-1}$.

The first summand of equation (2.2.69) takes into account the decrease in CRH production in the disorder of the hypothalamus function and at high levels of cortisol in the background of natural circadian rhythms. The second summand describes the stimulation

of CRH IL-1 production. The last summand is responsible for the natural elimination of CRH from the body.

CRH activates the production of ACTH hormone by the hypophysis. It is known from the literature that the hypophysis blocks the ACTH production when a certain cortisol level is reached. The general form of the equation describes the change in the rate of ACTH production, as follows:

$$\frac{dACTH}{dt} = \mu_1(1-D_3)\left(1-\mu_2\frac{K(t-\tau)^n}{c^n+K(t-\tau)^n}\right)CRH-\mu_3 ACTH\ , \qquad (2.2.70)$$

where $ACTH$ – the concentration of ACTH, pg/ml;

D_3 – the parameter of hypophysis synthetic function disorder ($D_3 \in [0;1]$);

μ_1 – the parameter of ACTH production, $hour^{-1}$;

μ_2 – the parameter of the cortisol effect on the ACTH production;

μ_3 – ACTH clearance, $hour^{-1}$.

When effecting the adrenal glands, ACTH stimulate the cortisol production, the production rate of which is given by the equation:

$$\frac{dK}{dt} = \nu_1(1-D_4)Acth(t-\tau)-\nu_2 K\ , \qquad (2.2.71)$$

where K – the cortisol concentration, pg/ml;

D_4 – the parameter of adrenal glands synthetic function disorder ($D_4 \in [0;1]$);

ν_1 – the parameter of cortisol production, $hour^{-1}$;

ν_2 – cortisol clearance, $hour^{-1}$.

Equation (2.2.71) reflects the increase in the rate of cortisol production in the increase of ACTH levels in the body taking into account the effects of disorders of the synthetic function of the adrenal glands and the temporary delay.

Thus, the regulation mechanism with the participation of elements of the neuroendocrine and immune systems taking into account the delay is written as follows:

$$\begin{cases} \dfrac{dM}{dt} = \beta_1(1-D_1)+\beta_2 IL\text{-}1\left(1-\dfrac{M}{M_{max}}\right)-\beta_3 M\left(1+\beta_4\dfrac{K(t-\tau)^n}{c^n+K(t-\tau)^n}\right), \\ \dfrac{dP}{dt} = \alpha_1+\alpha_2 P\left(1-\dfrac{P}{P_{max}}\right)-\alpha_3 M\left(\dfrac{\alpha_4 P}{1+\alpha_4 P}\right), \\ \dfrac{dIL\text{-}1}{dt} = \gamma_1 M\left(\dfrac{\alpha_3 P}{1+\alpha_3 P}\right)\left(1-\gamma_2\dfrac{K(t-\tau)^n}{c^n+K(t-\tau)^n}\right)-\gamma_3 IL\text{-}1, \\ \dfrac{dCRH}{dt} = \lambda_1(1-D_2)G(t)\left(1-\lambda_2\dfrac{K(t-\tau)^n}{c^n+K(t-\tau)^n}\right)+\lambda_3 IL\text{-}1-\lambda_4 CRH, \\ \dfrac{dACTH}{dt} = \mu_1(1-D_3)\left(1-\mu_2\dfrac{K(t-\tau)^n}{c^n+K(t-\tau)^n}\right)CRH-\mu_3 ACTH, \\ \dfrac{dK}{dt} = \nu_1(1-D_4)Acth(t-\tau)-\nu_2 K. \end{cases} \qquad (2.2.72)$$

The system of equations (2.2.72) with the initial conditions $M(t_0) = M_0$; $P(t_0) = P_0$; $IL\text{-}1(t_0) = IL\text{-}1_0$; $CRH(t_0) = CRH_0$; $ACTH(t_0) = ACTG_0$; $K(t_0) = K_0$ is a Cauchy problem recorded for a system of ordinary differential equations of first order with retarded argument. It is believed that all the constants in the equations are non-negative (this results from their biological sense), and D_j is continuous and non-negative function of time ($D_j(t)$), then any non-negative initial conditions ($M(t_0) \geq 0$, $P(t_0) \geq 0$, $IL\text{-}1(t_0) \geq 0$, $CRH(t_0) \geq 0$, $ACTH(t_0) \geq 0$, $K(t_0) \geq 0$) have solution of the problem and are unique in the entire determination area ($t \geq 0$). Moreover, the theorem on the existence and uniqueness of solutions of the Cauchy problem implies that a decision will be continuous and non-negative ($M(t) \geq 0$, $P(t) \geq 0$, $IL\text{-}1(t) \geq 0$, $CRH(t) \geq 0$, $ACTH(t) \geq 0$, $K(t) \geq 0$) under the stated conditions for $t \geq 0$.

The complexity and non-linearity of equations (2.2.72) complicate the obtaining of the analytical solutions and lead to the need for numerical methods. The difference scheme based on the Runge-Kutta method of the 4th power with constant pitch was used for the numerical solution of the system (2.2.72) [Butcher J.C., 2003].

The effectiveness of mechanism for bacterial invasion control along with the ability of monocyte - macrophage to produce cytokines is also determined by the number of cells participating in the immune response, i.e. the organs ability (in this case, of bone marrow) to replenish "spent" cells of immune system (synthetic function). The disorder of these functions leads to a deficiency of necessary cytokines and, as a consequence, the system's exit from a homeostasis state.

It is known that the functional activity of most organs, including the production of regulatory molecules (cytokines and hormones) and cells (monocytes) weakens [Roberts-Thomson I.C. et al., 1990; Wayne S.J. et al., 1990; Ferguson F.G. et al., 1995] with age, that may be correlated with the appearance of more severe forms of disease and longer periods of treatment and recovery, moreover chemical environmental factors enhance such effects [Sattar S.A. et al., 2007]. It should be noted that the immune system is in constant interaction with the neuroendocrine system as mentioned above and, thus, an excess or deficiency of hormones caused by disorders of the synthetic function of producing organs may also disrupt the immune response.

The identification of mathematical models describing complex biological processes in the human body is one of the most intractable problems, the solution of which is accompanied by a substantial uncertainty [Parakhonsky A.P., 2007]. In this case, the main problem is related to the inability to organize the targeted experiment varying values within a wide range, and a significant number of confounding factors characterizes a system of sample surveys. Therefore, the determination of the model parameters was carried out by structural identification allowing the use of the published results of researches in the analysis of the interaction of the individual elements of the neuroendocrine and immune systems. The missing part of the parameters was assessed according to our own laboratory researches.

Table 2.19 shows the identified parameters of the mathematical model of interaction between the neuroendocrine and immune system in the streptococcal pneumonia infection (chosen as a model example) taking into account the evolution of functional disorders of the bone marrow in the negative impact of chemical agents.

The consideration of other types of bacteria or influencing chemical factors requires additional identification of a number of parameters.

The identified parameters allow performing numerical experiment showing the behavior of the model obtained under different scenario conditions, which are defined as different degrees of functional disorder of production of cells or regulatory molecules associated with the impact of adverse chemical factors. The model of disorder of synthetic function of the tested organs determines the influence of several factors, the main of which are chemical substances entering the body from the environment. One of the possible

Table 2.19

Parameters of the model with the data source indication

Parameter	Value	Source
M_{max}	$1.3 \cdot 10^6$	Smith A.M. et al., 2011
β_1	3965.3	Coggle J., Tarling J., 1982
β_2	190	In-house studies
β_3	0.003	Van Oud Alblas, van Furth, 1979
β_4	1	In-house studies
c	120	In-house studies
n	5	In-house studies
τ	19	In-house studies
P_{max}	$2.3 \cdot 10^8$	Smith A.M. et al., 2011
α_1	0	In-house studies
α_2	0.0256	Todar K., 2002
α_3	0.0026	Hampton M. et al., 1994
α_4	0.01	Smith A.M. et al., 2011
γ_1	0.00029	Bergeron Y. et al., 1998
γ_2	0.05	In-house studies
γ_3	0.1245	Gloff C., Wills R., 1992
λ_1	106.176	Vinther F. et al., 2011
λ_2	0.05	In-house studies
λ_3	0.1	In-house studies
λ_4	10.3974	Felig P., Frohman L.A., 2001
μ_1	22.9212	Vinther F. et al., 2011
μ_2	0.05	In-house studies
μ_3	6.26976	Carroll B.J. et al., 2007
ν_1	9.2386	Vinther F. et al., 2011
ν_2	3.266136	Carroll B.J. et al., 2007
a_0	0.042	In-house studies
b_0	0.0000004	In-house studies
p_0^N	0.1	In-house studies

solutions of the equation (2.2.6) is shown in Fig. 2.25. Bone marrow was chosen as an example of the producing (synthetic) organ for the model because the central element of all immune reactions in the described example are the monocytes – macrophages – produced by this organ.

This decision reflects the possibility of bone marrow dysfunction resulting from natural aging processes, as well as the complex of "aging – chemical factors" effects. In this case, as can be seen from the graph, the impact of chemical factors can significantly accelerate the accumulation process of synthetic function disorders that are also confirmed by our earlier studies [Trusov P.V. et al., 2012].

To check the adequacy of the model, calculations were carried out for three scenarios varying in degree of functional disorders of monocyte production by the bone marrow associated with exposure to chemicals: $D_1 = 0$; $D_1 = 0.17$ and $D_1 = 0.2$. The specified damage parameter values may occur at different ages depending on the negative impact of chemical factors. At the same time processes of interaction between the elements of neuroendocrine and immune systems can vary considerably.

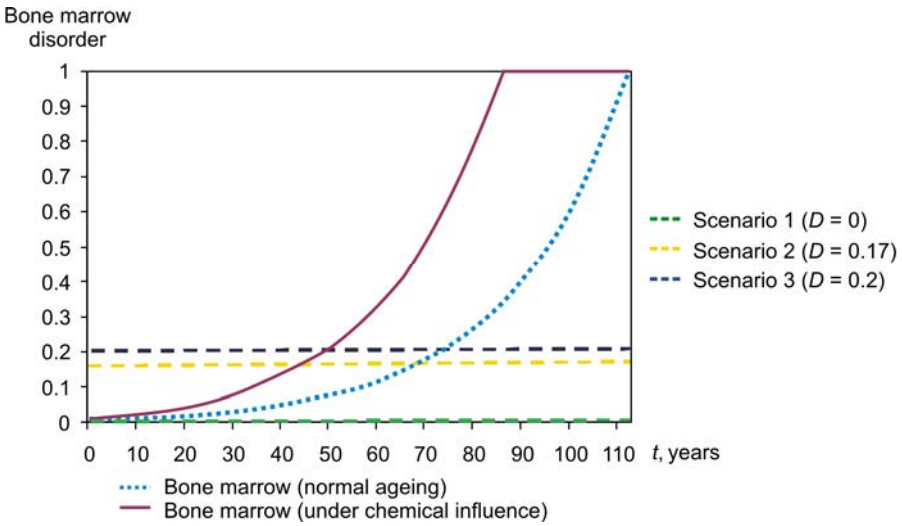


Fig. 2.25. The evolution of disorder of bone marrow function to produce monocytes in natural aging and under the additional impact of man-made chemical factors

The possible solutions of equations (2.2.72) are shown in Fig. 2.26, which shows the change in the three selected variables of the model in the case of a bacterial infection of the body: "monocytes – macrophages" complex; change in the number of bacteria (bacterial number), and the content of IL-1. These indicators were chosen because of their visual changes with the chosen parameters and initial conditions of the scenarios. The not included parameters of the model such as CRH, ACTH and cortisol differ slightly in view of the proper functioning of the elements of the neuroendocrine system under the conditions of the specified scenarios. Estimated simulation period is 10 days.

Each scenario assumes disturbing the balance of system by setting the initial level of streptococcus bacterial infection of 10^5 CFU. This dose obtained based on the experimental data [Smith A.M. et al., 2011], is able to induce the immune system's reserves activation with revealing the manifestation of the interaction of the elements of the neuroendocrine and immune systems. At a lower bacteria dose, a healthy body in a short time copes with bacterial invasion using local resources and has no significant impact on the regulatory circuit. The exponential growth of bacteria occurs even in a healthy body in the invasion of bacteria with a number more than the chosen dose; the body cannot cope with this growth and it leads to a total breakdown of the protective mechanisms.

Increase in the number of "macrophage – monocyte" and launch of regulatory mechanisms is observed at the initial stage (within 2–3 days) of all scenarios. The difference lies in reducing the ability of bone marrow to produce a sufficient number of monocytes-macrophages (synthetic function) for the second and third options resulting in a decrease in the concentration of the specified cells (monocytes and macrophages – Fig. 2.26, a), which in its turn reduces the efficiency of actions preventing the growth of bacteria.

In the first scenario, the bone marrow functionality level of which shown in Fig. 2.25, the system enters a state of stable equilibrium in 4–5 days, which corresponds to the suppression of bacterial infection and bringing the indicators (Fig. 2.26, blue line) to the standard state. The considered process flows against the background of stable circadian rhythm of changes in immune and neuroendocrine systems values. In clinical practice, such changes are consistent with either the absence of disease symptoms, or acute inflammation terminated by rapid recovery ("rehabilitation – recovery" scenario).

The second scenario simulates a minor breach of the synthetic function of bone marrow, when a balance of two processes is carried out: the growth of bacteria and their killing by macrophages. The level of synthetic function disorder in this scenario is shown

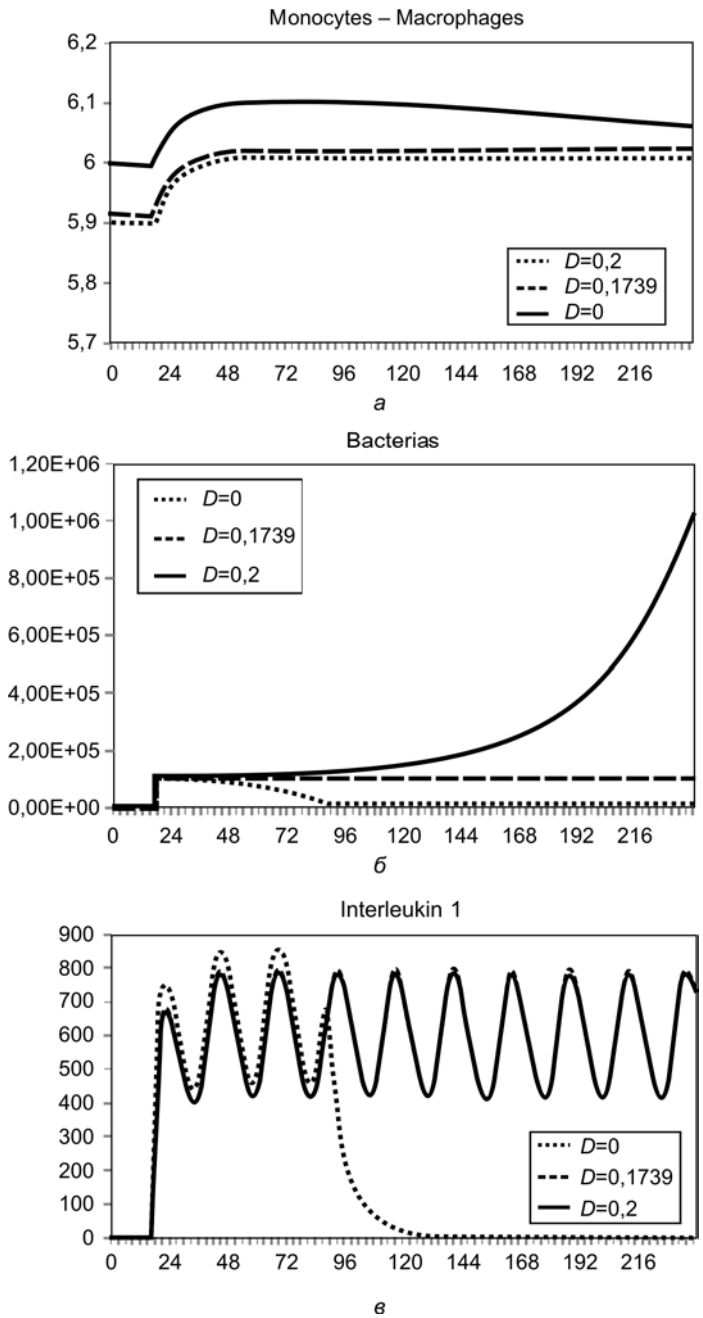


Fig. 2.26. The graphs of changes: *а* – the content of macrophages, *б* – the number of bacteria, *в* – the concentration of IL-1 in the blood. time in hours is specified along the abscissa, where the original point of the curve corresponds to the time 20 hours before bacterial invasion. The value obtained by computer simulation is specified along the ordinate. Different colors displayed three simulated scenarios with different functional damage of the bone marrow

in Fig. 2.25. The conditions of this scenario, as can be seen from the graph, occur much earlier when exposed to chemical factors in the bone marrow. At the same time the growth of bacteria does not occur and the immune system's stress persists (Fig. 2.26, the red line). In clinical practice, the remission or acute exacerbation of chronic diseases (scenario "chronic disease") may be an example of such conditions.

The third scenario simulates a significant violation of the production of monocytes – macrophages of bone marrow, the value of a violation of the synthetic function of bone marrow observed in Fig. 2.25. This condition occurs at a later age than in the first and second scenarios, but this level of disorder can also be observed at an earlier age in the case of the negative impact of chemical factors on the bone marrow. The change in the level of IL-1 is slightly different from the second scenario due to the adequate operation of the elements of the neuroendocrine system. You can observe an unlimited increase in the number of bacteria associated with a reduction in the number of monocytes – macrophages due to a decrease in their production by the bone marrow, which may be caused by the effect of chemical factors of the environment (Fig. 2.26, green line). This leads to the oppression of all regulatory indicators manifested in severe acute conditions or the severe exacerbation of chronic infection ("severe infection" scenario) that can lead to death.

The present task considers the mathematical model allowing to describe the mechanism of regulation of elements of neuroendocrine and immune systems in response to bacterial invasion taking into account the evolution of functional disorders of the elements under the influence of environmental factors. The work of individual structural elements of the systems in question is simulated, the description of the interaction of these systems allows to qualitatively show the features of the occurring regulation processes.

Numerical solution of the resulting system of equations is carried out using the difference scheme based on Runge – Kutta method of the 4th order with constant pitch. The identification of the model's parameters is made to describe the condition of bacterial infection (on the example of streptococcal lung infection) under the conditions of a change in production of monocytes by the bone marrow under the influence of technogenic chemical factors in order to demonstrate the qualitative results allowing to assess the impact of the environment on human health through its impact on the regulatory system.

Thus, the presented model adequately describes the processes of bacterial infection taking into account the effects of chemical environmental factors. Although the studied structure of the interaction of elements of the neuroendocrine and immune systems is not complete, and contains only a part of regulatory mechanisms, we can talk about the development of the basic model reflecting the essence of multi-component interaction of regulatory systems in inflammatory responses of bacterial genesis and ready to be complicated due to the introduction of additional parameters and relationships.

2.3. The assessment of risk and its evolution at the impact of chemical environmental factors on health

Currently, the concept of risk assessment in almost all countries and international organizations is considered as the main mechanism for the development and making of management decisions both at the international, national, or regional levels, and at the level of individual production or another potential sources of the environmental pollution.

Complete scheme for the assessment of public health risk under the influence of chemical factors provides four stages:

– hazard Identification is the establishment of qualitative evidences of the ability of the particular chemical agent to cause some harmful effects in a human;

– exposure Assessment is the identification and assessment of quantitative and qualitative severity of frequency, duration and route of exposure;

– dose – Response Assessment is the quantitative characterization of toxicological information and the establishment of the relation between exposure dose (concentration) of the pollutant and the incidences of harmful effects in the exposed population;

– risk Characterization is the integration of data obtained at all previous stages of researches, with the aim of quantitative and qualitative risk assessment, identification and assessment of the relative importance of the public health problems [EU, 2000; Benford D.J., 2001; P 2.1.10.1920-04; Instructions 2.1.6.11-9-29-2004].

Hazard identification

Hazard identification is more often considered as the process of establishing the potential health risk factors of the chemical nature and their ability to induce some harmful effects in man [EU, 2000; A guide to health risk assessment, in 2001; Onishchenko G.G. et al., 2002; Risk Assessment Of Chemicals, 2007].

Hazard identification is a qualitative process and depends on the type and reliability of the used data, as well as the weight of evidence from various sources. At that, data on the reliability and consistency of researches, the relevance of animal studies to humans are important [Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004].

Hazard identification has screening nature and provides the identification of all sources of chemical contamination of the environment and their possible effect on humans; the identification of pollutants; the characteristics of the potentially harmful health effects due to exposure to chemicals and the evaluation of scientific proof of the possibility of these effects in humans; the identification of chemical compounds priority for further study; the establishment of harmful effects caused by priority substances at the estimated exposure routes (including priority contaminated environment and the routs of the chemicals intake in the human body), the duration of exposure (acute, subacute, chronic, life-long) and routs of their intake in the human body (inhalation, oral, percutaneous) [EU, 2000; Benford D.J., 2001; A guide to health risk assessment, in 2001; P 2.1.10.1920-04; Instructions 2.1.6.11-9-29-2004; Commonwealth of Australia, 2004; Risk Assessment Of Chemicals, 2007; Environmental Legislation and Human Health, 2007].

The assessment of the completeness and accuracy of the available data on the contamination levels of various environmental objects is carried out; tasks for an additional collection of information on actual and/or simulated concentrations of chemicals in various media are defined; the availability of information on the quantitative criteria necessary for the subsequent health risk analysis (reference doses and concentrations, the factors of carcinogenic potential) is assessed at the stage of hazard identification.

In the assessment of health risk due to chemical factors, the list of the priority harmful chemical compounds is determined, the hazards indicators (carcinogenic and non-carcinogenic) are selected, a preliminary exposure scenario is formed, and preliminary exposure routes are identified at the stage of hazards identification.

The description of the physico-chemical properties of chemical, its behavior in the environment, the probability of cross-media transitions, its toxicological properties, including the impact on the genetic material at the cellular, organ level should be carried out within the chemical hazards identification [EU, 2000; Benford D.J., 2001; A guide to health risk assessment, 2001; EU, 2003; P 2.1.10.1920-04; Инструкция 2.1.6.11-9-29-2004; Commonwealth of Australia, 2004; FAO/WHO, 2006*b*; Risk Assessment Of Chemicals, 2007; WHO, 2010].

The analysis of a broad spectrum of effects caused by the analyte in the whole range of effecting doses and at different exposure duration is performed at the stage of hazard identification; generally, the response observed at the lowest dose loads during chronic animal experiment, is considered particularly relevant to humans and is considered as critical [US EPA, 1995]. In addition, it is necessary to take into account possible differences in the manifestations of the toxic effect at the different routes of the chemical intake. More often, the harmful effects characterization is based on localization of pathological changes (e.g., lesions of the central nervous system, gastrointestinal tract, reproductive system, etc.),

the assessment of the effects severity is also possible [Onischenko G.G. et al., 2002; Risk Assessment Of Chemicals, 2007; WHO, 2010].

The presence of reference (safe) levels for both acute and chronic effects (RfC, ARfC, the maximum permissible content level, the maximum permissible exposure level etc.), and the critical organs/system and effects corresponding to this reference level are established for non-carcinogenic chemicals at the stage of the hazard identification.

The analysis of the carcinogenicity evidence importance based on existing classifications (IARC, U.S. EPA, NTP, etc.) indicating the values of the carcinogenic potential factors (SF) for the conditions of inhalation (SFi) and oral (SFo) inctake and single risk index (URi) is performed for chemicals with carcinogenic potential [Onishchenko G.G. et al., 2002].

Thus, the establishment of chemical hazards, possible effects associated with their impact on human health, the definition of risk cohort will be a result of hazard identification within the evaluation of population health risk associated with chemical pollution of the environment.

Exposure assessment

The stage of exposure assessment is aimed at quantitative and/or qualitative [Benford D.J., 2001] establishment of chemical agent intake into the body through contact with different environmental medium (air, water, soil, food) [US EPA, 1992; A guide to health risk assessment, 2001; Onishchenko G.G. et al., 2002; EC, 2003; Commonwealth of Australia, 2004; WHO, 2010; ICCA, 2011].

The exposure in the evaluation of the health risks associated with chemical pollution of the environment is the body (receptor) contact with a chemical agent. The exposure value is defined as the measured or calculated amount of an agent in a particular environmental medium that is in contact with the so-called border organs (lungs, gastrointestinal tract, skin) for any set time. Exposure can be expressed as the total amount of the substance in the environment (in mass units, for example, mg) or as the value of the impact - mass of a substance per unit of time (eg, mg/day), or as the amount of exposure normalized taking into account body weight (mg/(kg·day)).

An important step in the exposure assessment is the development of exposure scenarios (including worst-case conditions) including a description of the specific conditions of exposure; set of facts, assumptions, and conclusions about the impact of the estimated harmful factor [US EPA, 1989; 1992; Onishchenko G.G. et al., 2002; EU, 2003; Commonwealth of Australia, 2004; Risk Assessment Of Chemicals, 2007].

Impact Assessment Methodology is based on the direct and indirect research methods including the direct measurement of samples in different environments, the personal monitoring of pollutants in the breathing zone, the use of markers, questionnaires, daily diaries, mathematical simulation.

Both qualitative and quantitative measurement and determination of the severity, frequency, duration and routes of exposure of harmful chemical factors, as well as a description of the nature of the impact, the sizes and nature of the exposed population is performed with the assessment of exposure routes in course of the exposure assessment [Commonwealth of Australia, 2004; US EPA, 2011].

Exposure assessment allows setting the distribution of harmful chemical factor in time and space in different environmental objects, populations with high and low risk, the contribution to the exposure levels from various sources of contamination, factors affecting the pollutants entry into the environment, distribution and intake routes of harmful substances into the human body, etc. [Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004; WHO, 2010; US EPA, 2011].

Exposure assessment also includes a description of the environment, including the main physical parameters of the studied area and the characteristics of the potentially exposed population; identification of exposure routes, pollution sources, potential distribution routes and points of human exposure; the quantitative characterization of the exposure with the establishment and assessment of the value, frequency, and duration of exposure for each analyzed intake route.

The mandatory part of the exposure scenario is to assess the impact route describing the mechanism by which an individual or a population is exposed to a chemical, exposure point and exposure route. The evaluation of the exposure route includes the characterization of the pollution source, the probable fate of a chemical compound (persistency, degradation, distribution, transportation, cross-media transitions). Exposure points and routes are determined for each route of exposure in terms of impact (potential human exposure to chemicals) [EU, 2000; Onishchenko et al., 2002; Instructions 2.1.6.11-9-29-2004; Commonwealth of Australia, 2004].

Priority exposure routes are identified for the final performance and the final formation of the exposure scenario, at that, principal (main) route in which the probability of human exposure to the agent is the highest and leads to the accumulation of agent concentration is allocated in the presence of several possible exposure routes. The concentration of chemicals in the point of impact is estimated using data from direct and/or indirect approach to the quantitative characterization of exposure [Onishchenko G.G. et al., 2002; WHO, 2010].

Direct research methods include, for example, personal monitoring of pollutants in the breathing zone and the use of biological markers; indirect methods – the direct measurement of samples in different environments, simulation of chemical substances propagation in the environment, questioning, the use of daily diaries and exposure models. The combination of the above methods is considered to be more effective in order to establish the most accurate levels of exposure to adverse environmental factors on the human body.

The basis of assessment of the effecting concentrations is the results of environmental monitoring, simulation, propagation and behavior of chemicals in the environment, the combination of monitoring results with data obtained with the use of simulation, exposure models [EU, 2000; Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004; WHO, 2010].

Exposure models are used to obtain conclusions about exposure to specific chemical contaminants on the target populations and predict the nature of the exposure on a human. In this case data on the concentration when exposed to specific pollutant per person, as well as the duration of such effects are used as background information [Onishchenko G.G., et al., 2002; WHO, 2010].

The direct methods for the exposure analysis include the use of biological markers: exposure markers, effect markers and susceptibility (sensitivity) markers [Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004; WHO, 2010].

Exposure marker is the exogenous chemical substance, or its metabolite or product of the interaction between the xenobiotic and any molecule or cell that are targets, the number of which is determined in various body compartments.

Effect marker quantifies the biochemical, physiological, behavioral, or other change in the body, the degree of which predetermine the actual or potential health impairment or disease progression.

Susceptibility (sensitivity) marker is a value of inherent (congenital) or acquired ability of an organism to respond to the effects of certain harmful agent.

Shared use of all three types of biomarkers allows assessing the impact levels (values of the absorbed or internal dose), the effects arising from chemicals and individual sensitivity to stress.

The exposure for each test chemical at a particular exposure route is quantitatively expressed using a level of intake, which has the dimension of mg/kg·day [US EPA, 1992; Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004; WHO, 2010].

The general formula for the calculation of the chemicals intake rate has the following form [US EPA, 1992; P 2.1.10.1920-04; Commonwealth of Australia, 2004]:

$$I = \frac{C \cdot CR \cdot EF \cdot ED}{BW \cdot AT}, \qquad (2.3.1)$$

where I – intake (amount of chemical on the exchange border), mg/kg of the body weight per day;

C – the concentration of the chemical; average concentration effecting at the exposure period (e.g., mg/l of water);

CR – the value of the contact; the amount of contaminated medium contacting with the human body at a time or in one case of exposure (e.g., l/day);

EF – exposure frequency, the number of days/year;

ED – exposure duration, the number of years;

BW – body weight: average body weight during the exposure period, kg;

AT – averaging time; exposure averaging period, the number of days.

The most important parameter reflecting the impact of the chemical on the body, is the dose, the amount of pollutant produced by the body with the increase of exposure time taking into account the body weight, as it directly refers to the number of contaminant with potential effect on the target organ.

The calculation of daily doses for different conditions of exposure of chemicals is carried out using standard formulas using standard exposure factors [R 2.1.10.1920-04; Commonwealth of Australia, 2004].

In this case, the concept of potential dose (the amount of chemical that is consumed or inhaled, or its amount contained in different environments and being in contact with the skin) (*TPD*) which is calculated using the following standard equation is highlighted:

$$TPD = C \cdot IR \cdot ED, \quad (2.3.2)$$

where *C* – the ambient concentration of the pollutant (air, soil, etc.) contacting the human body (expressed in units of weight/volume or weight/weight);

IR – intake rate (speed) depending on the speed of inhalation (lung ventilation volume), the volume of water consumed, etc.;

ED – exposure duration.

Total dose (the sum of the individual doses received by the human body as a result of the impact of individual pollutant for a certain period during the interaction with all the pollutant-containing media (air, water, food, soil)) is calculated in the case of multipath multimedia exposure, [EU, 2000; Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004; US EPA, 2011].

Average daily dose averaged taking into account the expected average life duration (70 years) is used when assessing carcinogenic risks. Such doses are referred to as *LADD*. The standard equation for LADD calculation is as follows:

$$LADD = [C \cdot CR \cdot ED \cdot EF]/[BW \cdot AT \cdot 365], \quad (2.3.3)$$

where *LADD* – average daily intake or intake (*I*), mg/ (kg·day);

C – the concentration of a substance in polluted environment, mg/l, mg/m^3, mg/sm^2, mg/kg;

CR – the intake rate of effecting medium (drinking water, air, food, etc.), l/day, m^3/day, kg/day etc.;

ED – exposure duration, years;

EF – exposure frequency, days/year;

BW – body weight, kg,

AT – exposure averaging period (for carcinogens *AT* = 70 years);

365 – number of days in a year.

Thus, the most important result of the exposure assessment within the evaluation of health risk associated with chemical pollution of the environment, is to form a complete exposure scenario which includes determination of the frequency, duration and routes of exposure of the chemical factors, a description of the nature of the impact, the size and nature of the exposed population with the assessment of exposure routes, as well as the establishment of the level of exposure of the investigated risk factor.

"Dose – response" dependency relation assessment

The assessment of risk associated with exposure to chemicals, the "dose – response" assessment is considered as a process of quantitative characterization of toxicological information and the establishment of a relation between exposure dose (concentration) of the

test chemical factors and the incidence of adverse effects in the exposed population [A guide to health risk assessment, in 2001; Onishchenko G.G. et al., 2002; EU, 2003; WHO, 2010].

Analysis of the "dose – response" relation provides for the establishment of causation of adverse effect under the action of the test chemical factor, identification of the lowest dose that causes the development of the observed effect, and the determination of the intensity of the effect increase with dose increase.

In addition, the study of "dose – response" relation is the basis for the establishment of toxicity indicators used in the future for the risk profile and includes:

– the collection of information about the toxic and carcinogenic properties of the substance;

– the selection of basic, critical research characterizing the "dose – response" dependence and observed adverse effects under the conditions of exposure that are most relevant to the chosen scenario and exposure routes;

– the analysis of additional supporting studies confirming the correctness of the choice of the critical observation;

– the determination of the required parameters of "dose – response" dependence, assessment of uncertainties and extrapolation parameters of "dose – response" relation for the exposed population;

– the generalization of toxicological information and selection of criteria for the subsequent risk assessment [WHO, 1999; A guide to health risk assessment, in 2001; Onishchenko G.G. et al., 2002].

When evaluating the ratio between the dose of the chemical and reaction of the body, it is believed that:

– the level of the reaction depends on the dose of the chemical;

– the higher the dose, the greater the percentage of the population that responds to a chemical effect;

– the higher the dose, the more severe the reaction occurring in humans;

– carcinogenic effects due to exposure to chemical carcinogens having genotoxic effects may occur at any dose that causes initiation of damage to genetic material (threshold effects);

– for non-carcinogenic substances and carcinogens with non-genotoxic mechanism of action, it is supposed to have thresholds below which adverse effects do not occur [Benford D.J., 2001; Onishchenko G.G. et al., 2002; Commonwealth of Australia, 2004].

A typical "dose – response" dependence for non-carcinogenic substances has the form of S-shaped (sigmoidal) curve, the left branch which tends to zero or is combined with abscissa at a point corresponding to the zero effect (Fig. 2.27), while no negative effects are observed at the lowest dose loads. Health responses are recorded when increasing the dose in a small number of people who represent the most sensitive group. Appropriate health responses are recorded as the subsequent increase in dose rates in most of the population, and gradually at the whole population. For the variable responses, their severity increases with increasing radiation dose [Benford D.J., 2001; Onishchenko G.G. et al., 2002].

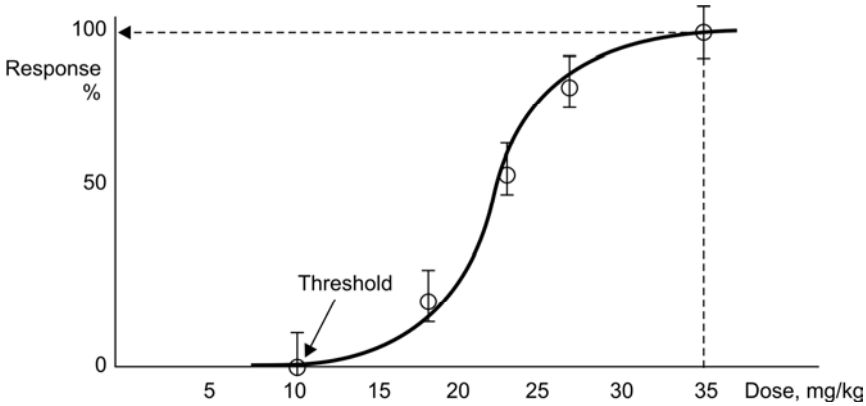


Fig. 2.27. Typical (sigmoidal) "dose – response" relation

The most commonly used in practice "dose – response" characteristics are:

1) the value of the dependence slope reflecting increase of the probability of negative response development with the increase of dose (concentration) of 1 mg/kg or 1 mg/m^3;

2) the level of impact associated with a certain effect probability;

3) the maximum nonperforming dose and the minimum dose causing a threshold effect (for non-carcinogenic and carcinogenic having non-genotoxic mechanism of action).

The parameters of the first and second groups are mainly used for the evaluation of carcinogenic risks, as well as health risks when exposed to some of the most common chemical contaminants; the indicators of the second group are used to establish reference doses and concentrations; the indicators of the third group, which is the basis for the establishment of reference doses and concentrations of chemicals are most commonly used for non-carcinogenic effects risk characterization.

The data used to establish the "dose – response" relation include the results of animal toxicology studies, clinical exposure studies, as well as the data of epidemiological studies with the highest priority [EU, 2000; Onishchenko G.G. et al., 2002; EC, 2003].

A wide range of harmful effects characterizes the effect of chemicals, but the risk assessment methodology should be focused on the harmful effect that occurs under the action of the lowest effective dose (critical effect, critical organs/systems). Other harmful effects caused by dosages exceeding the threshold ones should not be ignored. With appropriate epidemiological or experimental data, it is more justified to analyze all the action spectrum of the test chemical, which greatly increases the ability to forecast the possible harmful effects.

"Dose-response" dependency relation assessment for noncarcinogenic effects

The large number of levels reflecting the daily exposure (intake) of chemicals throughout the entire live, including the reference dose and concentration (*RfD* and *RfC*), acceptable daily Intake (*ADI*), tolerable daily intake (*TDI*), guidance level (*GV*), the recommended indicators of permissible health effect (*HA*), the projected non-effective level for humans (*PNEL*), minimum risk level (*MRL*), the recommended exposure level (*REL*), etc. are used to assess the chronic non-carcinogenic effects [EU, 2000; Onishchenko G.G. et al., 2002; WHO, 2010].

The safe levels of short-term effects are aimed at preventing of deaths, acute poisoning of varying severity or unpleasant subjective sensations at short-term but intense environmental pollution caused by adverse weather conditions (smog, toxic mists), emergency contingency situations, and volley emissions, the discharges and spills of toxic substances in high concentrations at hazardous production facilities. These levels are usually designed for continuous short-term chemical effect lasting from 5–30 min to 6–8 and 24 h. The reference level of acute inhalation effects on the population (*ARfC*) is the most commonly used – maximum concentration causing no harmful effects in the most sensitive individuals at regulated time of exposure averaging [Onishchenko G.G. et al., 2002; Instructions 2.1.6.11-9-29-2004].

The risk assessment of the development of non-carcinogenic effects is usually based on the assumption of a threshold of harmful action, below which adverse effects are not developed. Risk assessment methodology widely uses the following concepts:

– Adverse Effects Non-detection Level (*NOAEL*) – the highest dose or concentration at which modern research methods cannot detect any harmful effects on health;

– Lowest exposure level at which the adverse effect is observed (*LOAEL*).

Health safe level of chemicals effect is set by dividing the *NOAEL* by the value of the uncertainty factor (*UF*). In the absence of *NOAEL*, *LOAEL* is used to calculate a safe level [Onishchenko G.G. et al., 2002]:

$$RfC\ (RfD) = NOAEL\ (LOAEL) / (UF \cdot MF), \qquad (2.3.4)$$

where *RfC* (*RfD*) – reference concentration (dose);

NOAEL – Adverse Effects Non-detection Level;

LOAEL – Lowest exposure level at which the adverse effect is observed;

UF – uncertainty factor (ratio);

MF – modifying factor.

This methodical approach is clearly shown in Fig. 2.28.

The uncertainty factor (*UF*) is established taking into account the possible impact on the reliability of the safety assessment of the level of a number of factors. The lower the uncertainty factor, the better the conditions for establishing a safe level corresponds to the "ideal".

The above formula also contains the value of modifying factor (*MF*) the value of which depends on the professional assessment of the completeness and accuracy of all analyzed toxicological data, the availability of supporting and additional researches. The value of modifying factor can fluctuate in the range of 1<*MF* = 10. More often, *MF* shall be equal to 1.0.

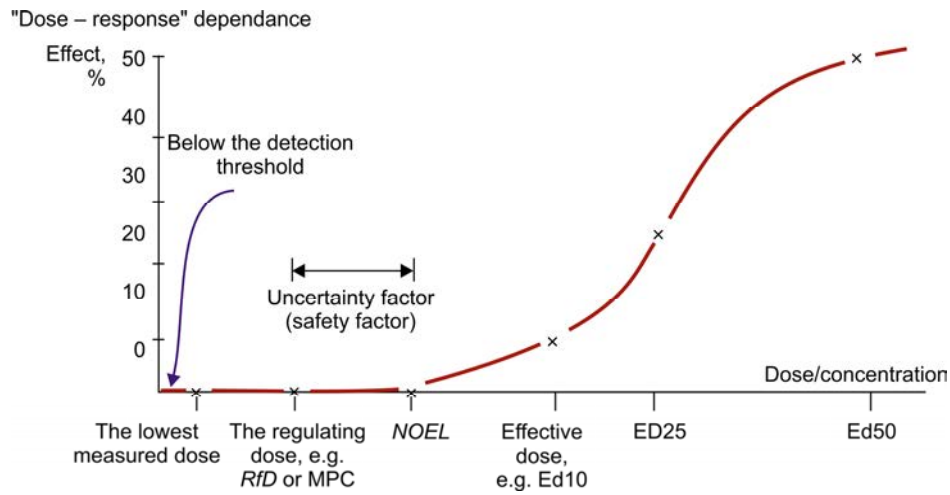


Fig. 2.28. The establishment of the reference exposure level on the basis of threshold or inactive dose

Experimental study on the use of uncertainty factors suggests the following categories:

– uncertainty factor to account for differences in the sensitivity of the people; this factor is introduced to take into account the variability of individual sensitivity in the human population (from 1 to 10 (1 – studies on the most sensitive subpopulations 10 – normal (average) sub-population));

– uncertainty factor for extrapolation of data from animals to human, which takes into account the variability in interspecies sensitivity (from 1 to 10 (1 – is observed in humans, 3 – observation on animals (unless HEC calculation is used), 10 – observation on animals in the absence of specific information about sensitivity));

– uncertainty factor for the extrapolation of data from subchronic to chronic exposure is used in studies in which the impact lasts for a shorter period of time than the whole life, and is based on the assumption that if a chemical affected the animals throughout their lives, and not for some of its interval, the Adverse Effects Non-detection Level could be lower (from 1 to 10 (1 – if the duration of the exposure is more than 12% of the average life expectancy, 3 – 8–12% of the average lifespan, 10 – less than 8% of the average life expectancy));

– factor for the extrapolation of data from the lowest observed adverse effect level (*LOAEL*) to the non-observed adverse effect level (*NOAEL*) (from 3 to 10);

– uncertainty factors to account for the effect of the substance on the developing organism (fetus, infant, child) (from 1 to 10);

– uncertainty factor that takes into account the transition from the minimum to the full database (less than or equal to 10).

The extrapolation of the results obtained at nonstandard exposure mode to the real conditions of human exposure should also be taken into account in the course of

establishing the value of uncertainty factor; extrapolation to the human equivalent concentration (HEC): the additional accounting of features of absorption and deposition of gases or aerosols in the respiratory tract of animals and humans; extrapolation from one exposure route to another (taking into account differences in toxicity for different intake routs); translation from more severe effects to less severe ones.

Decision on the amount of uncertainty factor is based on expert judgment.

The total value of the uncertainty factor is obtained by multiplying the selected values of each of the components of this factor.

Recommended levels do not have a legislative nature and are not a substitute for existing hygienic standards used as criteria for the quality of the environment, and serve only as criteria for a risk of substances exposure on the human body.

Recently, parameters of risk assessment obtained from *epidemiological studies* are preferred in the world practice. The *method of the reference (supporting) levels establishment* (Benchmark Dose (BMD), Benchmark Concentration (BMC)) is most popular. This approach provides a selection of types of studies of the examined response, the development of a mathematical model that approximates the real data on the exposure and appropriate responses, the construction of the best model that reflects the dependence of the response on the exposure levels, the selection of the frame response characterizing the degree of differences between the responses in the experimental and control groups, calculation of 95% upper confidence limit for the acceptable risk level and exposure level (BMD/BMC), which corresponds to this value [WHO, 1999; EU, 2000; Onishchenko G.G. et al., 2002; WHO, 2009*b*, 2010].

"Dose – response" dependency relation assessment for carcinogenic substances

Carcinogenesis is the main non-threshold effect. The assessment of the non-threshold effect assumed the linearity between the experimentally obtained lowest dose and zero dose [WHO, 1999; Benford D.J., 2001; A guide to health risk assessment, in 2001; Onishchenko G.G. et al., 2002; WHO, 2010] suggesting the presence of the calculable probability of an adverse health response development even at very low dose. The numerical values of the probabilities are obtained by selecting one or more models for the range of the experimental doses and extrapolation to more lower levels of external environmental impact [Commonwealth of Australia, 2004].

An example of "dose – response" relation for a carcinogen with non-threshold mechanisms of action is shown in Fig. 2.29.

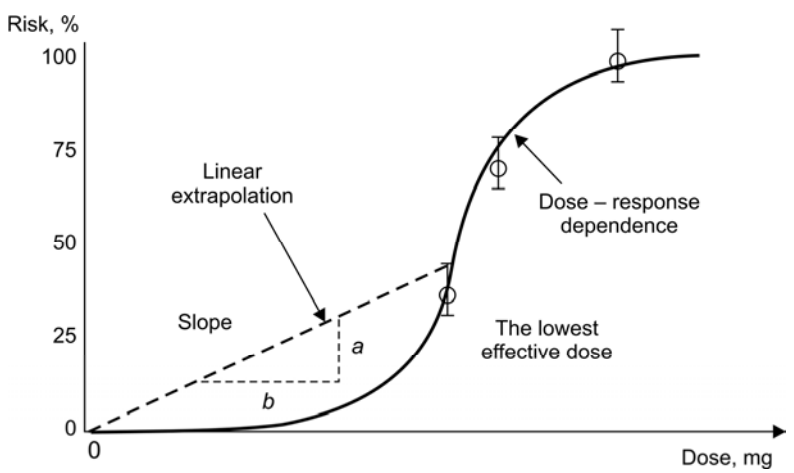


Fig. 2.29. "Dose – response" dependency relation for chemical carcinogen

The main parameter to assess the carcinogenic risk of exposure to carcinogenic agent with non-threshold mechanism of action – the carcinogenic potential factor (*CPF*) or slope factor (*SF*) characterizing the degree of carcinogenic risk increase with increase in the exposure dose per unit. Slope factor has dimension $(mg/(kg \cdot day))^{-1}$.

SF values are set separately for inhalation (*SFi*) and oral (*SFo*) intake of chemical carcinogens.

Another parameter for the carcinogenic risk assessment is the value of the so-called unit risk (*UR*), which is a top, conservative estimate of carcinogenic risk in humans exposed throughout their lives to constant exposure to an analyzed carcinogen in a concentration of 1 mg/m3 (ambient air) or 1 mg/l (drinking water).

Unit quantities *SFd* for epicutaneous exposure are calculated in risk assessment methodology based on the values of absorption coefficient in the gastrointestinal tract and the *SFo* value obtained upon oral administration of a chemical carcinogen.

Risk characterization

Risk characterization is the stage at which quality risk assessment, the calculation of parameters for semi-quantitative and quantitative risk assessment, and the classification of risk with the assessment of its admissibility is performed.

The characterization of the risks associated with the effect of chemical factors is carried out according to the following steps:

– the summation of the assessment results of exposure and "dose (concentration) – response" relations

– the calculation of risk values for individual exposure routes of chemicals;

– the calculation of risk for the conditions of aggregate (the intake of one chemical compound in the human body through all possible routes from different environmental medium) and cumulative (simultaneous exposure to multiple chemicals) exposure;

– the identification and analysis of the uncertainties of risk assessment;

– the summary of the results of risk assessment and presentation of the obtained data to the people participating in the risk management.

Risk characterization uses the value of conditionally accepted acceptable risk – the probability of an event occurrence, the negative effects of which are so small that a person or a group of people or society as a whole are ready to take that risk for the obtained benefit from risk factors [R 2.1.10.1920-04].

The characterization of the risk of carcinogenic and non-carcinogenic effects is controlled separately.

Carcinogenic effects risk characterization

Carcinogenic risk characterization includes:

– the summary and analysis of all available information on hazard, features of their effects on the human body, and exposure levels;

– the calculation of individual carcinogenic risk for each substance entering the body through the analyzed routes;

– the calculation of individual carcinogenic risk for each carcinogenic component of the test chemical mixture and the total carcinogenic risk for the whole mixture;

– the calculation of total cancer risks for each of the analyzed exposure routes, as well as the total carcinogenic risk for all substances and all their analyzed exposure routes;

– the calculation of population carcinogenic risks;

– the discussion and evaluation of the sources of uncertainty and variability of the results of the risk characterization;

– the summary and presentation of the results of the risk characterization [P 2.1.10.1920-04].

The calculation of individual carcinogenic risk is carried out using data on the amount of exposure and the values of the factors of carcinogenic potential (slope factor, unit risk). Typically, the additional probability of cancer development in an individual throughout the life

(*CR*) is estimated considering the lifetime average daily dose (*LADD*) for carcinogenic chemicals:

$$CR = LADD \cdot SF, \quad (2.3.5)$$

where *LADD* – lifetime average daily dose, mg/ (kg·day);
SF – slope factor, $(mg/(kg \cdot day))^{-1}$.

When using the value of the unit risk (*UR*), the calculation formula has the following form:

$$CR = LADC \cdot UR, \quad (2.3.6)$$

where *LADC* – the average concentration of the substance in the test environmental medium for the entire averaging period of exposure (drinking water, mg/l air, mg/m^3);
UR – unit risk of water (risk per 1 mg/L) or air (risk per 1 mg/m^3).

In the risk calculation and characterization, it is necessary to take into account the features of the estimated population group, exposure factors (descriptors) inherent to it and the exposure measure selected by researcher. Calculation of the carcinogenic risk is performed only for the range of doses (concentrations) of the chemical, which corresponds to the linear part of the "dose (concentration) - response" relation. If there are several types of exposure and the estimated population groups, the risk assessment should be carried out for each of these options individually.

The determination of the population carcinogenic risks (*PCR*) reflecting an additional (to the background) the number of cases of malignant tumors that can occur during the life due to the exposure to the test factor, should be conducted by the formula:

$$PCR = CR \cdot POP, \quad (2.3.7)$$

where *CR* – individual cancer risk;
POP – the number of the tested population, people.

Individual and population cancerogenic risks characterize the upper limit of the possible carcinogenic risk during the period corresponding to the average human life expectancy (70 years). The comparative risk characterization often uses the value of annual population risk (*PCRa*) – the estimated number of additional cases of cancer during the year. The amount of the annual population risk, as a rule, should not be used for any direct analogies between the levels of actual cancer incidence or mortality rates and the values of these risks.

The results of the characteristics of the carcinogenic risks are most valuable for the comparative assessment of the impact of environmental factors on different areas at different times, before and after recreational activities, to compare the effectiveness and potential impact on human health of various technological processes and environmental activities.

Carcinogenic risk in the complex intake of chemicals through different ways (oral, dermal, inhalation) and at the combined action of several chemical compounds is considered as an additive one.

Under the influence of several carcinogens, the total carcinogenic risk for a given exposure route (e.g., oral or inhalation) is calculated according to the formula

$$CR_T = \sum CR_j, \quad (2.3.8)$$

where CR_T – total carcinogenic risk for exposure routes *T*;
CR_j – cancer risk for *j*-th carcinogenic substance.

With simultaneous exposure to multiple carcinogenic substances entering the human body through various routs, the calculation of the overall risk (TCR) is performed according to the formula

$$TCR = \sum CR_T, \quad (2.3.9)$$

where *TCR* – carcinogenic risk for multiple routes of exposure;
CR_T – total carcinogenic risk for exposure routes *T*;

When calculating the total carcinogenic risks, it is necessary to take into account differences in the severity of carcinogenic effects of chemicals in different exposure routes. In cases, where the value of the carcinogenic potency factors in different exposure routes are different, the calculation of risk based on the total doses is legitimate only for the same exposure routes.

In the simultaneous presence of several carcinogenic substances in the environment, similar calculations are performed first for each tested substance, and then for the whole mixture.

Characteristics of carcinogenic risk is carried out in accordance with the acceptability criteria system (Table 2.20) [Onishchenko G.G. et al., 2002].

Table 2.20

The classification of the risk ranges in accordance with R.2.1.10.1920-04 "Guidelines on the assessment of risk for public health at the impact of chemical substances contaminating the environment:

Individual risk value	Characteristic
$R \leq 1 \cdot 10^{-6}$	Corresponds to one additional incidence of a severe disease or death per 1 mln. of exposed people, characterizes such risk levels that are perceived by all people as negligible small, not different from ordinary, everyday risks (*de minimis* level). such risks do not require any additional measures on their mitigation and their levels are subject to the periodical control only.
$1 \cdot 10^{-6} < R < 1 \cdot 10^{-4}$	Corresponds to maximum acceptable risk, i.e. the upper bound of acceptable risk. most foreign hygienic standards are recommended by international organizations for the population as a whole was established at this level (for example, who uses a value of $1 \cdot 10^{-5}$ as acceptable risk for drinking water, and $1 \cdot 10^{-4}$ for air). these levels are subject to the permanent control. in some cases at such levels of risk the additional measures on their mitigation can be taken.
$1 \cdot 10^{-4} < R < 1 \cdot 10^{-3}$	Acceptable for professional groups and not acceptable for population as a whole. the occurrence of such risk requires the development and implementation of the planned recreational measures. the planning of measures on the mitigation of risks in this case shall be based on the results of deeper assessment of different aspects of existing problems and establishment of the level of their priority in relation to the other hygienic, ecological, social and economic problems at this territory.
$R \leq 1 \cdot 10^{-3}$	Not acceptable both for population and professional groups. this range is defined as the *de manifestis risk* and if it is reached it is necessary to provide the recommendations for people making the decisions on the implementation of emergency recreational measures for the risk mitigation.

Noncarcinogenic effects risk characterization

The characterization of risk of non-carcinogenic effects development is carried out either by comparing actual exposure levels to safe exposure levels (the hazard index/quotient), or on the basis of parameters of "concentration – response" dependence derived from epidemiological studies.

The characterization of the risk of non-carcinogenic effects development for individual substances is performed based on the hazard quotient calculation by the following formula

$$HQ = AD/RfD \text{ or } HQ = AC/RfC, \quad (2.3.10)$$

where HQ – hazard quotient;

AD – average dose, mg/kg;

AC – average concentration, mg/m^3;

RfD – reference (safe) dose, mg/kg;

RfC – reference (safe) concentration, mg/m^3.

Hazard quotient is calculated separately for the conditions of short-term (acute), subacute, and long-term effects of chemicals. In this case, the averaging period of exposures and corresponding safe exposure levels should be similar.

The characterization of the risk of non-carcinogenic effects development under combined and complex exposure to chemical compounds is based on the hazard index calculation (*HI*).

Hazard index for the conditions of simultaneous intake of several substances through the same route (e.g., oral or inhalation) is calculated by the formula

$$HI = \sum HQ_i, \tag{2.3.11}$$

where *HQ* – hazard quotients for individual components of the mixture of effecting agents.

In the integrated chemicals intake into the human body from the environment through several ways at the same time, as well as in multiroutes and multimedium impact, the total hazard index (THI) calculated by the following formula is a criterion of risk

$$THI = \sum HI_j, \tag{2.3.12}$$

where HI_j – hazard index for the separate or individual exposure routes.

In the simultaneous intake of a substance through inhalation and ingestion, hazard index is calculated by the following formula

$$THI = C_a/RfC + D_0/RfD, \tag{2.3.13}$$

where C_a – estimated concentration of the substance in the air, mg/m^3;

D_0 – dose received through the oral route, mg/kg.

Hazard assessment for complex intake is carried out without taking into account the absorption coefficients of substances in the respiratory and gastrointestinal tract, i.e. based on the affecting doses and concentrations. This is stipulated by the fact, that the value of safe exposure levels of chemicals (RfD, RfC) is always set as exposure (effecting) ones rather than absorbed doses.

The value of the absorbed dose is usually estimated in percutaneous exposure to chemicals. Due to the lack of data on safety levels in percutaneous exposure for the majority of priority chemicals, the value of the absorbed dose calculated on the basis of the reference dose (RfD_o) in the oral intake route is used as indicative measures of acceptable epicutaneous exposure (RfD_d):

$$RfDd = D_0 \cdot GIABS, \tag{2.3.14}$$

where *GIABS* – the coefficient of absorption in the gastrointestinal tract.

It is appropriate to perform the calculation of the hazard indices taking into account the critical organs/systems exposed by test substances, as the additivity is the most probable type of their combined action under the influence of components of the mixture on the same organs or systems of the body. A similar approach adopted in the assessment of the risk for non-carcinogenic effects is quite conservative because it may exaggerate the health hazard, but it is more preferable in comparison with separate, independent evaluation of each of the components or the recognition of all the components as additively effecting ones.

If the calculated hazard quotient (*HQ*) of the substance does not exceed 1, the probability of harmful effect development in human is insignificant with daily intake of substance during the life, and this exposure is characterized as acceptable. If the hazard quotient is greater than 1, the probability of harmful effects development in human increases in proportion to *HQ* increase, however it is not possible to accurately indicate the magnitude of this probability.

Hazard quotients for each route and each exposure environment are summarized, and the total hazard index (THI) is calculated in complex and/or multimedia intake of one substance. The total hazard index characterizing the tolerable intake should also not exceed 1 [R 2.1.10.1920-04].

In the combined intake of several substances through any route, the total hazard index is determined for substances that affect the same system (organ). In the context of the combined effect, the total hazard index characterizes the risk of adverse effects on the critical organ (system). Priority organs and systems most affected by exposure to chemical environmental factors can be allocated according to this index.

Quantitative assessment of noncarcinogenic risk to health at the exposure to chemical factors on the basis of the evolution models construction:

At present, the risk evolution simulation within the assessment of carcinogenic health risks caused by exposure to chemical environmental factors, is considered as one of the most appropriate methods for solving problems of prediction and assessment of the probable impact of environmental factors on human health [Zaitseva N.V. et al., 2012].

Methodological approaches to quantitative assessment of the noncarcinogenic risk are presented in the MR 2.1.10.0062-12.

The use of quantitative evaluation of non-carcinogenic risk parameters based on evolutionary models under chronic exposure to chemicals allows the evaluation of the risks accumulation with regard to age and duration of exposure.

The assessment of population health risk when exposed to chemical factors taking into account the time of effects development allows:

– predicting the health harm including a reduction of life expectancy due to exposure to chemical factors of the environment on the basis of analysis of the dynamics and evolution of the risks;

– identifying chemical factors potentially affecting human life and health in the intake through different routes from different environmental mediums;

– performing quantitative risk assessment of health problems of varying severity under the influence of non-carcinogenic chemicals;

– performing the validation of measures aimed at risk minimization through the development and implementation of measures to prevent the contamination of the environment.

The fundamental algorithm of actions to quantify the non-carcinogenic health risk based on construction of evolutionary models is shown in Fig. 2.30.

Stages of hazard identification and exposure assessment within the framework of quantitative assessment of carcinogenic health risk based on evolutionary models are performed in accordance with R 2.1.10.1920-04 and include the establishment of chemical hazards, probable effects associated with their impact on human health, the definition of risk group, and the formation of a complete exposure scenario which comprises the determining of the frequency, duration, and route of exposure to the chemical factor, the description of exposure nature, the size and nature of the exposed population, the assessment of exposure routes, the setting of the exposure level of risk factor under study.

The stage of "exposure – response" and "exposure – effect" dependencies analysis involves the construction of an evolutionary model including all of the involved identified factors and the probable health responses. Detailed simulation procedure is presented in Section 2.2.

The process of a mathematical model construction to quantify the non-carcinogenic health risk when exposed to chemicals can use paired mathematical models listed in the guidance and recommendations of leading international organizations (WHO, OECD, etc.) and contained in the published scientific studies (EPA, ATSDR, etc.). The use of these models to analyze the evolution of health risk is accompanied with a mandatory procedure adaptation, basic relationships of which are represented by formulas (2.2.35)–(2.2.45)

The results of special regional epidemiological and controlled clinical studies should be used in the absence of "exposure – response" models. The simulation of "exposure –

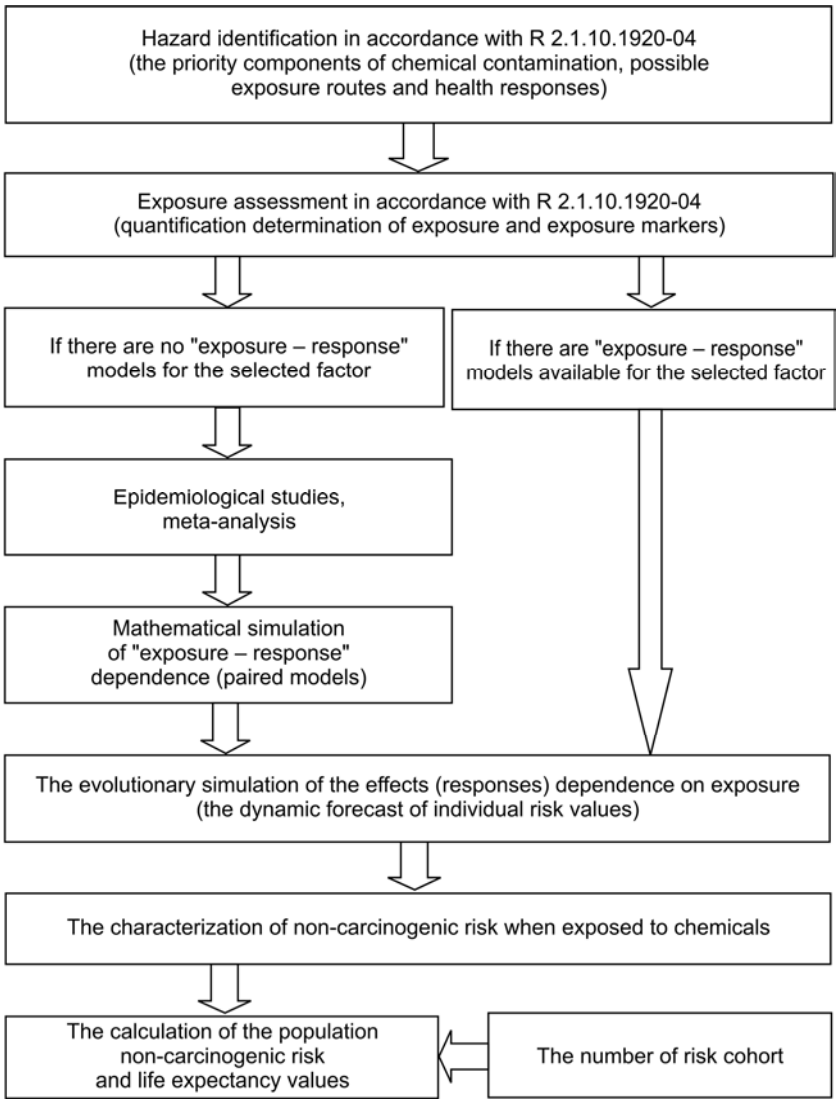


Fig. 2.30. The algorithm for quantitative assessment of public health non-carcinogenic risk when exposed to chemicals

response" dependencies when assessing carcinogenic risk establishes a threshold actions principle, according to which adverse health effects or responses appear starting with the reference level. The probability of negative effects can be determined using regional models that are adequate to a specific set of chemical factors.

In the absence of published data on the reference concentration/dose, such levels should be set on the basis of the results of epidemiological studies, in which the "odds ratio" (*OR*) indicators for the entire studied exposure levels range are calculated. Reference level is determined based on the condition $OR = 1$, the value corresponding to the upper 95% confidence limit of the resulting model should be set as the reference level.

Paired "exposure – response" dependencies adapted for use in the health risks evolution simulation and combined in the "model library" allow performing the calculation

and assessment of risk with a given chemical factors exposure scenario. In this case, the indicators used to evaluate the "exposure – response" relationship should be reviewed and amended as new scientific data that meet the requirements for completeness and quality of research is obtained.

Use of evolutionary models allows the calculation of non-carcinogenic risk at any given time based on the duration of exposure and age. This basis makes it possible to predict the expected life expectancy (projected life expectancy) and its reduction under the influence of risk factors.

Risk characterization is based on the calculation of the additional risk, reduced risk index, the structure of risk by factors and the probable responses. Methodology for the application of evolutionary simulation for problems of health risk assessment, presented in Section 2.2, involves the possibility to calculate the additional population indicators of morbidity and mortality.

The risk values under the impact of chemical factors reflect mainly the long-term trend of health indicators change emerging subject to all the initial conditions (for example, a certain duration and intensity of exposure, the exposure immutability through time, the specific values of the exposure factors, etc.) accepted in the calculations.

The results of the risk assessment are the most effective tool to compare the harmful effects of chemical factors in different areas at different times before and after the health measures to determine their effectiveness, etc.

The conclusion of the magnitude of the risk level associated with the subsequent decisions on reducing (or avoiding) contamination of the environment, which may require significant financial costs or appear to be feasible in practice. Therefore, the inherent assessment uncertainty should be characterized along with the risk value.

Uncertainty analysis

Uncertainty – a situation caused by the imperfection of knowledge about the present or future state of the considered system – describes the partial absence or degree of reliability of data on certain parameters, processes or models used in the risk assessment. Uncertainty ultimately determines the reliability and accuracy of risk assessments and can be reduced by additional studies or measurements [Commonwealth of Australia, 2004; Onishchenko G.G. et al., 2002].

Uncertainties assessment is an essential component of health risk assessment due to chemical factors and is aimed to establish the main sources of uncertainties, variability, and assumptions of all stages of health risk assessment [US EPA, 1992; NRC, 1994; WHO, 1995; Dourson M.L., 1996; EU, 2000; Benford D.J., 2001; Jager T., 2001; Onishchenko G.G., 2002; EC, 2003; Commonwealth of Australia, 2004; Risk Assessment Of Chemicals, 2007; WHO, 2008, 2009*a*, 2010; US EPA, 2011].

When discussing possible sources of uncertainties related to health risk assessment due to exposure to chemical factors, it is necessary to distinguish two basic concepts [EU, 2000; Onishchenko G.G., 2002; Commonwealth of Australia, 2004; Risk Assessment Of Chemicals, 2007; WHO, 2009*a*; US EPA, 2011]:

– *variability* representing the homogeneity or volatility of population parameters of plants, animals or human, the physical properties of the environment, etc.; the variability being a fundamental property of nature usually cannot be reduced by conducting additional studies or measurements;

– *uncertainty* which is a partial absence of the concept or certain data on certain parameters, processes, or models related to the risk assessment. Because uncertainty is a property inherent to the risk assessment process, in some cases it can be reduced by additional studies or measurements with a mandatory allocation of research priorities allowing the most effective reduction of the overall uncertainty [EU, 2000; Onishchenko G.G., 2002].

The main sources of uncertainty on the hazard identification stage are incomplete or inaccurate information on the sources of pollution of the environment, the qualitative and quantitative characteristics of the studied chemical hazards; errors in the prediction of the

fate and transport of chemical factors in the environment objects; the insufficient degree of completeness, reliability and representativeness of measurements results; poor evidence or lack of data on the harmful effects in humans [Onishchenko G.G., 2002; Commonwealth of Australia, 2004].

Hazard identification should include a critical review of each result, and the entire database, related to the analyzed chemical hazards with the conclusions on the hazard for the exposed human populations and the possibility to use data obtained in animals to predict adverse effects in humans [Onishchenko G.G., 2002].

The main sources of uncertainty that can occur when assessing "dose – response" relations include uncertainties:

– associated with the establishment of the threshold/reference/safe level of exposure;

– stipulated by the transfer of the results of epidemiological studies on the estimated population exposure;

– associated with the establishment of the degree of proof of adverse effect in humans, including carcinogenic one;

– the establishment of critical organs/systems and harmful effects;

– related to lack of knowledge of the mechanisms of interaction of factors studied at different exposure routes and at the simultaneous intake through different routes [EU, 2000; Benford D.J., 2001; Onishchenko G.G., 2002; Instructions 2.1.6.11-9-29-2004; WHO, 2010].

One of the most important components of uncertainty analysis is the assessment of the uncertainties associated with the "dose – response" dependence simulation [Onishchenko G.G., 2002] including incomplete information on the parameters used in the analysis, including both the properties of the population, and features of the effecting factor using the methods of Maximum Likelihood Estimation, bootstrapping, Markov chains.

In general, the uncertainties associated with the exposure assessment have a greatest impact on the accuracy of the final risk assessments [Onishchenko G.G., 2002; WHO, 2009*a*].

The following 3 groups of uncertainties are distinguished in the course of exposure assessment:

1) uncertainties associated with the exposure scenario;

2) simulation uncertainties;

3) parameters uncertainties [US EPA, 1992; EU, 2000; Commonwealth of Australia, 2004; WHO, 2008; US EPA, 2011].

The sources of exposure scenarios uncertainties include: description errors, aggregation errors (for example, conclusions about the homogeneity of the population, the assumption of a stable equilibrium of a dynamic process state, etc.), errors of judgments (choosing the wrong scenario, models, lack of experienced experts, etc.), as well as the selection or exclusion of various exposure routes from the analysis, assumptions about the frequency and duration of the various activities of the population, etc. [US EPA, 1992; Onishchenko G.G., 2002; EC, 2003; Commonwealth of Australia, 2004; Risk Assessment Of Chemicals, 2007; WHO, 2008].

Uncertainties associated with the model structure, including the auxiliary models, include functional errors (errors in the representation of the process); errors caused by simulation technique including the description errors of processes, models aggregation errors, etc.; technical errors (numerical errors, programming errors) [US EPA, 1992; Onishchenko G.G., 2002; EU, 2003; Risk Assessment Of Chemicals, 2007; WHO, 2008].

The sources of parameters uncertainties are measurement errors, sampling errors, the use of generalized or surrogate data, the standard values, the extrapolation of data, the values of physiological exposure factors chosen for intake value calculation [EU, 2000; Benford D.J., 2001; Onishchenko G.G., 2002; EU, 2003; EU, 2003; Commonwealth of Australia, 2004; WHO, 2007; Risk Assessment Of Chemicals, 2007; WHO, 2010].

Measurement errors may be accidental, resulting from inaccurate measurements, and systematic reflecting the deviation or tendency to measure anything other than that to be measured [US EPA, 1992; Onishchenko G.G., 2002; Risk Assessment Of Chemicals, 2007; WHO, 2008].

Variability analysis should be carried out along with an uncertainty analysis in the exposure assessment [Onishchenko G.G. et al., 2002; Instructions 2.1.6.11-9-29-2004; US EPA, 2011]. For example, impact variability is related with the activity of individuals, their behavior, with indicators of contaminant emissions, physical and chemical processes that change the concentrations of chemicals in various media, etc..

There are three types of variability in exposure assessment:

– the variability of the location (spatial variability), which can be evaluated at the regional (macro) or local (micro) level;

– variability in time (time variability) including the assessment of the exposure duration, seasonal changes in exposure;

– variability among individuals (interindividual variability), including human characteristics (age or body weight), as well as behavioral characteristics (nature of the activity, location and duration of the various types of activity) [R 2.1.10.1920-04; US EPA, 2011].

Uncertainties associated with the determination of the total risk and total hazard index at a stage of risk characterization in the case of health risk assessment due to chemical risk factors mainly concern the issues of synergy or antagonism of the effect of different mixtures of chemicals. Taking into account these uncertainties significantly expands the list of conditions that limit the possibility of the total risk determination [R 2.1.10.1920-04].

Uncertainty analysis is an important and integral part of all stages of assessment of population health risk associated with the chemical contamination of the environment, and allows making more accurate and reliable conclusions about the magnitude of the acceptable level of risk.

The use of the entire complex of risk assessment tools, including semi-quantitative, quantitative evaluation, as well as evolutionary simulation of the health risks caused by the exposure to chemical environmental factors, allows the full description of the established health risks, the identification of priority components forming it, as well as the most probable health responses, the occurrence of which can be expected at this risk. The proposed classification of health risk levels when exposed to chemical environmental factors can be the fundamental basis for the selection of risk management measures.

2.4. The assessment of public health risk associated with the microbiological contamination of living environment objects

Complete scheme for the assessment of public health risk under the influence of microbiological factors provides four stages:

– hazard Identification aimed at identifying a microorganism or microbial toxin in foods that pose a health risk, and the collection of scientific and practical data on the dynamics of microorganisms or microbial toxins (growth, reproduction, inactivation, or deletion) in this object; the risk profile is developed at the stage of hazard identification;

– exposure Assessment, which hold the establishment (taking into account the factors influencing microbial contamination at the stages of advancement of the food to microorganism and having an uncertainty) of the frequency of availability and content level of the pathogen microorganism at the time of intake to the macroorganism;

– hazard Characterization performing the description and assessment of the impact of harmful effects on the health associated with exposure of a specific pathogen microorganism on macroorganism, given their variability, as well as the simulation of the "dose – response" dependence;

– risk Characterization, which held the data integration obtained at the previous three stages of the assessment, in order to determine the risk levels (now and/or in the future) of injury to the health of the specific studied categories and groups of population, individuals from exposure to certain pathogen microorganisms based on the assessment of the impact of related uncertainties.

Hazard identification

Hazard identification is the first stage of the health risk assessment associated with microbiological contamination of the environment objects [WHO, 1998a; FAO/WHO, 1999a; Environment Canada and Health Canada, 1999; Revised framework for microbial risk assessment, in 2000; Benford D.J., 2001; Crumpton M.J., 1996; FAO/ WHO, 2006a], and is most often interpreted as a process of establishing the potential health risks of microbial origin, and the ability of a particular factor to cause some adverse effects in humans.

The objective of hazard identification is the maximum characterization of pathogen microorganisms and microbial toxins and metabolites, their genetic material, and structural components, the possible adverse effects on humans when present in food products.

At the stage of hazard identification as part of the assessment of health risk associated with microbiological contamination of environmental objects, the risk profile is formulated (in particular food as the main source of microbiological risk factor).

The risk profile includes the following elements:

– the definition of risk area (the identification of the type of product, the description of the manufacturing process, the evaluation of scientific data on the characteristics of the productions, the determination of the potential risk to consumers, the creation of a list of all microbial factors affecting the health of the population, typical for food, the assessment of the possible impact of pathogen microorganisms on the health, the analysis of existing standards for the assessment of microbiological hazards, the description of previously established risk among different segments of the population);

– risk indicators, which are dependent on the objectives of the study (e.g., the number of microorganisms in food products, the number of infectious diseases associated with infected products, rates of microorganism multiplication in foods);

– the analysis of the main elements of the security system (the monitoring of food products, quality manufacturing practices, the assessment of control points, the standardization of sanitary measures, the evaluation of the measures taken to ensure the safety of the product).

The risk profile should be detailed to indicate the connection of specific pathogen microorganisms with main source of their intake (for example, certain types of food) and with the factors under which these microorganisms will be concentrated in these sources. To do this, it is necessary to generalize information from appropriate sources on the incidence of certain infections and its consequences, to connect them with the frequency of food consumption and existing control measures [Revised framework for microbial risk assessment, 2000; MP 2.1.10.0067–12].

Data from scientific literature, public health monitoring, international organizations in the field of population health risk assessment when exposed to microbial factors contained in food can be used as the sources of required information, in addition, expert assessments can be used, as well as information on incidences of similar diseases [WHO, 1995; WHO, 1998*a*; FAO/WHO, 1999*a*; Environment Canada and Health Canada, 1999; Revised framework for microbial risk assessment, 2000; FAO/WHO, 2003*a*; Crumpton M.J., 1996; FAO/WHO, 2006*a*; USDA, FSIS and EPA, 2012; MP 2.1.10.0067–12].

Information useful to assess the health risks associated with microbiological contamination of environmental mediums may be contained in some statistical reporting forms.

Characteristics of pathogenic microorganisms in the assessment of the health risks associated with the microbiological contamination of environment includes:

– taxonomy;

– the presence and characteristics of pathogenicity and virulence factors;

– detecting frequency and concentration in food;

– survival and ability to reproduce in the relevant environments;

– resistance to influence of technological, disinfectants and other factors.

Data obtained in the clinical, epidemiological, laboratory and other researches can be used as background information for hazard identification in the study of the microorganisms

characteristics, in sporadic diseases, in the group breakouts or in the process of epidemiological monitoring.

The top selection criteria of priority microorganisms for risk assessment are the data of risk profile and epidemiological data evidencing about the possibility of an unacceptable health risk in the propagation of these microorganisms in foods and the lack of science-based measures for effective prevention of infections caused by them.

Hazard identification should include a description of raw materials, ingredients, and materials contacting the product, characteristics and use of the end product when assessing the microbiological risk within the HACCP system.

Hazard identification stage has screening nature and involves the identification of priority microbial contaminants in combination with certain foods that have potentially harmful factors for human health in the evaluated exposure routes [FAO/WHO, 2006*a*].

Hazard identification during the microbiological risk assessment can be carried out based on two perspectives. From the point of view of a products manufacturer, the purpose of hazard identification is to establish the possible hazards that should be excluded to ensure the safety of consumers. Furthermore, the hazard identification can be retrospective using data of epidemiological studies, of violations of food safety, and contain characteristic harmful effects among the exposed population with the establishment of a "guilty" product and pathogen. In addition to the characteristics of the microorganism or toxins and the probable sources of contamination, as well as the ability to reproduce during production and storage, it is necessary to take into account the effect of the processing and the possible sensitivity of consumers to the microbiological risk factor [Microbiological Risk Assessment in Food Processing, 2002].

As a result of hazard identification the variability in the behavior and induced effects between different types of one microorganism must also be evaluated so that at the subsequent stage of the exposure assessment the variation in the various conditions of production and use (e.g., during numbing or long-term storage in a cooled state) will be taken into account. Such differences may also affect the level of toxins production, growth rate, temperature sensitivity and survival [Microbiological Risk Assessment in Food Processing, 2002].

The following is defined based on the results of hazard identification: the list and description of priority microbial contaminants potentially hazardous to human health in the assessed exposure routs, and food that may be contaminated by them, susceptible populations and subpopulations, as well as the layout of the risk profile developed based on the earlier published studies [Revised framework for microbial risk assessment, in 2000; MR 2.1.10.0067-12].

Exposure assessment

Exposure assessment within the assessment of the health risk associated with microbiological contamination of environment is aimed at the establishment of the actual or expected number of pathogen microorganisms entering the human body through the consumption of contaminated food, and is based on an assessment of the degree of actual or potential food contamination with microorganisms or microbial toxins, and information about contingent consumption of food [FAO/WHO, 2008; MR 2.1.10.0067-12].

Exposure characterization also includes an assessment of the interaction of the pathogen, environment and human body [Revised framework for microbial risk assessment, 2000].

The exposure assessment determines the level of food contamination with bacteria in the study in view of its life cycle, and frequency and duration of its exposure on the selected population [FAO/WHO, 1999a; Benford D.J., 2001; MR 2.1.10.0067-12].

The stage of exposure assessment within the assessment of population health risk caused by microbiological contamination of environment requires to form different exposure scenarios that take into account all potential factors of causative microorganism transmission, levels of pathogen microorganisms content in foods [Revised framework for microbial risk assessment, in 2000; EU, 2000; MR 2.1.10.0067-12].

The assessment of the exposure to microbiological hazards requires to consider [FAO/WHO, 1998; FAO/WHO, 1999*a*; Revised framework for microbial risk assessment, 2000; Benford D.J., 2001; Microbiological Risk Assessment in Food Processing, 2002; FAO/WHO, 2008; USDA, FSIS and EPA, 2012; MP 2.1.10.0067–12]:

– the characterization of the pathogenic agent (e.g., its resistance to high temperatures etc.).

– the connection of the test microbiological agent with certain foods;

– food (product description, methods of its use and the manufacturer; products used in conjunction with the tested ones, the ability of the product to be a breeding ground for microorganisms, storage time);

– the processing of the food at the stages of production, use, consumption, and the impact of treatment on the level, physiological state and the virulence of microbial agents;

– food chain (results of investigations of microbiological contamination of the product components; production conditions; storage; transportation; use of detergents and disinfectants, etc.);

– the probability of cross-contamination with microbiological agents contained in other foods during production, storage, distribution, and consumption;

– the presence of preservative factors such as the specific temperature conditions, pH, humidity, etc. during packaging, storage, and propagation;

– the type of food and the ability to support or inhibit the growth of microorganisms in different environments;

– the features of test food products consumption (treatments, preparation);

– consumer (gender, age, health status, socio-economic factors, frequency and the amount of consumption of the product, the duration and conditions of product storage by the consumer, the conditions of preparation and handling).

At the stage of exposure assessment, it is necessary to form different exposure scenarios that take into account all potential factors of causative microorganism transmission, levels of pathogen microorganisms content in food. The principle of "best and worst ratings" with an assessment of the probability of the optimistic and pessimistic scenario should be considered when forming the scenarios. In accordance with the objectives of the risk assessment, exposure may be calculated based on the average values, the most probable ones (mode), or taking into account the proportion of product consumers, most often 95%.

Exposure assessment may be carried out for a variety of tasks such as:

– the assessment of the risk associated with a "pathogen – product" combination;

– the analysis of the relationship between the level of microbiological hazard of the product, followed by the exposure of consumers – in this case the exposure assessment can be used to determine the sanitary measures in international trade;

– the comparison of exposure levels under different scenarios and exposure routes;

– the determination of the information adequacy and the need for measures to improve the exposure assessment;

– the identification of the most effective measures to reduce exposure, adequate hazard of a particular product;

– the assessment of the effectiveness of protective measures;

– the identification and assessment of critical control points within the HACCP system.

It is advisable to use a schematic model of the risk process (RPM) to analyze the evolution of the studied population of microbes in time under certain conditions from the source of contamination to the receipt (contact) by macroorganism. Each stage (module) of RPM marked parameters and microbiological processes critical for causative microorganism. Thus, from 1 to 6 basic fundamental events effecting the transmission of dangerous microbial factors may be included to each module of schematically reproduced situations of food promotion to the table of a consumer. The example of RPM for microbiological risk assessment of verocytotoxin producing *E.coli* (*VT-E.coli*) in smoked meat products (SKMP) is shown in Table 2.21 [MR 2.1.10.0067–12].

Table 2.21

The model of risk process *VT-E.coli* in SKMP [Sheveleva S.A., 2007]

No.	Stage (module)	Microbiological process	Data required for microbiological risk assessment	Data sources
	Initial stage			
1	The slaughter of cattle in a slaughterhouse, eventration	The contamination of carcasses surface *VT-E.coli* caused by feces	*P VT-E.coli*, %, and *C* CFU in 1 g of cattle feces	Data based on veterinary monitoring, the results of the production control of manufacturers
2	Sawing into half carcasses, quarter carcasses, cuts	Dissemination *VT-E.coli*	P_{in} *VT-E.coli*, %, and C_{in}, CFU per cm^2 of meat surface	
3	The storage and transportation of meat	Growth with penetration into the inner layers or the inactivation depending on the conditions (time, *t*°, humidity, O_2 access, log-phase, growth velocity *VT-E.coli*)	$P_{ch.}$ *VT-E.coli*, %, and $C_{ch.}$ CFU in 1 g of meat	The results of production control and state supervision
	Intermediate stage			
4	Cuts clearing	Dissemination *VT-E.coli*	$P_{interm.}$ *VT-E.coli*, %, and $C_{interm.}$ CFU in 1 g of semi-finished products	The results of production control and state supervision
5	Separating the meat from the bones – mixing of boned meat from many carcasses	Re-contamination of *VT-E.coli* taking into account Fcc factor		
6	The trimming of meat, cutting, grinding	Dissemination *VT-E.coli*		
	Intermediate storage trimmed (minced) meat	*VT-E.coli* growth with penetration of meat pieces or minced meat depending on the conditions (time, *t*°, humidity, O_2 access, log-phase, growth velocity *VT-E.coli*, etc.)		
7	Adding components under the formulation	The reduction of C_{interm}, *VT-E.coli* KOE/r	The accounting of dilution factor	
8	Sediment or maceration	The growth of *VT-E.coli* depending on the conditions (time, *t*°, humidity, growth rate of *VT-E.coli*, etc.)	$P_{interm.}$ *VT-E.coli*, %, and $C_{interm.}$ CFU in 1 g of product	
9	Smoking and/or drying in compliance with the parameters of the technology and in the use of starter antagonists cultures	Inactivation or inhibition *VT-E.coli* according to the conditions (time, Aw, pH, presence of antimicrobial substances, necrosis rate, etc.)		
	Final stage			
10	SKMP	Survival or inactivation in the final product depending on the conditions during storage (time, Aw, pH, presence of antimicrobial substances, necrosis rate, etc.)	P_{fin}, %, and C_{fin}, CFU/g	Data from the adequate sources of outbreak investigations and incidences in the outbreak; scientific publications

Note: *P* = the frequency of microbe detection, %; *C* = concentration, CFU/g.

The construction of the RPM identifies stages where there is no necessary information for microbiological risk assessment, and uses a decision about its sources, including the use of different simulation methods of the microorganisms behavior on the basis of mathematical calculations (programmable models of direct and triangular distribution, Poisson, β-pert, β-, γ- and Vaybull, Monte Carlo, etc.).

The determination of the level of microbial pathogens or toxins with the possibility of falling into the food is also performed as part of the exposure assessment. It is allowed to classify risk according to the criteria of contamination level, the probability of infection or changes in its intensity on the route to the human organism for the purposes of the qualitative health risk assessment under the influence of microbial factors contained in food [FAO/WHO, 2008; MR 2.1.10.0067-12].

The classification of harmful effects levels of microorganisms is carried out for the qualitative assessment of population health risk when exposed to microorganisms contained in food products, and implementation of expert assessments. There are three levels of the harmful effects of microorganisms, their metabolic products, structural and genetic elements: low (microorganisms are limited, low levels of contamination, the duration and frequency of exposure does not ensure the survival, the distribution or reproduction of microorganisms in food); average (mean duration and/or frequency of exposure, the average food contamination level; microorganisms can remain in small amounts in food, only some of the living organisms can be exposed), and high (length and/or frequency of impact is large, a high level of food contamination, the microorganism has a high ability to survive, distribute, reproduce and preserve in food) [Revised framework for microbial risk assessment, in 2000; FAO / WHO, 2008; MR 2.1.10.0067-12].

For the quantitative exposure assessment a frequency of contamination with tested microorganisms, and their number per unit of weight (volume) of the food product (e.g., CFU/m^3; CFU/g CFU/l; CFU/ml for bacteria) are set with regard to their changes under the influence of external factors, such as pH, moisture, the content of nutrients, anti-microbial additives, the presence of competing microflora. Therefore, along with the initial level of food contamination, it is necessary to determine the dynamics of changes in exposure and factors that contribute both to its increase and to decrease [FAO/WHO, 2008.; MR 2.1.10.0067-12].

The establishment of the frequency and levels of microbial contamination of foods should consider the following factors:

– the quantity and quality of the operations performed with food (cooking, its parameters etc.);

– the probability of secondary contamination and cross-contamination, etc.

The determination of pathogenic microorganisms or their toxins, metabolites is carried out in accordance with techniques providing quantitative data on the content of these microorganisms in food products.

At the exposure assessment stage, it is also necessary to carry out the characterization of risk cohorts (population groups exposed to microbial agents) including demographics, age, and the behavioral characteristics of the population, number, health state, socio-economic and cultural conditions, which requires a study of food consumption (obtained data on the average per capita individual consumption), the consumption frequency and the sizes of the food portion, and the qualitative composition of food products should be set [FAO/WHO, 1998, 1999a; EU, 2000; Benford D.J., 2001; MR 2.1.10.0067-12].

For the quantitative assessment of population health risk associated with the microbiological contamination of environment, the exposure assessment should be done per unit of food consumption and based on the information on the extent of food contamination with microorganisms or microbial toxins at the time of intake to the human body. [Revised framework for microbial risk assessment, 2000; FAO/WHO, 2008; MR 2.1.10.0067–12].

Median value, 90th and 95th percentiles of the data samples on the microbial contamination of food products should be used to calculate the exposure.

Quantitative health risk exposure assessment should be carried out at the end point, that is, in the test product at the time of consumption. However, information on the results of such

studies is not always available. In these cases, the exposure simulation can be conducted using stochastic and deterministic approaches depending on the assessment objectives.

Exposure assessment models are currently widely adopted, these models are used to describe and analyze the interaction of all the above factors, and the structure, completeness and detailization level of which depends on the purpose of microbiological risk assessment [EU, 2000].

Simple models describing the exposure routes are developed for the qualitative or semi-quantitative microbiological risk assessment. It is possible to use more sophisticated approaches involving, for example, the analysis using the "event tree" allowing to set variables of risk or probable events, and enabling the semi-quantitative expression of some parameters and probabilities [FAO/WHO, 2008; MR 2.1.10.0067-12].

The dependences of mathematical models are used for quantitative exposure assessment. A significant place in the framework of quantitative exposure assessment is held by predictive models allowing the description of the change in the number of bacteria in time, and the influence of environmental factors on the rate of change [EU, 2000; FAO/WHO, 2008; MR 2.1.10.0067-12].

Exposure simulation in the chain from production to consumption, which can be used within the framework of HACCP system is the most time-consuming and requires a large amount of information and resources. At the same time, this exposure simulation method allows assessing it over time in different points of routes of product receipt by the consumer.

An example of a conceptual model describing the "production – consumption" exposure routes is shown in Fig. 2.31.

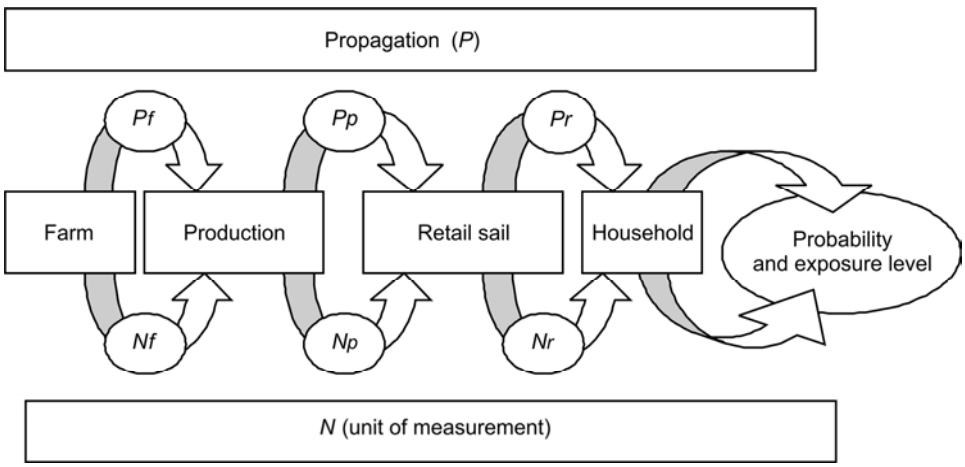


Fig. 2.31. An example of a conceptual model describing the "production - consumption" exposure routes. Exposure assessment requires the simultaneous consideration of the probability of food product unit contamination (denoted *P*) and to assess the level or amount of this harmful substance (indicated by *N*) during sales [FAO / WHO, 2008]

When simulating exposure in the chain from production to consumption, it is necessary to consider the processes of microorganisms growth and/or their inactivation. These processes are simulated depending on the exposure scenario taking into account the conditions of storage, transportation, handling, etc.; the problems of the cross-contamination analysis are also relevant.

Exposure assessment at the end point sets:

– the sizes of individual consumption of foods containing pathogen microorganisms by susceptible populations (daily diet and/or portions of these foods) and their consumption frequency;

– the amount (concentration) of microorganisms in the tested food product at the time of consumption;

– the dose of microorganisms entering the body with a particular food per a meal, per day, if necessary – per a week, month, year.

The dose of the microorganism entering the body per a day (or with a single portion of food) can be compared with the sizes of the known minimum infective doses (MID) of certain pathogen microorganisms for representatives of the various populations from the epidemiological observations, that is of paramount importance in determining the real risk of exposure on public health and is considered at stages of the hazard and risk characterization.

The following is defined based on the results of exposure assessment: priority scenario and the exposure models including the dimensions of the individual consumption of foods containing pathogens, assessment of the actual or expected number of pathogenic microorganisms entering the human body as a result of contaminated foods consumption in considered scenarios (amount (concentration) of the microorganisms in the tested food at the intake moment, the dose of microorganisms entering the body with a particular food per meal, per day, if necessary – per a week, month, year).

Hazard characterization

The severity and duration of adverse responses on the part of the human body are described at the stage of hazard characterization as a result of the test exposure levels, including clinical forms of the disease, pathophysiological and epidemiological characterristics (sporadic or epidemic disease level) of process, the probability of secondary distribution and change in quality of life.

At this stage of assessment of population health risk under the influence of microbial factors contained in food, the analysis of the "dose – response" dependence is performed, i.e. the relationship between the dose, virulence and manifestation (type, severity) of the health responses of susceptible populations with the use of statistical models, "dose – response" data obtained for both human and animals experiments, taking into account the exposure routes, sources and methods of preparing a material containing pathogens [Dourson M.L. et al., 1996; FAO/WHO, 1999*b*; EU, 2000; Microbiological Risk Assessment in Food Processing, 2002; FAO/WHO, 2003*a*, 2003*b*; Vragović N., 2011; MP 2.1.10.0067–12; USDA, FSIS and EPA, 2012].

For the qualitative assessment of health risk associated with microbiological contamination of environment, it is important to determine the level of microorganism hazard for public health, namely the assessment of:

– the natural abilities of the pathogen (phenotypic and genetic characteristics);

– the mechanisms of virulence and pathogenicity;

– host infections specificity;

– the mechanism of infection and the entrance gates of infection;

– the possibilities of re-distribution;

– the variability of strain;

– antibiotic resistance and its effect on the severity of the disease;

– consequences caused by effects;

– infection reversibility (takes place without treatment or requires it);

– the levels of morbidity, prevalence, mortality due to studied nosological entity;

– the severity of infection.

Depending on the severity of the objectives of the study, the infectious disease can be expressed in the duration of the disease (for gastrointestinal symptoms of moderate severity), the number of days of incapacity or treatment costs (for conditions requiring medical intervention or long-term states), the population mortality rate (in infectious diseases, caused by microorganisms having high pathogenicity), the portion of diseased or duration of the disease in the population, the level of economic losses, level of the life quality reduction (for chronic diseases).

The classification of microorganism hazards for public health is carried out on the next levels.

High:

– the development of severe long-term disease with serious consequences for human health;

– the possibility of death;

– the probability of propagation within a population;

– the development of lethal or severe incidence at the high levels of exposure in experimental infection.

Average:

– disease incidences are limited, localized and selfsolved incidences are possible, the reflection of data in the scientific literature;

– the probability of re-propagation within a population is low;

Low:

– information on the reported cases of infectious diseases either absent or infections of mild severity, asymptomatic or with a favorable outcome are predominantly recorded;

– there are no sufficient conditions for re-propagation;

– adverse effects development were not found in experiments on laboratory animals at high exposure levels.

The characteristics of the effect (response) dependence on the level of microorganisms exposure – the ranges and parameters of these dependencies are considered at the stage of hazard characteristics.

The assessment of the population health risk caused by microbiological factors of the environment uses the criteria of the minimum infectious doses of microorganisms identified based on the epidemiological studies results. These criteria include the minimum dose of microorganisms that can cause the disease in susceptible body (MID). Table 2.22 shows some values of this criterion obtained for a number of microorganisms – originators of food-born diseases [Rose J.B., Gerba C.P., 1991; FAO/WHO, 2001; Microbiological risk assessment in food Processing, 2002; Sheveleva S.A., 2007].

Table 2.22

MID of infectious agent transmitted through food, that allow the development of food-borne diseases

Pathogen type	Number of CFU in acute administration	
	Traditional	With altered properties
*Salmonella spp.**	$10^5 – 10^9$	1–10 for antibiotic resistant
Entero virulent *E.coli**	The groups of *ETEC*, *EPEC* – 10^6–10^{10} *EIEC* – 10^5	Groups *EHEC* – 10–100
Citrate assimilating coliforms (*Citrobacter*, *Klebsiella*, *Enterobacter sakazakii**)	10^8–10^9 CFU in 1 g	У *E. sakazakii* <3 CFU in 1 g for infants (not finally determined)
*Campylobacter spp.**	10^6	$5 \cdot 10^2$
*Vibrio parahaemolyticus**	$1 \cdot 10^6 – 10^9$	Reduced in the use of antacids and food with buffering properties
*Listeria monocytogenes**	Unknown; diseases at $<10^2$ in 1 g are documented	May be lower in persons susceptible to microbial agent
C. perfringens	10^5–10^9 CFU in 1 g	–
Bacillus cereus	10^5 CFU in 1 g	May be lower in persons susceptible to microbial agent
Staphylococcus entertoxin	1 mkg	Up to 0.1 mkg – in children up to 14 years and seniors over 60 years
Shigella spp.	$2 \cdot 10^2 – 10^4$	1

Note: * – priority microorganisms for microbiological risk assessment according to WHO.

To perform the quantitative assessment according to the stochastic microbiological risk assessment, which in the maximum extent takes into account the factors of variability of living systems and the existing uncertainty, the calculations are based on the mathematical treatment of the values obtained by the simulation of the value of pathogen content in food and physiological parameters of susceptible organism response, given the size of the daily individual consumption or exposure to microbial agents. The expected level of risk in these assessments has more complex and accurate nature.

Significant factors associated with both the pathogen and a susceptible organism should be considered during the selection of the model for a specific study at the stage of hazard characterization.

For microorganism, this factors include:

– the consideration of the variation of pathogen virulence during the interaction with the susceptible organism and the environment, for example, the probability of an exchange of genetic material between microorganisms in the microbial communities coexisting with the human body, which can lead to a change of some properties, such as antibiotic and virulence resistance, the degree of acidity inactivation in the stomach, the ability to reproduce in the intestine, the percentage of attachment to the intestinal epithelium cells or other critical organs and systems;

– ability to calculate the probability of exposure to microorganisms on organism with different levels of immunity;

– ability to save microorganisms in the sources and factors of infectious agent transmission.

The characteristics of the susceptible group (individual) should be taken into account in the simulation along with the factors of the infectious agent:

– age, nutritional status;

– immunological parameters (degree of gastrointestinal dysbiotic disorders, concentration of IgA, lysozyme, cytokines, interferon in mucosal secretions, etc. Parameters of cellular and humoral immunity);

– the presence of concomitant diseases, hypo- or achlorhydria, including the use of drugs;

– genetic predisposition;

– pregnancy, the presence of nutritional deficiencies;

– clinical symptoms remote in time from the exposure time;

– demographic, social and behavioral characteristics of the population.

The analysis models establish factors affecting the level of susceptibility and severity, and quantitative characteristics of their impact on health, as well as the most susceptible group.

Depending on the objectives of the study, the severity of the disease can be expressed in mortality level (for microorganisms having high pathogenicity level), the proportion of diseased people or duration of the disease in the level of economic loss [Revised framework for microbial risk assessment, in 2000; FAO/WHO, 2003*b*; MR 2.1.10.0067-12].

As far as possible, the characteristic of health responses must include the entire spectrum of clinical manifestations of the disease including symptomatic and asymptomatic flow, duration and severity of the disease, the selection of critical organs and systems damaged by disease, the possible consequences, the overall levels of morbidity, mortality due to this nosology in population, changes in the quality of life. The results of data collection on the apparent health disorders are presented separately for children (newborns, the first year of life, pre-school and school age) and adults [MR 2.1.10.0067-12].

Two hypotheses of infection process development are proposed to describe the "dose – response" dependency: the first – the presence of the minimum infective dose with the development of threshold models, the second – the development of an infectious process in the presence of at least one CFU of pathogen with the development of non-threshold impact models [FAO/WHO, 2003b; USDA, FSIS and EPA, 2012].

Most often, when determining the relationship between the response (for example, the proportion of the infected population) and the dose (e.g., the log-number of the received microorganisms), a graphic representation of "dose – response" relationship has a sigmoidal

shape, which may indicate the presence of a minimum infective dose below which infection does not develop [Buchanan R.L. et al., 1998]. However, it is rarely possible to determine this level, so it is believed that each bacterial cell has a small potential to grow in the host, and can cause the development of the disease [Microbiological Risk Assessment in Food Processing, 2002].

The hypothesis of non-threshold mechanism is often taken as default during the simulation of "dose – response" relation for infectious diseases, the occurrence of which is associated with the consumption of foods that can be explained by the presence of a large number of major disease outbreaks at a very low bacterial contamination of food, in addition, non-threshold models is considered more appropriate to assess the risk to health caused by toxicogenic microorganisms [Microbiological Risk Assessment in Food Processing, 2002].

Thus, the models based on the non-threshold assessment of an infectious case are most frequently used in practice, i.e. with the condition that a single microorganism can cause an infection, but in some cases, when a threshold of action is determined, the threshold models are considered. These threshold models use the criteria of the minimum infectious doses (MID) of micro-organisms the definition of which is based on the results of epidemiological studies and is expressed as the minimum dose of microorganisms capable of causing the disease in susceptible hosts [MR 2.1.10.0067-12].

Beta-Poisson and Weibull distribution models are considered most effective for the analysis of "dose – response" relation when conducting microbiological risk assessment [EU, 2000; FAO/WHO, 2006a; MR 2.1.10.0067-12].

To perform the quantitative assessment of microbiological risk according to the stochastic assessment, which in the maximum extent takes into account the factors of variability of living systems and the existing uncertainty, the calculations are based on the mathematical treatment of the values obtained by simulation both the value of pathogen content in environment (or combination of actual data and data obtained using predictive microbiology), and physiological parameters of susceptible organism response, given the size of the daily individual consumption or contact. The expected level of risk in these assessments has more complex and accurate nature.

During the selecting of the model systems at the stage of hazard characterization significant factors associated with both the pathogen and a susceptible organism must be considered [Dourson M.L. et al., 1996; FAO/WHO, 1999*b*; Revised framework for microbial risk assessment, 2000; EU, 2000; Benford D.J., 2001; Microbiological Risk Assessment in Food Processing, 2002; FAO/WHO, 2003*b*, 2006*a*; MP 2.1.10.0067–12; USDA, FSIS and EPA, 2012].

With respect to microorganism, these are: the virulence, the consequences of caused effects, reversibility of infection (managed without treatment or requires it), the levels of morbidity, prevalence, mortality due to studied nosological entity, severity and duration of infectious disease, accounting of variation in virulence of the pathogen in the course of interaction with the susceptibility organism and the environment, the ability to calculate the probability of exposure of microorganisms on organisms with different levels of immunity, the ability to save microorganisms in the source and factors of infectious agent transmission [EU, 2000; MR 2.1.10.0067-12].

The simulation, along with the factors of the pathogen, should take into account the characteristics of the susceptible group (individual), including age, race, nutritional status, the parameters of the immune status, the presence of concomitant diseases, genetic predisposition, demographic, social and behavioral characteristics of the population, the size of the exposed group and others.

The characteristics and properties of the medium involved in the transmission of the agent (food and water) are also noteworthy, namely properties affecting the microorganism survival during the passage of the gastrointestinal tract of microorganism, for example, the content of fat, iron, pH, temperature, background flora, the presence of preservatives, the physical condition of food, use conditions etc. [EU, 2000].

The use of retrospective models of the occurred diseases in the form of epidemiological investigations results of outbreaks or epidemiological analysis of sporadic cases of infectious diseases, as well as the results of animal experiments *in vitro*, studies of exposure biomarkers are very useful at the stage of the hazard characterization [Crumpton M.J., 1996; Benford D.J., 2001; Microbiological Risk Assessment in Food Processing, 2002; FAO/WHO, 2003*b*; FAO/WHO, 2006*a*; MR 2.1.10.0067–12].

The analysis models establish factors affecting the level of susceptibility and severity, and quantitative characteristics of their impact on health, as well as the most susceptible group.

The characteristic of "dose – effect" relation is an example for the non-typhoid bacteria of the Salmonella genus, obtained using the model of beta-Poisson distribution [Fazil A.M., 1996]:

$$P_{ill} = 1 - \left(1 + \frac{Dose}{\beta}\right)^{-\alpha}, \qquad (2.4.1)$$

where P_{ill} – the probability of disease development in the given population;

Dose – the dose of microorganisms;

α, β – model parameters.

Fig. 2.32 shows a graph of the model for the parameters of the beta-Poisson distribution model: alpha = 0.3126 and beta = 2885 (for initial data); alpha = 0.4047 and beta = 5587 (for data of once exposed population group) [Fazil A.M., 1996].

The examples of "dose – effect" assessments for *Salmonella enteritidis* made on the basis of the parameterized model of "dose – effect" Weibull $P = 1 - exp(-\theta d^b)$ dependence are shown in Fig. 2.33, 2.34 [Health Canada, 2000].

The use of the retrospective models of the occurred diseases in the form of epidemiological investigations results of outbreaks, epidemiological analysis of sporadic cases of infectious diseases, data obtained in the analysis of statistical information on the health of the population, the results of intervention studies and animal experiments in vitro, as well as participation of volunteers are very useful at the stage of the hazard characterization

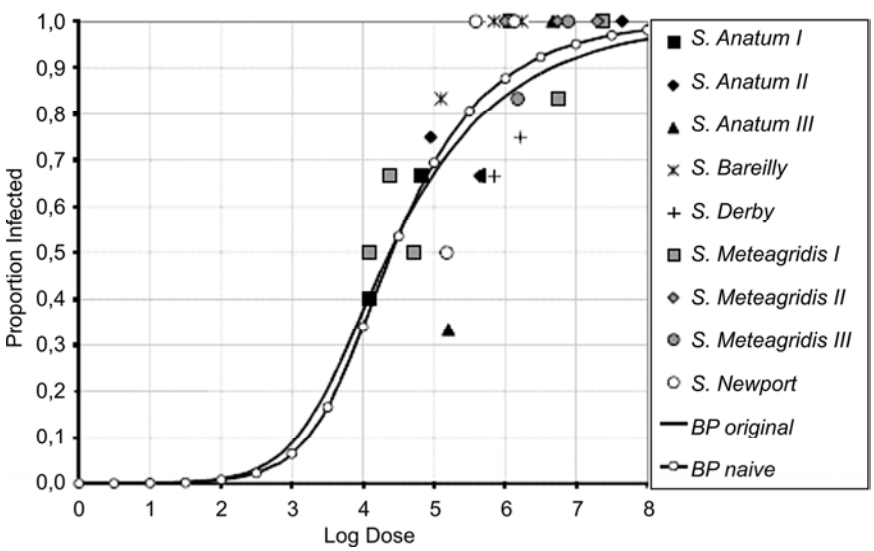
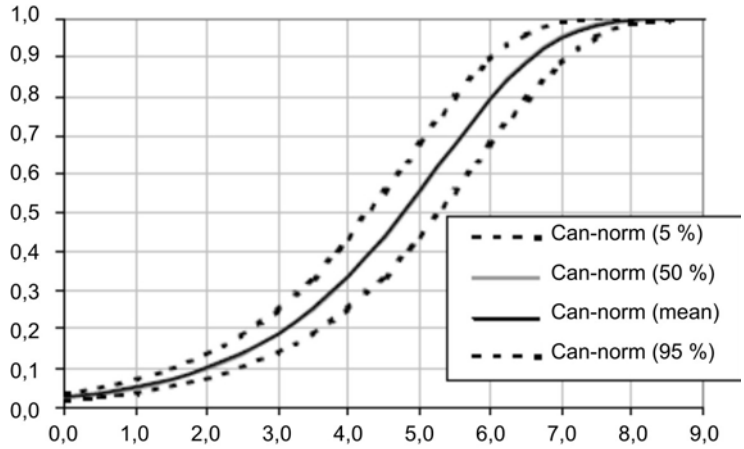
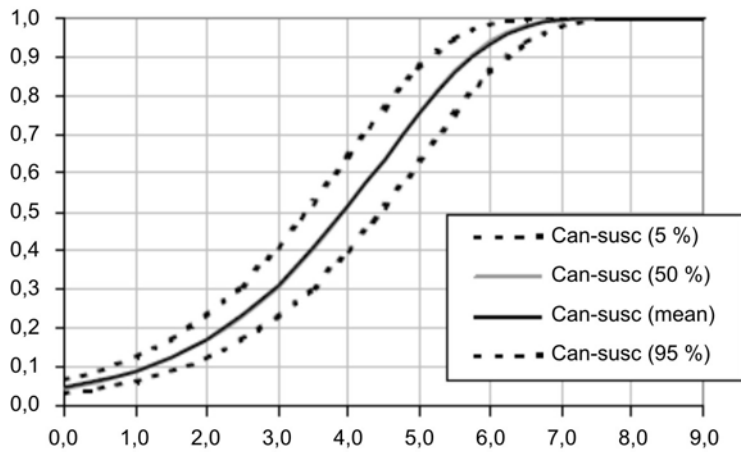


Fig. 2.32. The model of the "dose – effect" dependence based on the research results of *Salmonella spp.* content in food



а



б

Fig. 2.33. The model of the "dose – effect" dependence for a normal (*а*) and susceptible (*б*) population groups in the risk assessment for *Salmonella enteritidis* (the population of Canada) [Health Canada, 2000]

The data obtained through epidemiological analysis, can be used in the statistical models provided a validated and well-regulated collection.

The data of epidemiological investigations, including a description of the factors contributing to outbreaks can be used when creating the RPM for the critical stages and parameters of pathogen accumulation in foods.

The result of the hazard characterization stage is the description of the interaction between the "susceptible organism – microorganism" system, which will allow performing a qualitative and/or quantitative assessment of the pathological effects of the health and the quantitative analysis of the "dose – response" dependence in accordance with the studies scenario developed during the planning stage, that in its turn will allow proceeding to health risk characterization stage.

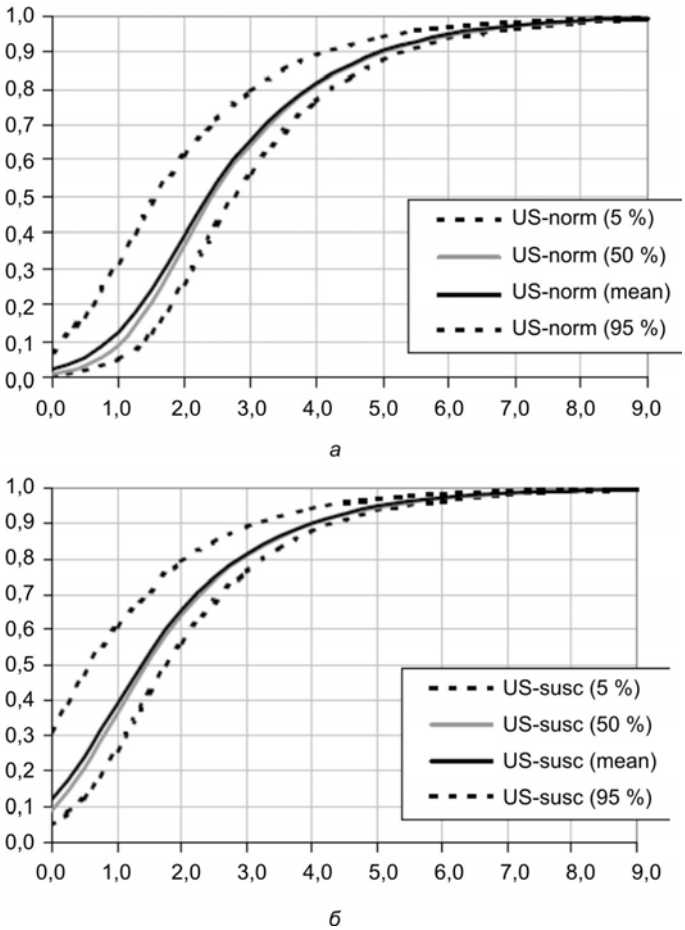


Fig. 2.34. The model of the "dose – effect" dependence for a normal (*а*) and susceptible (*б*) population groups in the risk assessment for *Salmonella enteritidis* (the population of USA) [Health Canada, 2000]

Risk characterization

Risk characterization is the stage at which quality risk assessment, the calculation of parameters, and semi-quantitative and quantitative risk assessment, and the classification of risk with the assessment of its admissibility is performed.

When assessing the health risks associated with the microbiological contamination of environment, it is recommended to allocate the two main components of risk characterization: risk establishment and description

The description of the types and severity of adverse effects is carried out when determining the risk. The probability of harmful effects development is determined for a specific exposure scenario by microorganisms based on exposure assessment data and possible health responses, including the resulting in dynamic simulation. For example, a number of microorganisms entering the body of an individual exposed for a certain time can be the result of the exposure assessment stage. The probability of the disease development at the intake of a certain number of microorganisms can be the result of the responses characterization.

The second risk characterization component (risk description) is carried out with regard to the nature, severity and the consequences of disease incidence. When describing risk, it is advisable to use descriptors, categories, and assessment health risk factors under the influence of microbial factors contained in foods [MR 2.1.10.0067-12].

The integration of all data obtained during the identification and characterization of hazards, exposure assessment is performed at the stage of risk characterization, also the probability and severity of pathological changes is determined qualitatively and quantitatively in the exposed population, including a description of related uncertainties. Qualitative, semi-quantitative, and quantitative microbiological risk assessment are allocated [FAO/WHO, 2009].

The qualitative assessment of microbiological risk is mainly used in screening to determine the need for further researches, which may be due to the following reasons:

– the qualitative assessment of the microbiological risk is easier to be performed and its results are understood more quickly;

– the results of the qualitative assessment of microbiological risk are more easily understood by persons making management decisions, including when they provide them to third parties;

– not enough complete data or a lack of resources for quantitative microbiological risk assessment.

The procedure for qualitative assessment of microbiological risk includes the analysis of data with an assessment of their uncertainty, estimates validation and justification report, which contains the answer to the questions posed in accordance with the objectives of the risk assessment. Essentially a qualitative microbiological risk assessment is based on expert opinions generated by the experts conducting the research. Due to the high degree of subjectivity of this approach, the qualitative microbiological risk assessment should specify all data used in the formation of such assessments describing the routes of exposure to a risk factor, the validation of each of the selected qualitative risk criteria (descriptors) with the orientation to the indicators used in international practice [FAO/WHO, 2009].

The final quality characteristics uses the risk descriptors presented in Table 2.23–2.25 [FAO/WHO, 2009].

Table 2.23

Qualitative probability assessment

Level	Key word	Approximate description
A	Specific	Expected in most cases
B	Probable	May happen in most cases
C	Potential	Happens or can happen sometimes
D	Hardly probable	May happen from time to time
E	Rare	May happen under exceptional circumstances

Table 2.24

The qualitative assessment of consequences or effects

Level	Key word	Approximate description
1	Insignificant	Insignificant impact, small disturbance of activity, low increase in the cost of risk management
2	Small	Small impact on the limited number of population, recoverable disturbances with a slight increase in the cost of risk management
3	Average	Small impact on the significant number of population, significant increase in the cost of risk management and monitoring
4	High	High impact on the limited number of population, significant increase in the cost of risk management and monitoring
5	Catastrophic	Significant impact on a large number of the population, total disturbance of the body systems functioning

Table 2.25

The matrix of qualitative microbiological risk assessment

Probability	Impact				
	1	2	3	4	5
A	Average	High	Very high	Very high	Very high
B	Average	High	High	Very high	Very high
C	Low	Average	High	Very high	Very high
D	Low	Low	Average	High	Very high
E	Low	Low	Average	High	High

The statement that the risk is "small" (this can be interpreted as risk, that "do not differ from 0", or «as low as (is) reasonably achievable» (ALARA), "low", "medium", "high" and "very high" can be made on the basis qualitative assessment of microbiological risk.

Semi-quantitative microbiological risk assessment allows a more adequate ranging by the categories of microbiological risk compared with a qualitative assessment.

Semi-quantitative microbiological risk assessment classifies the possibility and frequency of exposure for each microbiological risk factor (Table 2.26). After that, each category is assigned a rank score (Table 2.27).

Table 2.26

The categories of probability and frequency of exposure [FAO / WHO, 2009]

Probability rank	Category		Frequency rank	Category
0	Negligible		0	Negligible
$<1\cdot10^{-4}$, not 0	Very low		1–2	Very low
$1\cdot10^{-3}$–$1\cdot10^{-4}$	Low		3–10	Low
$1\cdot10^{-2}$–$1\cdot10^{3}$	Average		10–20	Average
$1\cdot10^{-1}$–$1\cdot10^{-2}$	High		20–50	High
$<1\cdot10^{-1}$, not 1	Very high		> 50	Very high
1	Limiting		–	–

Table 2.27

The rank assessments of probability and the frequency of exposure [FAO / WHO, 2009]

Category	Probability assessment	Frequency assessment
Very low	1	1
Low	2	2
Average	3	3
High	4	4
Very high	5	5

The evaluation of the general microbiological risk "severity" (overall severity score, OSS) of food products is performed based on the criterion of common logarithm of rank estimations sum:

$$OSS = \ln(10^{a} + 10^{b} + \ldots + 10^{n}), \quad (2.4.2)$$

where *a*, *b*… *n* – the sum of rank assessments of the individual factors of microbiological risk. When assessing the microbiological risk for solving the risk management tasks, it is recommended to distinguish the three levels of the risk "severity" (green – low, yellow – average, red – high) in accordance with Table 2.28.

Table 2.28

Levels of microbiological risk "severity" [FAO / WHO, 2009]

Exposure levels						
	Very high	7	8	9	10	11
	High	5	6	7	8	9
	Average	4	5	6	7	8
	Low	3	4	5	6	7
	Very low	2	3	4	5	6
		Very low	Low	Average	High	Very high
	Exposure (events per year)					

The analog of a semi-quantitative microbiological risk assessment under the simplified characterization of microbiological hazards is the use of the estimated coefficients that take into account the severity and duration of disease caused by the microbiological contamination of food [MR 2.1.10.0067-12] (Table 2.29).

Table 2.29

Evaluation coefficients for health risk level characterization at the influence of the microbial factors contained in the food products

The probability of disease (*p*)*	Severity (the probability of death from disease) (*s*)	Duration (the duration of disease), days (*t*)	Final evaluation factor, scores (*R*)
Less than $1 \cdot 10^{-5}$	Less than $1 \cdot 10^{-5}$	Less than 4	1
$1 \cdot 10^{-5} – 10^{-3}$	$1 \cdot 10^{-5} – 10^{-3}$	4–10	2
More than $1 \cdot 10^{-3}$	More than $1 \cdot 10^{-3}$	More than 10	3

Note: * – established as a result of "dose – response" dependence simulation.

The description of health risk dependence when exposed to microbial factors contained in foods is performed using risk category value (RI_{cat}), which is calculated by the formula (2.4.3), and the grading scale of population health risk levels under the influence of microbial factors contained in food (Table 2.30).

$$RI_{cat} = R_p R_s R_t, \quad (2.4.3)$$

where R_p – the evaluation factor of disease probability;
R_s – the evaluation factor of disease severity;
R_s – the evaluation factor of disease duration;

Table 2.30

Evaluation scale for the public health risk level characterization at the influence of the microbial factors contained in the food products

Risk category indicator (RI_{cat})	Risk level
$9 \le RI_{cat} \le 27$	High (red)
$3 \le RI_{cat} < 9$	Average (yellow)
$1 \le RI_{cat} < 3$	Low (green)

The High level of risk ($9 \le RI_{cat} \le 27$): the high risk of development of serious, long-term and widely spread adverse changes in health within the probable scenarios of exposure as a result of established contact with microorganisms. In case of such health risk level, it is recommended to develop and implement the risk control and management measures in the form of development and/or correction of sanitary and epidemiological standards and guidelines, hygienic regulations, standards for improving the systems to

control quality and safety at production, the development of inter-industry target settings (terms for elimination or reduction of the diseases risk level), increase the efficacy of sanitary training and promulgation, hygienic education of employees.

Simultaneously, the priority directions of studies aimed at the reduction of uncertainties and development of new control or prevention strategies are determined based on these results.

The Average level of risk ($3 \leq RI_{cat} < 9$): adverse changes in the public health within the probable scenarios of exposure are presented mainly by the individually solved cases of average severity. It is recommended to develop and implement the risk control and management measures in the form of improving the systems for the control of quality and safety at production, the development of recommendations for industry, trade, consumers, hygienic education and training of employees of the food industry and catering enterprises and population.

The Low level of risk ($1 \leq RI_{cat} < 3$): adverse changes in the public health within the probable scenarios of exposure are presented by the quite rare, individually solved, cases of light degree. It is recommended to develop and use the risk control and management measures in the form of hygienic education and training of population.

Quantitative microbiological risk characterization can be performed using probabilistic and deterministic models. The quantitative (numerical) assessment is more informative than the qualitative one, but it increases significantly the uncertainty of the obtained results.

The characterization of microbiological risk considers the disease probability after a single use of a standard portion of the food product and/or the disease probability in the use of food for a certain period. 100 grams of finished product or 30 grams of protein, or the amount of product containing 1,000 calories can be considered as a standard portion in the first approach. The second approach is closer to the deterministic models, as it implies that the exposure can be repeated with a certain frequency.

Effect (response) can be recorded both as diseases, and as indicators taking into account economic aspects (disability days, QALY, etc.).

Individual risk can be identified as the probability of a random individual in the studied population (subpopulation) to fall ill due to infection in the single consumption of food for a certain period or a lifetime, as well as the expected number of negative effects in an individual in the consumption of a certain amount (for example, 1 kg) of the food product.

The expected number of disease incidences or the number of disability days associated with the consumption of food in the population, the probability of one incidence of disease or death in the population over one year, etc. are used as the population risk parameters.

Justification for the choice of the model analyzing the adequacy of the model chosen for this study to the available data, the task at hand, simulation uncertainty, the possibility of extrapolation to other scenarios is of particular importance in quantitative risk characterization. It is advisable to carry out a quantitative risk characterization based on stratification of the studied population by age, sex, national/regional eating habits, food consumption characterization (frequency, volume), accommodation conditions and other features in accordance with the objectives of the study. This allows to identify cohorts exposed to the largest risk with the identification of foods determining this risk. The accumulation of information about the microbiological risk taking into account the population gradation over the age will allow the formation of recurrent equations and move on to the evolutionary risk simulation.

Risk characterization established the probability of disease development in the intake of a certain number of microorganisms in accordance with the scenarios defined to solve the risk assessment tasks; and risk level is described taking into account the nature, severity, and consequences of disease incidence.

Uncertainty analysis

The description and consideration of the effect of related assumptions (restrictions) and uncertainties arising at all stages of the study is a necessary component of population health risk assessment procedures under the influence of microbial factors.

The main sources of uncertainty at the hazard identification stage are incomplete and inaccurate information about the potential hazards, the qualitative and quantitative characteristics

of the microbial contamination of the environment, lack of completeness, accuracy and representativeness of the data.

Uncertainties associated with impaired studies planning, inaccuracies in determining the level of microorganisms in foods, including those associated with the choice of determination methods, lack of data on the level of body exposure can be identified at the stage of exposure assessment.

The main sources of uncertainty in the hazard characterization stage are associated with the establishment of a threshold exposure level with the establishment of the evidence degree of adverse effect in humans with the definition of critical organs/systems and the harmful effects with lack of knowledge of interaction mechanisms of pathogens or infectious process features in different ways and factors of transmission and combinations.

The reliability rate of the final results of the risk assessment depends on the variabilities, uncertainties, and assumptions (restrictions) related to the assessment and extrapolation of data from epidemiological, microbiological and experimental studies, study model selection. Biological variability includes both of the differences such as the virulence within the microorganisms population and the differences of susceptibility level within the entire human population and its subpopulations.

2.5. The assessment of risk and its evolution at the impact of physical environmental factors on health

The impact of physical factors (noise, ionizing and non-ionizing fields, vibration) on human health has been studied for a long time, but in the historical aspects, the studies were primarily related to the effect of working conditions.

According to the WHO, hearing loss due to noise amounts to 16% of global scope of diseases related to occupational factors, and is in the second place (after back pain), they outrun chronic obstructive pulmonary disease, bronchial asthma, injuries and other types of health problems. The same organization recognizes that the electromagnetic field (EMF) of artificial origin is one of the most dangerous and important factors to human health characterized by an extremely active biological effect. EMR negative impact on the activity of the brain, functional disorders of the central nervous system, the change in hormonal status of human is proved, EMR may cause the leukemia development, etc. [Tomenius L., 1986; Stuchly M.A, Mild K.H., 1987; Olsen J.H. et al., 1993; Verkasalo P.K. et al., 1993, 1996; Grigoriev Y.G., Grigoriev O.A., 2013].

In general, according to the Medical Service of the Russian Federation, the specific weight of occupational pathology related to exposure to physical factors, amounts to 46.65% in 2013, which is considerably higher than the contribution of other factors (chemical, physical overload factor, etc.). At that, the stable reduction of the contribution of factors of this group to professional pathology is not registered.

In recent decades, more and more areas are referred to the zones of acoustic discomfort due to the rapid development of all types of transport (primarily road and air ones) and the approach of noise sources to the places of permanent residence. According to the European Union, the number of people who are constantly exposed to noise is 20% of the world's population. Consequently, about 80 million of people suffer from unacceptable noise levels that cause sleep disturbance, irritability, and have adverse effects on health. Another 170 million European citizens live in areas where the population is exposed to noise attacks in the daytime. In the Russian Federation, the portion of citizens' complaints about the acoustic impact of the total number of complaints about the impact of physical factors is 58%, and in some subjects of the Russian Federation, it exceeds 70%.

The identified types of health disorders associated with noise factor include sleep disorders, cognitive disorders, nervous disorders, lesions of cardiovascular system and hearing [Babisch W., 1999, 2006; Meister E.A, 2000; Ising H., 2004; Stansfeld S., Prasher D., 2005].

The financial terms of cost of society for the addressing of environmental noise problem range from 0.2 to 2% of gross domestic product. Even the smallest of these figures is a huge amount. All this makes the problem of correct health risks assessment due to noise extremely important.

The problem of health risk assessment under the impact of electromagnetic fields is not less acute. Avalanche development and the implementation of technologies based on electromagnetic fields in daily life required large-scale and diversified medical, biological, and epidemiological studies of the effect of electromagnetic radiation of varying frequency and intensity on health of both working, and the whole population. The results of these studies were the evidence of negative influence of EMR on the health of workers of electrical plants and telecommunication facilities. The relation between the exposure of EMR on working places and the formation of leukemia, brain tumors, and breast cancer is confirmed in the publications by S.J. London (1991), D. Savintz et al. (1995) and a number of other studies. A significantly higher frequency of health problems development in children who have been exposed to EMF (living near power lines, the impact of household equipment, and other sources of EMF radiation) has been found in studies by N. Wertheimer, E. Leeper (1979), L. Tomenius (1986), Feychting, A. Ahlbom (1992, 1993), J.H. Olsen et al. (1993, 1995). Thus, the fact of the possibility of tumors development in the children and adolescents population was confirmed in the publications by L. Tomenius (1986). Studies had been carried out from 1958 to 1973. A group of children and adolescents aged from 0 to 18 living within 150 m from the substations, transformers, underground, under the electric lines of railroads, and power lines (PL) was examined. It has been found that the tumors of the nervous system and leukemia occurred 2 times more often in this group than in the comparison groups. J.P. Goldsmith (1997) summarizing the results of epidemiological studies showed that the adverse effects of EMR on the hematopoiesis and chromosomes, the development of leukemia and tumors of the female genital organs, the development of tumors of hematopoietic tissue in workers of radar installations, leukemia in children living near radio stations, an increased incidence of abortions of female therapists using microwave radiation in diathermic plants were determined.

All of this raises the problem of developing methodologies for health risks assessment in terms of exposure to noise and electromagnetic fields. The problem is urgent because currently this aspect of risk assessment is much less developed than the aspects of chemical and microbiological risks.

2.5.1. Risk assessment and its evolution at noise exposure

Risk assessment under the influence of noise on the population can be done in full accordance with the general algorithm that includes hazard identification, the assessment of "exposure – response (effect)" dependence, exposure assessment and risk characterization. Of course, the nature of the factor requires to take into account the specificity of this factor in the performance of each stage of the risk assessment.

Thus, the hazard identification stage involves the identification, collection, and analysis of all possible information on the sources of the noise effecting the population, in order to determine:

- the level and frequency characteristics of noise;
- the distribution of noise in residential areas;
- the time of exposure to noise: day, week, month, year, etc.;
- the number of population affected by the noise influence.
- possible health problems associated with exposure to noise.

The main sources of information for hazard identification is the data of instrumental measurements of noise, noise maps of settlements received during the social-hygienic monitoring and other objective laboratory control of sources and calculations of noise propagation and distribution of its intensity in residential areas.

Due to the fact that the inner-city traffic noise is one of the most significant sources, it should be thoroughly considered. Thus, the total noise load is defined as a set of noise generated by vehicles in separate linear sections of the street and road network (SRN) which include the crossroads and roundabout elements. The calculations of noise from the linear section of the road were carried out on the basis of its technical inventory based on the following parameters:

- traffic density in the SRN section of the studied area, units of cars/h at different times of day, days of the week, months of the year;
- the average speed of traffic on the SRN section, km/h;
- the slopes and type of road surface;
- the condition of the road surface;
- the structure of traffic by type of road transport: trucks, cars, motorcycles, and special vehicles, while buses with a capacity of less than 9 passenger seats are equal to passenger transport, the others to the cargo transport.

The calculation of the noise from the linear sections of railroad tracks, including urban rail ground electric transport is performed taking into account the following parameters:

- the assessment of traffic density of rolling stock during the day;
- the type of rolling stock (passenger or cargo);
- the length of rolling stock and average speed of its movements on the linear section of the road;
- the average number of rail joints per kilometer;
- railroad tracks conformity with technical regulations.

To calculate the level of aircraft noise in residential areas, the following data is collected:

- characteristics of aircraft "corridors" (takeoff/landing and approach zones);
- the type of aircraft;
- traffic density (the frequency of flights of certain types of aircrafts);
- traffic distribution by time of day, days of week, month, etc.

The negative effects in the form of specific nosologic forms recorded in the ICD-10, which can be formed in the population living under the influence of traffic noise are presented in Table 2.31 and are the result of generalization of domestic and foreign scientific data over the past few decades.

Table 2.31

The types of health disorders of the population living under the influence of the traffic noise [Rosenlund M. et al., 2001; Stansfeld S.A., 2002; Haines M.M., 2003; Haralabidis A.S. et al., 2008]

Affected organs and systems	Deterioration of health	The code of heals deterioration according to ICD-10	Data on threshold noise levels, dB
Nervous system	Nervousness (nervous tension, excitation)	R 45.0	35
	Sleep disorder	G 47	40
	Cognitive deterioration	R 41	42
	Vegetovascular dystonia	G 90.8	60
Circulatory system	Nonspecific increase in blood pressure without diagnosis of hypertension	R 03.0	65
	Hypertensive heart disease	I 11.9	70
	Ischemic heart disease	I 24, I 25	70
	Stenocardia	I 20	70
	Miocardial infarction	I 21	70
Diseases of the ear and mastoid process	Tinnitus aurium	H 93.1	45
	Conductive and sensory neural hearing loss	H 90	80
	Hearing loss due to noise	*H 83.3*	80

It should be noted that the literature contains a significant amount of data on the different donozological effects that are the premonitory signs of more serious health problems under conditions of constant repetition (Table 2.32). At the same time, according to WHO experts' opinion, the effects have a high or medium degree of proof.

Table 2.32

Effects for population health when exposed to night noise, established in epidemiological studies [Medical effects of aircraft noise, 1977; Ising H. et al., 2004; Fridman K.B., Lim T.E., 2009]

Effect	Indicator	Threshold, db	Proof degree
Sleep anxiety (shuffle)	$L_{Amax,inside}$	32	High*
Disorder during different stages of sleep, sleep "fragmentation"	$L_{Amax,inside}$	35	High
Complaints	$L_{night,outside}$	35	Average*
Awakening at night and/or very early in the morning	$L_{Amax,inside}$	42	High
The protracted sleep onset phase (difficult to fall asleep)	*	*	High
Sleep fragmentation, reduced sleep time	*	*	High
The increase in the average level of restless movements during sleep	$L_{night,outside}$	42	High
The feeling of sleep disruption	$L_{night,outside}$	42	High
The use of sedatives or other drugs	$L_{night,outside}$	40	High
Insomnia associated with environmental factors	$L_{night,outside}$	42	High

Note: * – effects which have enough amount of reliable accumulated data is according to WHO experts are referred to a high degree of validity; effects which have limited data are referred to the average degree of validity.

Exposure assessment involves determination of the normalized parameters of noise at a given time and the duration of its effect (through the registration of a number and duration of sound events), as well as the assessment of the daily weighted noise as a measure of population exposure to harmful factor.

The combination of design data and instrumental studies is optimal. This interface of data provides the most extensive and at the same time correct results. The calculations of noise levels in residential area, in residential and public buildings allow setting the acoustic characteristics of a large territory, simulating a variety of different situations, but with a certain degree of approximation. Instrumental studies provide the most accurate data, but can only characterize a specific point (zone, site) under the specific conditions of noise events.

Indicator L_{den} (equivalent level of the average weighted daily noise), which can be determined by the equation (2.5.1) with the daytime and nighttime noise levels is accepted as the basic unit of the existing noise levels in the risk assessment:

$$L_{den} = 10 \lg \frac{1}{24} \left(16 \cdot 10^{\frac{L_{day}}{10}} + 8 \cdot 10^{\frac{L_{night}+10}{10}} \right), \qquad (2.5.1)$$

where $L_{day} = L_{Aeg,16}$ – equivalent adjusted 16-hour level of daytime noise;

$L_{night} = L_{Aeg,8}$ – equivalent adjusted 8-hour level of nighttime noise.

The levels of the evening noise can be considered in the presence of data.

The assessment of the equivalent level of noise can also be performed according to the formula (2.5.2) over a specified period of time:

$$L_{Aeg,t} = 10\lg\frac{1}{t}\int_t\left(\frac{p_A(t)}{p_0}\right)^2 dt\ , ... \quad (2.5.2)$$

where L_{Aeg} – equivalent adjusted noise level over a specified period of time;

$pA(t)$ – the current value of the average square sound pressure taking into account the correction "A", Pa;

p_o – the original sound pressure in the air $p_o = 2 \cdot 10^{-5}$, Pa (reference sound pressure);

T – the noise duration, h.

The conversion of noise levels (dB) into the units of sound pressure in Pascal (Pa) is performed by means of the following formulas

$$p = 10^{\frac{L}{20} + \lg p_0}\ , \quad (2.5.3)$$

$$p^2 = 10^{\frac{L}{10} + \lg p_0^2}\ , \quad (2.5.4)$$

where p – sound pressure at the observation point, Pa;

$p_o = 2 \cdot 10^{-5}$ Pa – the threshold value of sound pressure, which is the hearing threshold in human with normal hearing at a frequency of 1000 Hz.

If there is data on the hourly dynamics of the noise situation, it is preferably to calculate the average noise according to the following formula

$$L_{den} = \frac{L_{t1}^i p_1 + L_{t2}^i p_2 + ... L_{tn}^i p_n}{p_1 + p_2 + ... p_n}, \quad (2.5.5)$$

where L_{day}, L_{even}, L_{night} are set as the average values for a given period of time (7–19 hours, 20–23 hours, 23–7 hours) based on the result of a number of tool or model studies covering the maximum possible number of noise events in the territory of the settlement. At that, the L_{day}, L_{even}, L_{night} values can be used as stand-alone exposure characteristics in the studies of the effects of daytime and/or nighttime noise on population health.

The indicators of daily weighted noise levels are used to assess the average long-term exposure of the population:

$$L_{den,t} = \frac{\sum_{i=1}^{N} L_{den}}{N} .., \quad (2.5.6)$$

where $L_{den,t}$ – the equivalent level of the average weighted daily noise during the studied period (t) measured for N times.

The calculated values of equivalent noise obtained empirically or by the three-dimensional mathematical simulation of the propagation and attenuation of noise through the use of certified (recommended) methods can be used, if the expected exposure is assessed (for example in the design).

When assessing the exposure taking into account aircraft noise, it is obligatory to perform instrumental measurements with noise events time (the duration of aircraft flight) recording. The selection of points for acoustic calculations is determined by the location of places of permanent residence, recreation zones, internal building areas, childcare centres, and places with a given scenario of risk assessment.

The stage of "exposure – response" ("exposure – effect") dependency analysis is performed on the basis of proven established, quantified relationships between noise exposure and the frequency, prevalence, type and severity of expected harmful effect in the population exposed to the harmful effects of noise. Table 2.33 shows examples of such dependencies obtained in various epidemiological studies.

Attention is drawn to the fact that a number of researchers present models allowing the assessment of the change in the probability of formation of a particular health disorder in the exposure change. At the same time, as a rule, the term "probability" is identified with the concept of "risk" as the researchers do not provide the quantitative characterization of the

Table 2.33

"Exposure – effect" dependence set in epidemiological studies

No.	Effect	Dependence	Data source
3.1.	The diseases of the circulatory system organs	$OR = 1.63–6.13\cdot10^{-4} L^2_{day,16} + 7.36\cdot10^{-6} L^3_{day,16}$ (for range of 55–80 dB)	Haralabidis A.S. et al., 2008; Stansfeld S.A. et al., 2008
3.2.	The proportion of persons irritated with night noise, *HA*,%	$HA = 0.5118\cdot(L_{den} – 42) –1.436\cdot10^{-2} (L_{den} – 42)^2 + 9.868\cdot10^{-4}\cdot(L_{den} – 42)^3$	Stansfeld S.A. et al., 2008
3.3.	Irritation with noise	$R = 100/1 + exp\ (10.4–0.132\ L_{den})$	Haralabidis A.S. et al., 2008; Stansfeld S.A. Stansfeld et al., 2008; GOST R 53574–2009
3.4.	The proportion of persons with stable sleep disorders in aircraft noise, *HSD*,%	$HSD = 18.147–0.956L_{night} + 0.0149\ L^2_{night}$	Stansfeld S.A. et al., 2008
3.5.	The proportion of persons with stable sleep disorder in the railway noise, *HSD*,%	$HSD = 11.3–0.55\ L_{night} + 0.00759\ L^2_{night}$	Stansfeld S.A. et al., 2008
3.6.	The proportion of persons with stable sleep disorders in road noise, *HSD*,%	$HSD = 20.8–1.05\ L_{night} + 0.0149\ L^2_{night}$	Stansfeld S.A. et al., 2008
3.7	The genesis of non-specific effects:	$Risk^{NSP} = \frac{1}{\sqrt{2\Pi}} \cdot \int_{-\infty}^{\Pr NSP} e^{\frac{x}{2}} dx,$ where $\Pr^{NSP} = –4,551 + 0,8531 \lg\left(\frac{Dt}{0,511}\right)$	Altena K. et al., 1988
3.8	Complaints from the public about noise:	$Risk^{SOC} = \frac{1}{\sqrt{2\Pi}} \cdot \int_{-\infty}^{\Pr SOC} e^{\frac{x}{2}} dx,$ where $\Pr^{SOC} = –6,5027 + 0,8891 \lg\left(\frac{Dt}{4,8 \cdot 10^{-4}}\right)$	Altena K. et al., 1988
3.9	The genesis of specific effects:	$Risk^{SP} = \frac{1}{\sqrt{2\Pi}} \cdot \int_{-\infty}^{\Pr SP} e^{\frac{x}{2}} dx,$ where $\Pr^{SP} = –6,6771 + 0,7041 \lg\left(\frac{Dt}{0,511}\right)$	Altena K. et al., 1988
3.10	Miocardial infarction	$OR = 0.0000001\ L^2_{Aday} + 0.0001\cdot L_{day} + 0.0035$	Haralabidis A.S., 2008; S.A. Stansfeld et al., 2008
3.11	Sleep anxiety (the total number of movements during sleep), M	$M = 0.0587+0.000192\ L_{night,inside} – – 0.00133ag + 0.0000148ag^2$, where *ag* – age of the person, years	Stansfeld S.A. et al., 2008
3.12	The risk of cardiovascular diseases	26 % per each 5 dB	Rosenlund M. et al., 2001; Greiser E., 2007

Table 2.34

"Exposure – effect" dependence obtained in epidemiological studies

Noise indicator	Noise level, dbA	Risk level	Main sources
The diseases of the circulatory organs			
L_{den}	> 62	50 % compared with the background of < 62 dBA	Knipschild P., 1977
L_{night}	–	10 % per each 10 dBA	Jarup L. et al., 2008
L_{den}	> 55	60 % compared with the background of < 55 dBA	Rosenlund M. et al., 2001
L_{den}	> 72	80 % compared with the background of < 55 dBA	Rosenlund M. et al., 2001
L_{den}	–	26 % per each 5 dBA	Kempen V. et al, 2002
L_{den}	65–70	30 % compared with the background of < 65 dBA	Babisch W., 2006
L_{den}	61–70	30 % compared with the background of < 60 dBA	Babisch W., 2006
L_{den}	> 65	Increase compared with the background of < 65 dBA	Health Canada, 2006
L_{den}	> 65	20 % compared with the background of < 65 dBA	Ising H., 2004
L_{den}	66–70	30 % compared with the background of < 66 dBA	Babisch W., 1999
L_{day}	> 60	30 % compared with the background of < 60 dBA	Babisch W., 1999
L_{day}	> 60	Increase compared with the background of < 60 dBA	Babisch W., 2006
L_{den}	65–70	Increase compared with the background of < 65 dBA	Prasher D., 2002
L_{day}	60–65	Increase compared with the background of < 60 dBA	Report, 2004
L_{night}	50–55	Increase compared with the background of < 50 dBA	Report, 2004
L_{den}	–	Proportional dependence	Meister E.A., Donatelle R.J., 2000
General morbidity			
L_{den}	–	50 % per each 10 dBA	Franssen E.A.M. et al., 2004
L_{day}	> 60	Increase compared with the background of < 60 dBA	Ising H., Kruppa B., 2004
L_{night}	> 50	Increase compared with the background of < 50 dBA	Ising H., Kruppa B., 2004
L_{day}	> 65	Increase compared with the background of < 60 dBA	Ising H., Kruppa B., 2004
L_{den}	> 75	Increase compared with the background of < 75 dBA	Prasher D., 2002
L_{night}	> 50	Increase compared with the background of < 50 dBA	Report, 2005
L_{den}	75–80	Increase compared with the background of < 75–80 dBA	Prasher D., 2003
L_{eq}	> 90	5 % compared with the background of < 75 dBA	Prasher D., 2003
L_{den}	> 75	Increase compared with the background of < 75 dBA	Prasher D., 2002

severity for the health. This approach does not allow comparing the health risks: for example, according to W. Babisch (2006) the risk of the circulatory system diseases increases with an increase in the average weighted daily noise by 20% compared to the background; according to D. Prasher (2003) the risk of hearing disorders increases with an increase of L_{den} up to 90 dB in relation to the background (Table 2.34) etc. Integrated risk assessments are not proposed by researchers.

Using the models of the risks evolution, which take into account both the severity of the individual body systems disorders, and the relationship between the individual organs and systems will eliminate the existing shortcomings of individual pairs of models of "noise exposure – response" dependency. All paired mathematical models have been grouped on the basis of the system, which includes the effect of: the models describing the impact of noise on the nervous system, the models describing the impact on the cardiovascular system, and the models affecting the hearing. At that, effects occurred at the lowest noise levels were identified for each system. For the nervous system, such "threshold" amounted to 43 dBA (sustainable sleep disturbance, insomnia) for the cardiovascular system – 58.8 dBA (high blood pressure, hypertension), for hearing – 50 dBA (tinnitus).

The system of three recurrence equations is shown in (2.5.7) and its solution allows to calculate the risk of disorder of each of the systems depending on the average weighted exposure and assess the risk to the health of the exposed person as a whole taking into account the probability and severity of disorders of each of the systems.

$$\begin{cases} R_{t+1}^{\text{Асл}} = R_t^{\text{Асл}} + \left[0{,}0118R_t^{\text{Асл}} + 0{,}001\left\langle \dfrac{L_{\text{den,t}}(1-R_t^{\text{Асл}})}{50} - 1 \right\rangle \right] K, \\ R_t^{\text{Асс}} = R_t^{\text{Асс}} + \left[0{,}0052R_t^{\text{Асс}} + 0{,}015\left\langle \dfrac{L_{\text{den,t}}(1-R_t^{\text{Асл}})}{58{,}5} - 1 \right\rangle \right] K, \\ R_t^{\text{Анс}} = R_t^{\text{Анс}} + \left[0{,}0074R_t^{\text{Анс}} + 0{,}0016\left\langle \dfrac{L_{\text{den,t}}(1-R_t^{\text{Асл}})}{43} - 1 \right\rangle \right] K, \end{cases} \quad (2.5.7)$$

initial levels:

$R_0^{\text{Асл}} = 0{,}023,$

$R_0^{\text{Асс}} = 0{,}007,$

$R_0^{\text{Анс}} = 0{,}02855,$

where $R_t^{\text{A}_i}$ – the risk of the *i*-th organs system disorder at an initial (given) time *t*;

$R_{t+1}^{\text{A}_i}$ – the risk of the *i*-th organs system disorder for the next time step (*t* + 1) (depending on *K*);

$R_t^{\text{Асл}}$ – the aggregate risk of hearing disorders of varying severity (tinnitus, conductive sensory neural hearing loss, hearing loss caused by noise) at the time *t*;

$R_t^{\text{Асс}}$ – the aggregate risk of cardiovascular system disorders development of the varying severity (high blood pressure, hypertensive heart disease, ischemic heart disease, cardiac angina, myocardial infarction) at the time *t*;

$R_t^{\text{Анс}}$ – the aggregate risk of development at the time *t* of the nervous system disorders (nervous tension, sleep disorder, cognitive impairment, vegetative-vascular dystonia);

$L_{den,t}$ – average weighted noise level in the studied period *t*, dB;

K – temporary empirical coefficient taken according to Table 2.1;

$\langle\rangle$ – Kelly's brackets with values $\langle x\rangle = 0$ at $x < 0$ and $\langle x\rangle = x$ at $x \geq 0$.

Empirical coefficients values take into account both the severity of the clinical course and outcome of diseases and disorders of the functional systems of the body. On the whole, the model allows calculating the risk at any given time *t.*

The prediction of the health risk in the model is performed through the design value of the risk at the current time. In the first year of life, the risk value is assumed equal to 0.01. Based on the known variation of the noise load over time, it is possible to determine the long-term forecast for the period of the expected life expectancy. Thus, paired models adapted to the problems of evolutionary modeling, obtained in the course of authoritative epidemiological studies, recognized at the international level, allow assessing the health risk in general.

In this case, risk classification is performed in full compliance with the general methodology discussed in p. 2.2. The unity of approaches allows taking into account the noise load in the assessment of associated risks, which is extremely important for the hygienic assessment of the impact of harmful factors of working conditions for workers, and for hygienic assessment of the living conditions of the population.

2.5.2. Risk assessment and its evolution under the influence of electromagnetic fields of radio-frequency range

The general algorithm of population health risk assessment under the influence of EMR is harmonized with the generally accepted approaches and includes the stages of hazard identification, the assessment of "exposure – response" dependency, exposure assessment, risk characterization. The approach involves an assessment of uncertainty and preparing data for risk communication, including for decision-makers.

Each stage of risk assessment is completed with intermediate results that have intrinsic value and can be used for various tasks and management decisions making. The "Hazard identification" stage involves the identification and the maximum comprehensive collection and analysis of initial information on the sources of electromagnetic exposure of the population in the studied area based on the frequency characteristics of the radiation, source operation time, the number of the exposed population and the probable responses to the impact.

It should be noted that currently the collection of the information about the sources of electromagnetic interference, including the relation to the settlements maps has much smaller practices than on the sources of chemical pollution and noise. This increases the requirements for hazard identification phase and imposes an obligation on researchers to thoroughly acquaint themselves with the design and technical documentation, the passports of electromagnetic radiation sources, the results of previous studies, examinations, sanitary-epidemiological conclusions on the allocation of transmitted radio-technical facilities, analytical reviews, reports, reference books, etc.

The objective of the hazard identification stage is to identify the main cohorts exposed to electromagnetic interference, the probable changes in health status with established exposure characteristics and the determination of the priority sources of EMR. The results of identification in the subsequent stages are used to select and assess the "exposure – response" dependencies, exposure, the formation of the plan of the subsequent studies, etc. The assessment of the completeness and accuracy of the available data on the EMR levels in the studied area and the availability of information on the quantitative criteria required for further analysis of health risk is carried out at the stage of hazard identification.

The typical anthropogenic sources of EMR forming the impact in terms of settlements are all sources of resonant circuits and wave generators. The grouping of objects by radiation frequencies is performed in accordance with generally accepted classification (Table 2.35).

The data used for risk assessment are subject to expert assessment and adjustment in terms of the completeness of the EMR sources recording, the correctness of the source of electromagnetic parameters and the locations of individual sources

The application of all EMR sources to an electronic map of the settlement is optimal for the development of an electromagnetic map of the territory of the radio frequency with the ability to analyze and simulate different situations and scenarios of electromagnetic

Table 2.35

The frequency range and the type of device or electromagnetic radiation source service

Frequency range	Frequency	The type of the device or service
0–30 kHz	LF (extremely low)	Induction furnaces, video display terminals of personal electronic computing machines, household appliances, and power lines
30–300 kHz	LF (low)	Low-frequency broadcasting and long-wave radio
300–3000 kHz	MF (medium)	Medium-wave radio, radio navigation, communication with ships
3–30 MHz	HF (high)	High-frequency radio, amateur radio, high-frequency radio communications and broadcasting
30–300 MHz	VHF (very high)	FM-radio, television, emergency rescue services communication
300–3000 MHz	UHF (ultra-high)	UHF TV, paging, mobile phones, amateur radio
3–30 GHz	EHF (extremely high)	Microwave ovens, satellite communication, radiolocation, super-high frequency point-to-point, wireless Wi-Fi-connection
30–300 GHz	EHF (extremely high)	Radars, radiolocation, radio astronomy, high-speed radio relay communication

fields change. The electronic EMR map of the territory allows estimating the number of population under the influence of a certain level. It is appropriate to collect data and refer them to the map to assess sex-age composition of the exhibited population.

The phase of the "exposure – response" analysis provides the establishment of a relation between the effecting exposure, mode, duration of exposure and the degree of severity, prevalence of adverse effects in the exposed population.

In the risk assessment, health disorders under the influence of EMR factor are based on the assumption of a threshold for adverse effect, below which adverse effects are not developed.

The known changes in the human body under the influence of EMR are summarized in Table 2.36–2.38.

Table 2.36

Known changes in the human body under the influence of electromagnetic fields (frequency of 0–30 Hz) of different intensity

Current density, $\mu A/sm^2$	The observed changes	Data source
0.1	There is no response of the nervous system at the cellular level	Bridges D., Prich M., 1981; Lee J. et al., 1989
1.0–10	The phenomenon of electro- and magnitophosphenes. The production of membrane potential	Bridges D., Prich M., 1981; J. Lee et al., 1989
10–50	The thresholds of stimulation of sensory receptors and nerve and muscle cells	Bridges D., Prich M., 1981; Smith C.W., 1984
>100	The probability of ventricular fibrillation. The possibility of cardiac arrest, respiratory tetanus	Bridges D.D., Prich M., 1981; Smith C.W., 1984

Hazard identification should take into account all types of effects that can be generated in the population exposure to EMR of different frequencies in accordance with modern scientific data[1]. The generalized and systematic information on the probable sources of electromagnetic effect, radiation parameters, and locations of sources regarding residential development, the population potentially exposed to the influence, and probable expected health effects.

[1] Health disorders related to the following force majeure circumstances are not considered: military operations, accidents, natural disasters.

Table 2.37

Known changes in the human body under the influence of electromagnetic fields (frequency of about 50 Hz) of different intensity

Field parameter	Exposure time	Observed response	Data source
1.15 and 20 kV/m	Up to 2 hours	Change in the response time within the physiological standard	Michaelson S.M., 1983; Savin B., Rubtsova N., 1978
0.2 mt	3 hours	No effect on the response time and electroencephalogram	Savin B., Rubtsova N., 1978
Up to 10 mctl	Up to 10 hours with a break	Changes in blood pressure, heart rate	Savin B., Rubtsova N., 1978; Komarova A.A., 1983
4–7 mctl	From 1 to 7 years	The increased incidence of children's leukemia. The appearance of tumor of different localization and types	Tomenius L., 1986; Verkasalo P.K. et al., 1993; Olsen J.H et al., 1993, 1995; Szmigielski S. et al., 1996

Table 2.38

Known changes in the human body under the impact of electromagnetic fields of different intensity [B.A. Minin, 1974]

Energy flux density, mcW/sm^2	The observed changes
600	Pain during the irradiation
200	The inhibition of redox processes
100	Increase in blood pressure followed by its reduction. In cases of chronic exposure – sustainable hypotension. Bi-directional cataractogenic effect in the frequency range of 1.5–10 GHz
40	Warmth sense. In the irradiation during 0.5–1 hours - increased pressure by 20–30 Mmhg
20	Stimulation of the redox processes of tissue
10	Neuro asthenic syndrome. Asthenia after 15 minutes of exposure, change in electrobiological brain activity
8	Undefined shifts from the blood with a total exposure time of 150 hours, the change in blood clotting
6	Electrocardiographic changes, changes in the receptor apparatus
From 4 to 5 years	Change in blood pressure during multiple exposures, a short-term leukopenia, erythropenia
From 3 to 4 years	Vasotonic response with bradycardia symptoms, the multiplication of the heart electrical conductivity
From 2 to 3 years	The pronounced nature of decrease in arterial pressure, tachysphygmia, fluctuations in the blood volume in heart
1	Decrease in blood pressure, the trend toward tachysphygmia, slight variations in blood volume in a heart. The reduction of ophthalmotonous pressure with daily exposure for 3.5 months. The reduction of the perception thresholds, increase in the time of psychophysiological test execution
0.5	Increase in the irritant perception threshold
0.4	Auditory effect when exposed to pulsed EMF
0.3	Some changes in the nervous system in chronic exposure for 5–10 years
0.1	Electrocardiographic changes. The absence of change in psychophysiological indicators
Up to 0.05	Trend to pressure reduction in chronic exposure

Despite the considerable number of effects caused by exposure to EMR, which is specified in the scientific literature, WHO recognizes proven effects with respect to the leukemia in children exposed to EMR of populated areas and the formation of brain tumors (meningioma, glioma) during long-term (more than 10 years) intensive (more than 1 hour per day) use of cell phones (Table 2.39, 2.40).

Table 2.39

The generalized results of studies on the risk of cancer (leukemia) in children who have been exposed to EMF (living near power lines, the impact of household equipment, cell phones, and other sources of EMF radiation)

Publications	Long-term effects	Yes (+), no (–)
Wertheimer N., Leeper E., 1979 (США)	Leukemia	+
Tomenius L., 1986 (Швеция)	Leukemia	+
Myers A.D. et al. 1985 (USA)	Leukemia	–
Savitz D. et al., 1988 (США)	Leukemia	+
London S.J. et al., 1991 (США)	Leukemia	+
Feychting M., Ahlbom A., 1992; Ahlbom A., Feychting M., 1993 (Sweden)	Leukemia	+
Verkasalo P.K. et al., 1993 (Finland)	Leukemia, encephalomas	– +
Pearson T. et al., 1995 (USA)	Tumors	+
Olsen J.H. et al., 1993, 1995 (Denmark)	Leukemia, encephalomas, lymphadenomas	+ + +
Petridou E. et al., 1997 (Greece)	Leukemia	–

Note: hereinafter:
(+) – effect is proved;
(+) – effect is not proved;

Table 2.40

Generalized results of studies on the risk of cancer (leukemia) in the adult population, who had contact with the EMF outside industrial activity (living near power lines, radar station, the use of electrical appliances and other sources of EMF radiation)

Publications	Long-term effects	Yes (+), no (–)
Robinette C.D. et al., 1980	Leukemia	+
Wertheimer N., Leeper E., 1979	Leukemia	+
Szmigielski S. et al., 1996	Leukemia, malignant thyroid neoplasm, lung cancer	+ + +
Floderus B. et al., 1993	Acute leukemia, chronic lymphoma, encephalomas	– + +/–

Based on the analysis of a set of domestic and foreign data on the dynamics of development of gliomas, meningiomas and leukemia under the influence of EMR on the background of the natural occurrence of these diseases, evolutionary and statistical mathematical models of adverse effects development are developed under the influence of high-frequency electromagnetic radiation.

The assessment of the probability of meningioma, glioma, or leukemia disease occurrence is performed by the solution of evolutionary recurrence equations (2.5.8)–(2.5.10).

The equation for the calculation of the probability of glioma has the following form:

$$P_{t+1}^{G} = P_{t}^{G} + \\ + \left(\left(-2{,}43 \cdot 10^{-5} \left(K\mathrm{t} \right)^{3} + 2{,}6 \cdot 10^{-3} \left(K\mathrm{t} \right)^{2} - 7{,}42 \cdot 10^{-2} K\mathrm{t} + 0{,}48 \right) + 0{,}03 \left\langle \frac{I^{H}}{0{,}075} - 1 \right\rangle \right) K, \quad (2.5.8)$$

where P_t^G – the probability of gliomas at initial (specified) time *t* per 100 thousand people;

P_{t+1}^G – the probability of gliomas for the next time step (depends on K) per 100 thousand people;

I^H – the intensity of radiation during the studied period of time (t/m^2);

K – temporary empirical coefficient taken according to Table 2.1;

$\langle\ \rangle$ – Kelly's brackets, taking the values $\langle x \rangle = 0$ at x < 0 and $\langle x \rangle = x$ at x $\geq$ 0.

The morbidity level at the first year of life is defined by the rate of 1 accident/100 thousand people.

The equation for the calculation of the probability of meningioma has the following form:

$$P_{t+1}^M = P_t^M + \left(0{,}02P_t^M + 0{,}00006\left\langle \frac{I^H}{0{,}075} - 1 \right\rangle\right)K, \tag{2.5.9}$$

where P_t^M – the probability of meningiomas at initial (specified) time *t* per 100 thousand people;

P_{t+1}^M – the probability of meningiomas for the next time step (depends on K) per 100 thousand people;

The equation for the calculation of the probability of leukemia has the following form:

$$P^L(t) = \left(-9{,}12\cdot 10^{-7}(K\mathrm{t})^4 + 1{,}68\cdot 10^{-4}(K\mathrm{t})^3 - 9{,}2\cdot 10^{-3}(K\mathrm{t})^2 + 0{,}1K\mathrm{t} + 2{,}8\right)\cdot \left(1 + \left(0{,}2\left\langle \frac{I^L}{0{,}1} - 1 \right\rangle + 1{,}5\left\langle \frac{I^H}{0{,}075} - 1 \right\rangle\right)\left(e^{-Kt\cdot 0{,}035} + 0{,}07\right)\right), \tag{2.5.10}$$

where $P^L(t)$ – the probability of leukemia at initial (specified) time *t* per 100 thousand people;

I^L – the intensity of low-frequency radiation during the studied period of time (mT);

I^H – the intensity of high-frequency radiation during the studied period of time (W/m^2);

The equations allow calculating the risk at any given time *t.*

The prediction of the risk of glioma and meningioma in the equations is calculated by the value of the risk at the current time. In the first year of life, the value of individual risk is equal to 10^{-5} for gliomas and 10^{-7} for mengliomas. Long-term forecast for the whole period of life can be incrementally build based on the dynamics of the change in EM-load. Studies on the assessment of the frequency and severity of diseases at the studied area are carried out at ($P_t \neq 0$), to build an evolutionary model and evaluate the initial risk value at a given time.

The following can be used to solve the system of recurrence equations: Standard office software Microsoft Excel, different mathematical packages such as MatLab, Mathematica, and others with similar capabilities.

Exposure assessment involves determining the electromagnetic characteristics of the radio frequency band at a given time, and duration of the preservation of certain levels of EMI, as well as the assessment of the weighted level of EMR as a measure of population exposure to harmful factor.

The different characteristics of EMF are used to assess the level of exposure to electromagnetic fields: within the range of 0...10 MHz – the density of electric current; within the range of 10–300 MHz – electric and magnetic field density, within the range of 0.3...300 GHz – the energy flux density.

The assessment of exposure as a quantity characterizing the established long-term level of the electromagnetic field can be performed through instrumental measurements and/or through calculation. The measurement of parameters of exposure to electromagnetic fields is performed using standardized instrumental methods [MG 4.3.043-96; MG 4.3.044-96; MG 4.3.1167-02; MG 4.3.679-97; MG 4.3.1676-03; MG 4.3.1677-03; MG 4.3.2501-09; MI 4109-86; GOST R 54148-2010].

Energy exposure can be considered as the average quantity characterizing the intensity and duration of exposure to a specific type of EMR:

$$\overline{ЭЭ} = \frac{\sum_{i=1}^{n} ЭЭ_j^i}{N}, \quad (2.5.11)$$

where $ЭЭ_j^i$ – the i-th measured or calculated value of the energy exposure of the j-th type (the density of the induction current, the intensity of electric or magnetic field, the energy flux density);

N – the number of measurements (results of calculations) during the studied period

Weighted average exposure is calculated if there is data on the exposure (taking into account the periods of the work of sources and/or the length of stay of the population under the influence):

$$\vec{ЭЭ} = \frac{ЭЭ_{j1}^i \cdot p_1 + ЭЭ_{j2}^i \cdot p_2 + ... ЭЭ_{jn}^i \cdot p_n}{p_1 + p_2 + ... p_n}, \quad (2.5.12)$$

where $P_{1,2,n}$ – the ration of the residence time of the population under the influence of EMR with intensity of $ЭЭ_j^i$.

With simultaneous exposure to the electromagnetic fields of different frequencies, additive effect is taken into account as follows.

With simultaneous exposure to the electromagnetic fields of different frequencies, additive effect is taken into account as follows.

$$J_\Sigma = J_1 + J_2 + J_n, \quad (2.5.13)$$

where $J_{1,2,n}$ – the density of the induced current generated by different sources

If the radiotechnical objects are equipped with several transmitters and systems operating in the frequency bands of up to 300 MHz, the total electric or magnetic field intensity in each of these ranges on the adjacent territory is determined according to the formulas:

$$E_\Sigma = \sqrt{\left(E_1^2 + E_2^2 + ... + E_n^2\right)}, \quad (2.5.14)$$

$$H_\Sigma = \sqrt{\left(H_1^2 + H_2^2 + ... + H_n^2\right)}, \quad (2.5.15)$$

where E_Σ,H_Σ – total field intensity;

E_1,H_1, E_2,H_2, …H_n,E_n – field intensity generated by each transmitter at a certain point of the range.

The total energy flux density (S_Σ) on the analyzed territory for the frequency ranges of 0.3–300 GHz is determined by the formula:

$$S_\Sigma = S_1 + S_2 + S_n, \quad (2.5.16)$$

where $S_{1,2,n}$ – the energy flux density generated by each transmitter at the determined point.

The results of the calculation or instrument assessment of the exposure are used for hygienic assessment and the calculation of health risk. The result of this stage is a field (measured) and/or estimated data on the levels of electromagnetic radiation in the studied area, taking into account the time factor and the number of population living under the conditions of a particular exposure level.

In simultaneous exposure to electromagnetic fields with different frequency, it is necessary to determine whether the combined effect of fields with different frequencies is additive in terms of effect. Additivity should be considered separately for the effects of thermal and electrical stimulation.

In fact, the risk assessment is performed through the solution of the recurrence equation (2.5.8–2.5.10). When characterizing the risk of gliomas, meningiomas or leukemia formation, you can use the standard criteria for carcinogenic risk assuming the value of $1 \cdot 10^{-4}$ as an acceptable level. It is also possible to perform the calculation of the additional risk and reduced risk index, and use a single scale for risk assessment based on the evolutionary simulation method.

2.5.3. The assessment of public health risk when exposed to the radiation factor (using the example of consumer products)

The assessment of public health risks under the influence of radiation factors is an integral part of the legislation in the area of product safety and population health protection both by a state – members of the Customs Union and by the rest of the world community.

In most countries of the world and international organizations the concept of risk assessment is considered as the main mechanism for the development of policies, strategies, and priorities of actions aimed at the maximum, economically viable reduction of the negative impact on public health.

The complete scheme of the public health risk assessment when exposed to radiation factors provides the conduction of four stages in full compliance with the classical scheme of health risk assessment [US EPA, 1989]:

– hazard Identification providing for the establishment of qualitative evidences of the ability of the particular agent to cause some harmful effects in a human;

– exposure Assessment is the establishment of human-equivalent radiation dose from potential sources of radiation exposure taking into account all the possible intake routes;

– dose – Response Assessment is the establishment of the relations between the dose of radiation exposure and the incidences of harmful effects in the exposed population;

– risk Characterization integrating the data obtained at all previous stages of researches, with the aim of quantitative and qualitative risk assessment, the identification and assessment of the relative importance of the public health problems.

Hazard identification when assessing the radiation risk for the consumer health

Hazard identification determines a probability of harmful health effects frequency establishment due to the exposure to a radioactive contaminant [US EPA, 1989].

At the stage of hazard identification, the main task is to identify the source of ionizing radiation, physical object or procedures that are able to create the quantitative dose of the human or group of people.

It is believed that under the condition that individual doses are much lower than the threshold of harmful deterministic effects, the effect created by the dose from a single source does not depend of those created by doses from other sources. In many cases, each source or group of sources can be considered separately. Then the exposure of individuals from a given source or a group of sources should be considered. This procedure is called "the source oriented approach".

The following is classified as the potential source of radiation exposure in addition to food products [EC, 2007]:

a) products containing intentionally made artificial radionuclides:

– smoke detectors with an ionization chamber in which the air located between the electrodes is ionized using a radiation source (eg., ^{241}Am, ^{85}Kr, ^{226}Ra, ^{238}Pu, ^{239}Pu);

– items glowing through special paints containing 226Ra, tritium, 147Pm, and the sources of glow of gaseous tritium (watches, navigation devices, such as compasses, lights, key rings, floats, etc.);

– the starters of electroluminescent lamps;

– various electronic devices (voltage regulator, current ripple protector, signal lights, and etc.).

– anti-static devices (^{210}Po, ^{241}Am);
– lightning protection system (^{241}Am, ^{226}Ra);
b) products containing intentionally made natural radionuclides:
thoriated gas mantles;
– thoriated lenses;
– thoriated tungsten welding electrodes;
– glassware, tableware, decorations and tiles containing uranium;
– uranium-containing dental materials;
c) the gems irradiated to intensify or change the colour (^{60}Co, neutron irradiation in a nuclear reactor, a beam of electrons in a linear accelerator);
d) antiques (such as coins and bank checks containing ^{14}C, identity cards and driver's license containing ^{147}Pm, lighting systems with ^{226}Ra and tritium, ointments, creams and powders containing natural uranium and others.).

In accordance with the "A Review of Consumer Products Containing Substances ..." [EC, 2007], the potential exposure routes of ionizing radiation in the operation of the relevant consumer products include:
– external exposure under normal operating conditions;
– internal exposure due to inhalation, ingestion or skin absorption of radioactive material;
– internal and external effects caused by improper operation.

The principal source of direct external exposure are the highly active sources of gamma particles, while the largest proportion of the dose of radiation incoming through inhalation and oral routes is associated with alpha particles. The most important radionuclides for each of the routes of exposure may vary and are determined according to their relative concentrations, half-life, mobility in the environment and the factors applicable to each of the intake routes [US EPA, 1989].

Intakes through inhalation, ingestion and absorption are the potential intake routs of radionuclides, although the intake of radionuclides is usually expressed in units of activity (Bq or Ci), and not in terms of mass units. Radionuclides incoming through the above ways can spread systemically and release alpha, beta and gamma particles to organs and tissues.

Risk assessment should include radionuclides the content of which exceeds the levels defined in the blank sample, or significantly exceeds the background levels in at least one sample of the products. Experts provide the conclusion about the need to include radionuclides in the risk assessment the presence of which in the samples of products is not determined, but there is a suspicion of their presence. The grouping of radionuclides within a quantitative risk assessment is considered unnecessary and inappropriate. The dose level of ionizing radiation and the associated health risk depend on the characteristics of the individual radionuclides. However, in some cases, it is possible to combine different isotopes of one element that have similar radiological properties (e.g., Pu-238/239/240, U-235/238), or belong to the same series of radioactive decay. The conduction of grouping must be justified, and rarely gives any advantages for risk assessment. In the case of the definition of a large number of radionuclides, the risk assessment should focus on a selected group of radionuclides that contribute to the dose of ionizing radiation and levels of exposed population group health risk.

Risk assessment can be carried out for the following groups of the irradiated population [MI 2.1.10.3014-12]:
– children at the age from 0 to 14;
– teenagers at the age from 15 to 17;
– children and teenagers at the age from 0 to17;
– adult population at the age from 18 and older;
– all population at the age from 0 to 85.

The most serious biological effects of radiation exposure can be grouped into two main categories:
– deterministic effects (harmful tissue reactions), mostly related to the death or malfunction of cells at higher doses of radiation;

– stochastic effects, i.e. cancer and inherited diseases associated with the development of cancer in exposed individuals due to mutations in somatic cells, or with an inherited disease in the offspring of exposed persons due to mutations in the reproductive (functional) cells.

The following biological radiation effects in embryo and fetus as well as non-cancerous diseases are also considered. The induction of tissue responses is characterized by a threshold dose. The reason for the existence of this threshold dose is that the radiation damage (severe malfunction or death) critical for the population of cells in this tissue should arise before tissue damage will manifest itself in an appropriate clinical form. In the exceedance of a threshold dose, the severity of damage including impaired restorability of the tissue increases with increasing dose.

"The biological basis for dose limitation in the skin" (1992) indicates that early (within days – weeks) tissue responses to radiation may have inflammatory nature due to the release of cellular factors when the threshold dose was exceeded, or they may have the nature of responses resulting from cells decrease.

Late deterministic effects emerging in the months and years after exposure may have general nature, as they are a direct result of damage to this tissue. On the other hand, according to W. Dorr, J.H. Hendry (2001), some other tissue responses may have the nature of radiation consequences if they occur as a result of early cell damage. Table 2.41 presents the thresholds of some tissue effects for some organs of an adult person.

Table 2.41

The assessments of thresholds of tissue effects in the testes, ovaries, the eye-lens and bone marrow of an adult [*ICRP*, 1984]

Tissue and effect	Threshold		
	The total dose of single short-term irradiation (gy)	The total dose of high-fractional or protracted irradiation (gy)	The dose rate per a year in high-fractionated or protracted irradiation during many years (gy · yr^{-1})
Testes			
Temporary sterility	0.15	NA[1]	0.4
Permanent sterility	3.5–6.0[2]	NA	2.0
Ovaries			
Sterility	2.5–6.0	6.0	>0.2
Eye-lens			
Noticeable opacities	0.5–2.0[3]	5	>0.1
Vision disorders (cataract)[4]	5.0[4]	>8	>0.15
Bone marrow			
Hematopoiesis depression	0.5	NA	>0.4

Note: [1] – NA – not applicable since the threshold dependents on the dose rate rather than the total dose;

[2] – see UNCEAR (1998);

[3] – see also Otake and Schull (1990);

[4] – defined as 2–10 Sv (NCRP 1989) for the threshold acute radiation dose.

There are epidemiological and experimental studies for oncology diseases, which give an assessment of radiation risk and its uncertainty for doses of about 100 mSv or less.

The main target of radiation exposure is chromosomal DNA, which was confirmed by a huge number of studies of cell cultures and animal species that are genetically deficient in responses to the DNA damage – many of these specific genetic defects increase the frequency of radiobiological effects.

Several studies have found that post-radiation cell response leads to genomic rearrangement and/or cellular effects without obvious evidence for direct-induced DNA damage. In the broadest sense, these processes can be called epigenetic ones; they are

contrast to well-known radiobiological concept of direct DNA damage due to the tracks of ionizing radiation. Although a part of these categories overlap, such epigenetic effects can be divided into two categories: (*a*) radiation-induced genomic instability and (*b*) the post-radiation effect of signal transmission between adjacent cells ("bystander effect").

The so-called "bystander effect" (post-radiation signal transmission by adjacent cells) refers to the expression of cell death/apoptosis, genetic/chromosomal mutation, genomic instability and/or the changed patterns of proteins' intake in cells that do not fall directly under the tracks of radiation. In *in vitro* studies, the phenomena of induced genomic instability and the "bystander effects" can have some commonality regarding their mechanisms associated with cellular stress. However, these are still not enough, and there are some controversies regarding the evaluation of the relative contribution of a signal transmit to a neighboring cell into cellular effects in general, as well as regarding the fact how this effect depends on dose.

It is determined that the structure of the organs and tissues plays a major role in their response to radiation. Paired organs or organs the functional sub-elements (FSE) of which have parallel, not sequential organization, are able to withstand inactivation of many FSU without clinical signs of disorder, as they have a considerable reserve and are compensated by the remaining FSO. This is one of major reasons for the existence of a dose threshold for these disorders, particularly high tolerance to radiation of the body when the critical part of these systems has functionality margin.

Late tissue responses have not only a durable, dose-dependent latent period before its expression, but also a long period of development, with a possible output after decades of exposure. Late responses may have a "common" nature, which means their origin directly in target tissue. On the contrary, some late tissue responses can be "consequences", which means their appearance in the form of consequences of severe early responses in the target tissue [The biological basis for the dossier limitation in the skin, 1992].

In accordance with current guidance on risk assessment [US EPA, 1989], when assessing the health risks associated with radiation factor of consumer products, it is appropriate to consider only the chronic effects, since the development of critical health responses is usually associated with exposure to extremely high levels of ionizing radiation not specific for the conditions of the use of consumer products.

The carcinogenic, mutagenic, and teratogenic effects are the main adverse health effects associated with exposure to ionizing radiation. The development of other harmful effects is also characterized for radiation exposure, but they are developed under the conditions of acute exposure to high, more than 1 Sv, radiation levels not typical for conventional non-emergencies and wartime everyday actions.

The damage of the molecules by electrically charged particles (e.g., free radicals) takes place as the result of exposure to ionizing radiation, which in turn leads to an chemical restructuring and irreversible cellular changes. The levels of biological damage from various types of radiation exposure are different [US EPA, 1989].

The carcinogenic potential of ionizing radiation is widely studied and confirmed by numerous scientists and reflected in a number of synthesis documents: Sources and Effects of Ionizing Radiation Nations (UNSCEAR), 1982; Ionizing Radiation: Sources and Effects Nations. New York, NY; United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1988; The Effects on Populations of Exposures to Low Levels of Ionizing Radiation (BEIR Report), 1988; The Health Risks of Radon and Other Internally Deposited Alpha-Emitters Report, 2006.

Depending on the metabolic features, radionuclides can be selectively accumulated in specific tissues and organs, which in turn may lead to an increase in the radiation dose and higher than usual incidence of cancer in these organs and tissues.

Ionizing radiation is considered pancancerogen, as it is also the initiator and the promoter of carcinogenesis and can induce the development of cancer in almost every tissue and organ, such as the thyroid gland, mammary gland, lung, bone marrow, stomach, liver, colon, brain, salivary glands, bones, rectum, esophagus, small bowel, bladder, pancreas, lymphoid tissue, skin, larynx, uterus, ovaries, cranial sinus mucosa and kidney.

The cancer of the above mentioned localization was detected in populations exposed to high levels of radiation, including survivors after the explosion of atomic bombs, miners, patients injected with thorium-containing radiopaque thorotrast or radium, patients treated with high-dose X-ray irradiation in various treatment programs.

On average, approximately 50% of cancers associated with exposure to ionizing radiation are lethal ones. The portion of lethal outcomes is different for different types of cancer and varies from 10% in the case of thyroid gland cancer to 100% in the case of liver cancer. The data for the study of mutagenic potential of ionizing radiation is based mainly on the results of animal studies, and demonstrates all forms of mutagenesis, including lethal mutations, translocations, inversions, nondisjunction, and point mutations. Mutation frequency established by the results of these studies is extrapolated to human and forms the basis for assessing of the impact of ionizing radiation on human genetic apparatus [UNSCEAR 1982, 1988]. It was found that the consequences of mutations observed in the germ cells are both the increase in mortality and morbidity [UNSCEAR, 1982]. Serious genetic diseases developed as a result of mutations and chromosomal aberrations due to radiation exposure include hereditary diseases, the disorders of physical and mental development, in addition, the shortening and reduction of life quality, increase in the frequency of hospitalization. However, the frequency of genetic disorders associated with exposure to ionizing radiation is relatively lower when compared with spontaneously occurring genetic diseases.

It is widely known that ionizing radiation has teratogenic potential, as the fetus is more sensitive to radiation than the mother. The most important factor effecting the extent and type of damage to the genetic material is a fetal age at exposure to ionizing radiation. In addition, the abnormal development of the embryo depends on which cells, tissues or organs were more actively differentiated at the time of exposure [Hassan O.A., 1998; Korolev Y.N. et al., 1999; Yurchenko O.B., 2001; Zolotukhina I.V., 2004; Vorobyev A.P., 2005; Alexandrov A.G. et al., 2006]. The embryo is relatively resistant to radiation at the later stages of development, and the most vulnerable from the implantion to the end of the period of organogenesis (from two to eight weeks after fertilization). The effects from the nervous system, skeletal system, eyes, genitals, and skin are observed more frequently [Brent, 1980]. The highest level of the damage risk to the fetal brain occurs during the period from the 8th to the 15th week of development, when the most rapid differentiation and cell proliferation is observed in the nervous system [Otake M., Schull W., 1984].

Furthermore, the result of exposure to ionizing radiation may be an increase of the risk of other diseases development, in particular cardiovascular (under the action of high doses). However, there are no direct evidences that the risk of non-carcinogenic health responses development increases under the conditions of low-dose exposure. In addition, radiation exposure is associated with the increase of the risk of certain types of benign tumours, but the available data does not allow calculating the level of the risk [Health risks from exposure to low levels of ionizing radiation, 2006].

It was found that the risk of carcinogenic effects is limiting and may be used as a basis for the assessment of health responses associated with exposure to ionizing radiation [Recommendations, 1991; Ivanov V.K. et al., 2005; Preston D.L., 2008; Steyter J.L. et al., 2010]. It is also important to establish the risk of diseases development associated with damage to the genetic material and transmitted to succeeding generations, in children whose parents were exposed to ionizing radiation, for example, as cystic fibrosis, as well as diseases the occurrence of which is influenced by both genetic and environmental factors, such as diabetes mellitus [Hoffman D.A. et al., 1989; Balewa L.S. et al., 2003; Bondarenko N.A., 2005; Podsonnaya I.V. et al., 2008; Balewa L.S. et al., 2011].

The purpose of genetic risk assessment is to establish an additional risk of genetic diseases with respect to the background frequency of such diseases among the population, these diseases include:

– Mendeleev diseases caused by mutations in a single gene, including autosomal dominant diseases (achondroplasia, neurofibromatosis, Morfana syndrome, myotonic dystrophy); autosomal recessive diseases (cystic fibrosis, phenylketonuria, hemochromatosis, Bloom syndrome, syndrome Louis-Bar); and recessive diseases coupled with the X chromosome (Duchenne muscular dystrophy and others.);

– Multifactorial diseases, including developmental defects (neural tube defects, cleft lip, heart defects) diagnosed at birth and adult chronic diseases, such as coronary heart disease, hypertension, diabetes mellitus [D.A. Hoffman et al., 1989];

– Chromosomal diseases associated with changes in the size, number (eg., Down syndrome) and structure (eg., Cri du chat) of chromosomes.

Thus, in the products hazard identification in the case of radiation risk assessment, it is required to:

– identify the source of ionizing radiation capable of creating quantified dose in a person or a group of people;

– identify risk cohorts (possible product consumers);

– establish the harmful health effects, the probability of increasing the frequency of which is possible due to exposure to ionizing radiation source.

Exposure assessment

Radiation effect is considered as a transfer of energy from the radiation fields of X-ray or gamma-rays per unit of air mass, a measurement unit of which is roentgen (*R*) (1 $R = 2{,}58 \cdot 10^{-4}$ C/kg).

The term "effect" also defines the physical contact between the human body and ionizing radiation.

The exposure of the population covers all types of population exposure not related to occupational exposure or medical exposure of patients (occupational exposure includes any exposure of personnel resulting from its work; the radiation exposure of a patient arises in course of diagnostic, interventional, and therapeutic procedures).

In planned exposure, the limit of dose that individuals can get from this source is called a critical dose. The concept of critical risk is relevant for potential exposure. Reference level is a limit focused on the source under emergency or current exposure. The concept of critical dose and reference level are used in the process of measures optimization to ensure radiation protection, facilitating the insurance of exposure retention at such a low level as reasonably achievable taking into account socio-economic factors.

Internal exposure occurs when radionuclides incoming through inhalation, peroral, injection and other ways affect the tissues and organs.

External exposure is an effect on tissue by ionizing radiation from sources located outside the body, scattered in air or water, on the skin surface, ground.

Internal exposure can be formed by all types of ionizing radiation, while a significant proportion of the outer dose is formed with photon, beta and neutron radiation.

It is believed that the ionizing radiation can cause harmful effects from the biological tissues, unless the energy released as a result of radioactive decay is absorbed by tissues. Exposition assessment for radioactive contaminants should include the detailed calculation of equivalent dose.

It should be borne in mind that the term "dose" in relation to radionuclides characterizes the energy transferred per unit of tissue mass. Gamma particles and X-rays have the highest penetration ability and determine the greatest contribution to the radiation dose in terms of external exposure to ionizing radiation. Alpha particles cannot penetrate through the outer skin integument, so they do not have a significant influence on the level of external dose.

In accordance with the "Risk Assessment Guidance for Superfund" [US EPA, 1989], exposure assessment includes:

– the characterization of exposure conditions;

– the identification of exposure routes;

– the quantitative characterization of exposure.

The method of direct measurement is the most preferred method for the assessment of the radioactive contaminants concentration in the probable place of contact. However, in cases when it is impossible to carry out direct measurements, in order to predict the contaminants content it is possible to use the results of behavior assessment of the tested

substance in the environment and transport models. Simulation is recommended when it is impossible to obtain samples containing studied radionuclides, when the level of radioactive contaminant did not reach the exposure point, the level of contaminant is below the detection limit, but still can create a significant health risk.

Special dosimetric quantities based on measurements of the energy absorbed by organs and tissues of the human body have been developed to estimate the radiation doses. In order to relate the radiation dose and a radiation risk (harm), it is necessary to take into account the differences in biological effectiveness of different types of radiation of different quality and differences in the sensitivity of organs and tissues to ionizing radiation.

ICRP introduced the values of dose equivalent in organs and tissues of the human body and the equivalent of the effective dose in 1977. Definitions and methods to calculate these values were changed in Publication 60 [ICRP, 1991b], which led to the introduction of the equivalent dose and effective dose concept and allowed to summarize doses of total body and its parts irradiation due to the external irradiation of various types and the supply of radionuclides in the human body.

The equivalent and effective dose in body tissues and the human body cannot be measured directly; therefore the concept of operating variables was introduced, these values can be measured and be a basis for an equivalent and effective dose assessment.

In the definition of the effective dose concept and its calculation, the use of the corresponding tissue weighting factors, w_T, allow consideration of the difference in sensitivity of different organs and tissues to stochastic effects induction. Radiation weighting factors having a high linear energy transfer, the so-called high LET radiation were obtained for stochastic effects at low doses.

Radiation can cause deterministic effects at high doses, especially in emergency situations. Such clinically observed lesions occur in excess of dose thresholds. Lesion size depends on the level of the absorbed dose and dose rate, and the quality of radiation and tissue sensitivity. In general, it was found that the relative biological effectiveness (RBE) for deterministic effects caused by high LET radiation was lower than those that were obtained for stochastic effects during irradiation in small doses; in such case the relative sensitivity of the tissue differs.

The concept of equivalent and effective dose should not be used for the quantitative assessment of increased radiation doses when making decision on the need for any treatment in the event of tissue responses development. For such purposes, doses should be assessed as the absorbed doses (Gy), and in the case of exposure to high LET radiation (e.g., neutrons or alpha particles) – absorbed doses weighted according to the corresponding LET.

The procedure of the effective dose assessment involves the assessment of the absorbed dose as a fundamental physical concept when averaging it on specific organs and tissues, and using the properly selected weighting factors to account for the differences in biological effectiveness of different types of radiation and different sensitivity of these organs and tissues to stochastic biological effects.

The values of equivalent dose in organs and tissues weighted by their radio sensitivity are summed to obtain the value of the effective dose, the value of which is based on the exposure to external radiation fields and incorporated radionuclides and on the processes of primary physical interactions that occur in irradiated tissues, and on the conclusions concerning the biological responses resulting in the development of stochastic effects.

The absorbed dose, D, is a basic physical quantity used for all kinds of ionizing radiation exposure and any radiation geometries, and is considered as an average energy of ionizing radiation per unit of tissue mass. Its concept is defined as the quotient of *dE* on *dm*:

$$D = \frac{dE}{dm}, \tag{2.5.17}$$

where *dE* – an average energy imparted by ionizing radiation;

dm – substance weight.

The measurement unit of the absorbed dose is Gray (1 J/kg). The conventional unit of absorbed dose designations is Rad (1 rad = 100 erg/g = 0.01 Gy). The absorbed dose is obtained from the average value of stochastic quantity of the transferred energy *E*, and does not reflect the random fluctuations of interaction events of the radiation in tissue.

In determining substance at each point, its value is obtained as an average for the mass element *dm* and hence for a variety of atoms or molecules of a substance. The absorbed dose is a measurable value, and there are primary standards to measure it.

When using the concept of the absorbed dose in the practice, the dose is averaged over a volume of tissues. At that, it is assumed that the average value of absorbed dose averaged over a specific organ or tissue for the low doses of radiation may be associated with radiation harm of stochastic effects for this tissue with sufficient precision in the context of radiation protection. Averaging of absorbed doses for tissues or organs, and the summation of weighted average doses in various organs and tissues of the human body are the basis for the definition of protective variables that are used to restrict the output of stochastic effects at low doses. This approach is based on the linear no-threshold model and thus allows summing the dose of external and internal exposure.

The averaging of absorbed dose is performed for the whole organ weight (e.g., liver) or tissue (e.g., muscle tissue), or for sensitive volume of tissue (e.g., endosteal skeleton surface). The extent to which the value of the average dose is representative for the absorbed dose in all parts of organs, tissues or tissue sections, depends (for external radiation) on radiation uniformity and from the path of the radiation incident on the surface of the human body. The uniformity of dose distribution in low doses range also depends on microdosimetric radiation properties. For those types of radiation which have a low penetration ability or lower paths (e.g., low-energy photons or charged particles) as well as for those tissues or organs that are distributed over a large volume of human body (e.g., red bone marrow, lymph nodes or skin), the absorbed dose distribution within a given organ or tissue will be less uniform. Tissue damage can occur in the cases of the extremely uneven exposure of the body even if the average dose to the organ or tissue radiation or an effective dose is below the dose limit.

The distribution of the radiation absorbed dose emitted by radionuclides inside organs or body tissues, the so-called internal emitters, depends on the permeation power and energies range of the emitted radiation. Thus, the distribution of the absorbed dose when exposed to the incorporated radionuclides emitting alpha particles, low-energy beta particles, or low energy photons or electrons can also be extremely uneven. This unevenness is especially characteristic for radionuclides deposited in the respiratory and digestive system, and the skeleton. Special dosimetric models were developed to measure the inequality in the distribution, activity retention, and when locating the sensitive sections of these systems.

The thresholds of absorbed doses to the whole body for some types of health responses are presented in Table 2.42.

Most values are rounded to the whole Gy; ranges indicate the dependence of the affect area for skin, and on the differences in medical care for the bone marrow.

The permissible values of exposure are used in order to set exposure limits and to achieve the lowering of the level of stochastic biological effects below the unacceptable levels, and total elimination of deterministic effects.

The determination of these values is based on the average absorbed dose of radiation *R* in the scope of this organ or tissue *T* (Table 2.43).

Radiation R is given as a type and energy of radiation incident on the surface of the body or emitted by radionuclides incorporated in the body.

According to the ICRP Publication 103 (Recommendation of the International Commission on Radiological Protection made in the year 2007, 2009) the protective value – the equivalent dose in an organ or tissue – is determined in accordance with the following formula

$$H_T = \sum_R w_R D_{T,R}, \tag{2.5.18}$$

where w_R – radiation weighting factor *R*.

Table 2.42

The assessment of the thresholds of doses absorbed by the whole body, corresponding to a yield of 1% on the morbidity and mortality due to destruction of organs and tissues of an adult by gamma irradiation of the whole body

Effect	Organ/tissue	Effect development time	Absorbed dose (Gy)[e] 1 % of yield
Morbidity			
Temporary sterility	Testes	3–9 weeks	0,1[a,b]
Permanent sterility	Testes	3 weeks	6[a,b]
Permanent sterility	Ovarium	< weeks	3[a,b]
The depression of hematopoietic process	Bone marrow	3–7 days	0.5[a,b]
Main phase of erubescence	Large area	1–4 weeks	<3–6[b]
Skin burns	Skin (large area)	2–3 weeks	<5–10[b]
Temporary hair loss	Skin	2–3 weeks	4[b].
Cataract (vision disorders)	Eye	several years	1.5[a,c]
Mortality			
Marrow failure			
– without medical care	Bone marrow	30–60 days	1[b].
– with a good medical care	Bone marrow	30–60 days	2–3[b,d]
Gastrointestinal syndrome:			
– without medical care	Small intestine	6–9 days	6[d]
– with a good medical care	Small intestine	6–9 days	>6[b,c,d]
Pneumonia	Lung	1–7 month	6[b,c,d]

Note: *a* – ICRP (1984);
b – UNSCEAR (1988);
c – Edwards and Lloyd (1996);
d – Scott and Hahn (1989), Scott (1993).

Table 2.43

The recommended values of the radiation weighting factors, w_R

Radiation type	Radiation weighting factor
Photons	1
Electrons and muons	1
Protons and charged pions	2
Alpha particles, fission fragments, heavy ions	20
Neutrons	Continuous function of neutron energy

The summation is performed for all types of considered radiation. The unit of equivalent dose is $J \cdot kg^{-1}$, which has a special name "sievert" (Sv).

All values are given for the radiation incident on the body surface, or (for the sources of internal radiation) emitted by incorporated radio nuclides.

The values of w_R were selected on the basis of expert assessments from a wide range of data on the RBE for stochastic effects. RBE values reach a maximum (OBEM) at a dose radiation reduction. OBEM values were used in order to select w_R and fixed values were assigned for these coefficients, w_R, in the context of radiation protection (Table 2.44).

Photons, electrons, and muons are radiations with LET of less than 10 keV/μm. The weighting factor equal to 1 was always assigned to these types of radiation. There are reliable arguments for the further use of w_R equal to 1 for all types of low LET radiation. However, this does not mean that the photons of various energies do not differ in their capacity. The proposed simplification is sufficient only to use equivalent and effective dose, that is, to limit, assess, and control doses in the range of low doses. The proposed simplification is sufficient only to use equivalent and effective dose, that is, to limit, assess,

and control doses in the range of low doses. More detailed information on the radiation field and acceptable values of RBE may be required when it is necessary to perform the retrospective assessment of individual risk, if the necessary data are available.

Table 2.44

Recommended values tissue weighting factors

Tissue	w_T	Σw_T
Red bone marrow, large bowel, lung, stomach, mammary gland, other tissues*	0.12	0.72
Gonads	0.08	0.08
Urinary bladder, esophagus, liver, thyroid gland	0.04	0.16
Surface of the bone, brain, salivary glands, skin	0.01	0.04
Total		1.00

Note: * – other tissues: adrenals, extrathoracic segment, gall bladder, heart, kidneys, lymph nodes, muscles, oral mucosa, pancreas, prostate, small intestine, spleen, thymus, uterus/cervix.

Neutrons. Weighting factor for neutrons reflects their relative biological effectiveness with external irradiation. The biological effectiveness of neutrons as they fall to the surface of the human body is highly dependent on their energy. It is recommended to describe the weighting factor for neutrons as a continuous function (Fig. 2.35). However, it should be noted, that the use of a continuous function is based on the practical consideration that the neutron with energy range are considered in most cases of the neutrons impact.

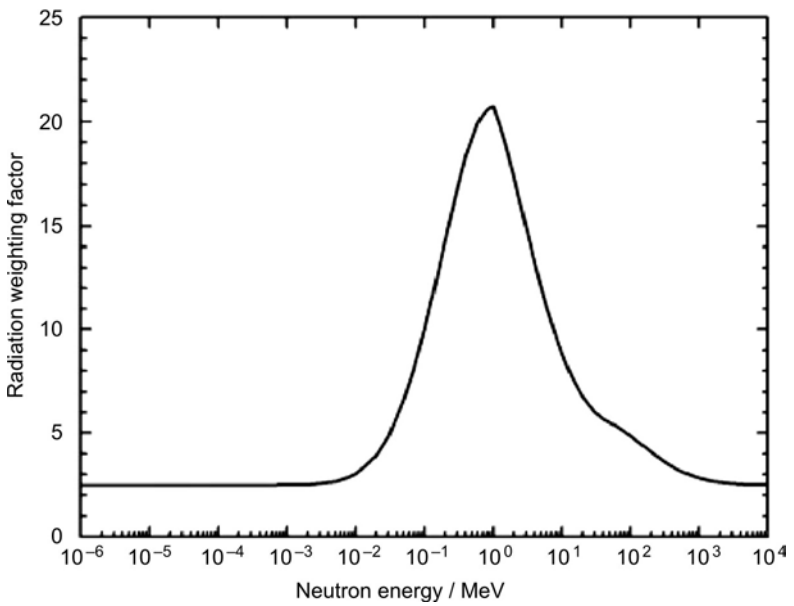


Fig. 2.35. Radiation weighting factor, w_R, for neutrons depending on their energy

The following continuous dependence on the neutron energy, En (MeV) is recommended when calculating the weighting factors of the neutron radiation.

$$W_R = \begin{cases} 5,0 + 17,0e^{-[\ln(2E_n)]^2/6}, 1MeV \le E_n \le 50MeV, \\ 2,5 + 3,24e^{-[\ln(0,04E_n)]^2/6}, E_n \rangle 50MeV, \\ 2,5 + 18,2e^{-[\ln(E_n)]^2/6}, E_n \langle 1MeV. \end{cases} \quad (2.5.19)$$

Only external exposure is important when considering the impact of protons in the practice of radiation protection. Protons of extremely high energies are the dominant components of the fields of cosmic radiation and space near the high-energy particles accelerators. Protons with the energy of few MeV have little value, even taking into account their increased biological effectiveness at low energies. It was quite appropriate to take a single value of w_R for protons of all energies, based on radiobiological data on high-energy protons with energies of above 10 MeV. The path of protons with the energy of 10 MeV in the tissue is 1.2 mm and decreases with energy decrease. These protons are absorbed into the skin. General and uniform weighting factor for protons equal to 2 is recommended for external proton irradiation. It replaces a value equal to 5 recommended in Publication 60 [ICRP, 1991*b*].

Negatively or positively charged or neutral particles are pions appeared in radiation fields as a result of the interaction of primary cosmic rays with nuclei in the upper atmosphere of the Earth. These particles have an impact in air travel. They are also found in complex radiation fields for the protection of high-energy particle accelerators contributing to the occupational exposure of accelerators personnel. Assuming that the energy distribution of the pion radiation fields is broad in scope, it is recommended to use a single weighting factor equal to 2 for all charged pions.

Alpha particles. A person can be irradiated with alpha particles from internal emitters, for example, due to the inhalation of radon decay daughter products or the ingestion of alpha-emitting radio nuclides such as isotopes of plutonium, polonium, radium, thorium, and uranium. A number of epidemiological studies, as well as data from animal studies provide information on the risks associated with the incorporated alpha emitters. However, the distribution of radionuclides in organs and tissues is complex, and the assessment of doses depends on models used for this purpose. Therefore, calculated dose values are characterized by uncertainty, which leads to a wide range of RBE values according to data of epidemiological and experimental studies. Despite the significant uncertainties in the estimates of dose and risk in the intake of alpha-emitting radionuclides to the body, the available data on humans and animals indicate that the RBE depends strongly on the considered biological effects. The limited volume of human data allowing to assess the RBE value for alpha particles assumes that they are approximately equal to 10–20 for lung and liver cancer and somewhat lower for bone cancer and leukemia. w_R value for alpha particles is equal to 20.

Fission fragments and heavy ions. The doses of irradiation with fission fragments and heavy ions are important for radiation protection, mainly for internal radiation dosimetry, and the situation involving their weighting factor is similar to the situation involving alpha particles. The short paths of heavy ions and fission fragments in organs and tissues, and the ionization density have a heavy influence on their biological effectiveness. Weighting factor equal to 20 that was introduced for alpha particles is also recommended for fission fragments and heavy ions.

Heavy ions are present in the fields of external exposure during air travel at high altitudes and in space exploration. The data on the RBE for heavy ions is extremely limited and mostly based on experiments *in vitro*. The quality of heavy charged particles incident on the human body and dwell in it, varies greatly throughout the particle track. The selection of a single value w_R equal to 20 for all types and energy of heavy charged particles is a conservative estimate and is recommended as sufficient for general use in radiation protection. Perhaps when irradiated in space where these particles make a significant contribution to the dose of human exposure, a more realistic approach should be used.

The concept of the effective dose, E, is determined as a weighted sum of the equivalent doses in tissues:

$$E = \sum_T w_T H_T = \sum_T w_T \sum_R w_R D_{T,R} , \qquad (2.5.20)$$

where w_T – tissue weighting factor T and $\sum w_T = 1$.

The summation is performed over all organs and tissues of the human body, is considered to be sensitive to the induction of stochastic effects. w_T values are chosen to represent the contributions of individual organs and tissues as the total radiation damage on the development of stochastic effects. The unit of equivalent dose is $J \cdot kg^{-1}$, which has a special name "sievert" (Sv). Units of equivalent and effective dose are equal, and therefore it is required to control that the value in question will be clearly understood when specifying the value.

The equivalent and effective dose are not practically measurable quantities. Mathematical phantoms used to estimate the dose in various radiation fields were used to calculate the conversion coefficients for external irradiation. Biokinetic models of radionuclides transfer in the body, reference physiological data, and mathematical phantoms were used to calculate the conversion factor from the radionuclides intake.

The estimates of equivalent doses for a conditional male and a conditional female, and an effective dose for a conditional human are based on the use of anthropometric models (phantoms). The specific phantoms were not identified in the past for calculations, so various mathematical phantoms such as hermaphrodite phantoms MIRD [Snyder et al., 1969], heterosexual phantoms [Kramer et al., 1982], or the phantoms of human body of different ages [Cristy and Eckerman, 1987] were used in practice. Today the reference mathematical phantoms of an adult conditional male and a conditional female are used widely to calculate the equivalent doses in organs and tissues. These phantoms are based on medical tomographic images [Zankl et al., 2005]. They are made in the form of a set of three-dimensional volumetric pixels (voxels). Voxels composing specific organs, have been chosen in order to approximate the weight of a conditional male and a conditional female. In order to ensure the practical approach to the assessment of equivalent and effective doses, transfer factors linking them with physical quantities, such as a stream of particles or kerma in the air for external exposure and intake activity for internal exposure, were calculated for standard radiation reference phantoms.

These models are a numerical representation of a conditional male and a conditional female and are used to calculate the average absorbed dose (*DT*) in an organ or tissue (*T*) from the reference radiation fields at external exposure and from the radioactive decay of radionuclide after their incorporation in the human body. They are used to calculate the factors to transfer to a dose from external radiation fields and to a dose from radionuclides intake. These doses in organs and tissues are multiplied by a weighting factor to obtain equivalent doses in organs and tissues of a conditional male and a conditional female (Fig. 2.36). The reference mathematical phantoms were also designed for children of different ages, as well as for pregnant females and a fetus.

Radiation risk assessment requires a single value of the effective dose for both sexes. Tissue weighting factors listed in Table 2.44 are averaged by gender and age for all organs and tissues including the mammary gland of male and female, the ovaries and testes (gonads: carcinogenic and hereditary effects). This averaging means that the use of such an approach is limited by the evaluation of effective dose and, in particular, cannot be used for individual risk assessment.

Thus, the effective dose is calculated based on the equivalent dose estimated for the organ or tissue (*T*) of a conditional male (H_T^M) and a conditional female (H_T^F) according to the following equation:

$$E = \sum w_T \left[\frac{H_T^M + H_T^F}{2} \right], \qquad (2.5.21)$$

where H_T^M – equivalent dose for an organ or tissue of a conditional male;

H_T^F – equivalent dose for an organ or tissue of a conditional female;

w_T – tissue weighting factor *T*.

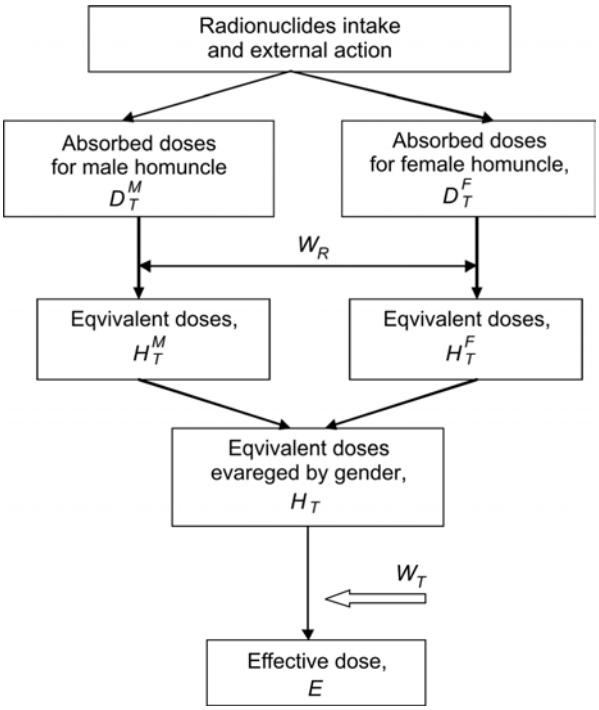


Fig. 2.36. Averaging over a gender for the assessment of effective dose

Similar to the approach used for the organs and tissues of the "others" category, the equivalent dose for the tissues in this category estimated separately for a conditional male and a conditional female are included in equation (2.5.22, 2.5.23) – Fig. 2.36. Equivalent dose for all the tissues of the "others" category is calculated as the arithmetic mean value of the equivalent doses for tissues listed in the note after Table 2.44. The equivalent doses of the tissues of the "others" category for a conditional male (H_{rmd}^M) and a conditional female (H_{rmd}^F) is calculated as (2.5.22, 2.5.23):

$$H_{rmd}^M = \frac{1}{13}\sum_T^{13} H_T^M \qquad (2.5.22)$$

and

$$H_{rmd}^F = \frac{1}{13}\sum_1^{13} H_T^F \,, \qquad (2.5.23)$$

where T – the tissue of the "others" category indicated in Table 2.44;

H_T^M – equivalent dose for an organ or tissue of a conditional male;

H_T^F – equivalent dose for an organ or tissue of a conditional female;

The summation in equation (2.5.22, 2.5.23) is performed by an equivalent dose for the tissue of the "others" category for a conditional male and a conditional female.

The effective dose is based on the average doses in organs and tissues of the human body. Its concept is defined, and its value is estimated for a conditional person. This value is the value that takes into account these conditions of exposure, rather than the

characteristics of a particular individual. In particular, weighting tissue factors have values averaged over a large number of individuals of both sexes. Equivalent doses in the organs and tissues of a conditional male and a conditional female are also averaged. The averaged dose is multiplied by the appropriate tissue weighting factor. The sum of these products provides the effective dose averaged on a gender for a conditional human.

As stated, the equivalent dose and effective dose are not measurable in practice. Therefore, operational values introduced to obtain the conservative estimation of protective variables associated with the exposure or potential exposure of persons under the most conditions of radiation exposure are used to assess the effective dose or the average equivalent doses in tissues or organs.

Operating values used in the medium monitoring include the ambient dose equivalent, H^* (10), and the directional dose equivalent, H' (0.07, Ω).

Operating value for individual monitoring is an individual dose equivalent $H_p(d)$ equal to dose equivalent in the ICRU of (soft) biological tissue at a corresponding depth d below a certain point in the human body. This particular point is usually a place of a personal dosimeter use. Depth d = 10 mm is selected to evaluate the effective dose H_p (10), and individual dose equivalent H_p (0.07) at a depth of d = 0.07 mm is used to assess a dose in the skin, hands, and feet. Depth d = 3 mm has been proposed for the rare cases when it is necessary to monitor the exposure of an eye pupil. However, H_p (3) is measured rarely in practice, and H_p (0.07) can be used for such monitoring.

There are no operating values set for the direct assessment of equivalent or effective dose in internal exposure. In general, different measurements of incorporated radionuclides levels are performed first, and then biokinetic models are used to assess the intake of these radionuclides in the body. Equivalent dose or effective dose values are calculated based on the value of such intake using the reference dose factors (dose per intake unit, Sv Bq^{-1}).

"Health Risks from Exposure to Low Levels of Ionizing Radiation" (2006) and the guidance "Risk Assessment Guidance for Superfund" [US EPA, 1989] requires to consider the fact that external impact is observed only in the presence of ionizing radiation, while the effect on internal organs and tissues continues for a long time even after the termination of radionuclide intake. However, the internal dose for a certain type of tissue and organs appears as the expected equivalent dose ($H_{E,50}$) defined as the equivalent dose for tissue T after 50 years of radionuclides intake.

Furthermore, the specific indicator is determined – the equivalent energy of alpha particles contained in 1 liter of air ($2.1 \cdot 10^5$ J/m^3) (WL), which is used to describe the effects of temporary products of radon radioactive decay (Rn-222) and is defined as combination of temporary products of radon radioactive decay per liter of air, and corresponds to the emission of alpha particles of $1.3 \cdot 10^5$ MeV.

For the cases of the inhalation of radionuclides intake, the dose is determined taking into account the radionuclide concentration in the inspired air (Bq/m^3), respiratory rate (m^3/day (year)), the duration of exposure (day (year)) and the magnitude of the dose conversion factor (DCF) (Sv/Bq), an expected equivalent effective dose (Sv) will be obtained as a result of this calculation.

It was found that the skin exposure route in the case of the inhalatory exposure of radionuclides is not significant, except in the event of exposure to vapors of tritiated water, which is actively absorbed by the skin, in this situation the dose conversion factor for inhalation exposure to tritium includes an adjustment factor that takes into account dermal absorption [Steimer J.L. et al., 2010].

In addition, the concentrations of beta-emitting and/or photon-emitting radioactive contaminants can also cause outdoor exposure. Equivalent effective dose resulting from external impact is calculated using the radionuclide concentration in the air (Bq/m^3), the conversion factor of dose outdoor exposure ((Sv/h) / (Bq/m^3)), exposure time (h).

External impact as a result of submergence in the water contaminated with radionuclides is similar to external impact related to the impact of air contaminated with radionuclides. However, this exposure route is not considered significant due to the shielding effect of water and the short term of impact. The value of the effective equivalent dose is

calculated using a value of the concentration of radionuclide in water (Bq/m^3) corresponding to the magnitude of the dose conversion factor ((Sv/h) / (Bq/m^3)) and the exposure time (h).

Doses assessment at the external sources of radiation exposure is usually performed either on the basis of data of individual monitoring using personal dosimeters worn on the human body surface, or, for example, in the case of retrospective estimates by measuring or assessment H^* (10) followed by the use of the respective transition factors. Operational quantities for individual monitoring are H_p (10) and H_p (0.07). If the personal dosimeter was located in a point on the human body surface, which is representative for its exposure, the value Hp (10) gives an estimate of the value of effective dose with accuracy sufficient to ensure radiation safety subject to low dose irradiation and assuming that there is a uniform irradiation of the whole body.

The assessment system of internal radiation dose due to the intake of radionuclides in the human body is based on the calculation of radionuclide intake that can be considered as operating value when assessing the internal radiation doses. The intake can be assessed either by direct measurements (e.g., monitoring of the radiation emitted from the surface of the entire body of a person or individual organs or tissues) or by indirect measurement (e.g., measurement of urine or feces), or by the measurements of environmental samples followed by the use of biokinetic models. Thereafter, the effective dose can be calculated based on the intake value and using dose factors recommended for a large number of radionuclides. These dose factors are given separately for the persons of different ages and for adults exposed to occupational radiation.

Radionuclides incorporated into the human body irradiate the body tissue for the periods of time determined by the period of their physical half-life and biological retention in the body. Thus, dose increase in tissues may occur for many months or even years after the radionuclide intake to the body. The need to manage the impact of radionuclides and the accumulation of radiation doses for the long periods of time forced to introduce the concept of "expected dose value". The expected dose of incorporated radionuclide is the total dose that would be expected for a certain period of time; expected equivalent dose H_T (τ) in a tissue or organ T is determined as

$$H_T(\tau) = \int_{t_0}^{t_0+\tau} H_T(t)dt \ , \tag{2.5.24}$$

where τ – integration time after radionuclide intake at time t_0.

Thus the value of the expected effective dose is defined as

$$E(\tau) = \sum_T w_T H_T(\tau) \ , \tag{2.5.25}$$

where T – the tissue of the "others" category indicated in Table 2.44.

In order to comply the dose limit, it is recommended that the expected dose was attributed to the period of one year, during which the intake occurred. Expected effective dose from the intakes of radionuclides is used for the prospective assessment of population exposure. In such cases, the period introduced for its calculation is equal to 50 years for adults, and for children of younger and older age groups this dose is estimated before they reach the age of 70.

To assess the expected effective dose $e(\tau)$ [2] at radionuclides intake, the dose factors averaged by gender t are calculated as

$$e(\tau) = \sum_T w_T \left[\frac{h_T^M(\tau) + h_T^F(\tau)}{2} \right], \tag{2.5.26}$$

where w_T – tissue weighting factor T;

$h_T^M(\tau)$ and $h_T^F(\tau)$ – the dose factors of the expected equivalent dose in tissue T over the expected period of time in the body of a male and female respectively.

The summation in equation also applies to the dose factors of the expected equivalent dose in the tissue of "others" category both in male and female.

The annual effective dose for the population is calculated as the sum of the effective dose received within one year from the effect of external radiation and expected effective dose from radionuclides incorporated into the body during the same year. This dose is not obtained by direct measurement of the individual exposure, but is mainly determined by the data of emissions measurements and the researches of environment, lifestyle, and subsequent simulation.

Thus, the dose component associated with radioactive emissions can be estimated by monitoring emissions from current levels, or by predicting the effects of the radiation source at the stage of its construction. Information on the radionuclides ambient concentrations are used in conjunction with radioecological simulation (the analysis of exposure pathways using environmental transport to humans through air, water, soil, sediment, plants and animals) allowing measurement of the external radiation dose and radionuclides intake.

The main objectives of the use of effective dose for the radiation safety of the population are prospective dose assessment to plan and optimize the protection, and retrospective dose assessment to demonstrate the compliance with the dose limits or to compare it with the dose constraints or reference levels.

In the practical implementation of measures to ensure radiation safety, the effective dose is used to manage the risks of stochastic effects of the population. The calculation of the effective dose or the corresponding coefficients of the transition to it for external exposure, and dose coefficients for internal exposure is based on the absorbed dose, weighting factors (w_R and w_T), and reference values of the parameters of the human body, its organs, and tissues. In such a general application, the effective dose does not allow assessing the individual dose, but the assessment for a conditional person under the given conditions of exposure.

The effective dose is intended for use within the assessment of radiation safety and is not recommended for use either for epidemiological assessments, or for detailed retrospective assessments of individual exposure and risk. In such cases it is necessary to use the most appropriate data for biokinetic biological effectiveness and risk factors. Doses in organs and tissues are required to assess the likelihood of cancer induction in exposed individuals rather than effective doses.

The use of effective dose is not allowed for the tissue responses assessment. In such situations, it is necessary to estimate the absorbed dose, taking into account the appropriate RBE values as the basis for any assessment of the radiation biological effects [ICRP, 1991*a*].

Collective dose values [ICRP, 1991*b*] have been introduced in order to optimize the provision of radiation safety, especially in the context of occupational exposure. Such values take into account the exposure of all the individuals comprising a group that was exposed over a given period of time or during a specific operation within the designated radiation zone. In practice, the collective equivalent dose is used only under special circumstances. Collective effective dose, S [ICRP, 1991*b*], is calculated as the sum of all the individual effective doses for a certain period of time or during a specific operation. Special name used for the collective effective dose – "man-sievert". The comparison of the different measures of radiation protection and operational scenarios in the form of evaluation of the relevant expected individual and collective effective dose is performed in the course of the optimization process.

Collective effective dose, S, is based on the assumption of a linear non-threshold dependence of "dose – effect" ratio for stochastic effects. This basis makes effective doses additivity possible.

The collective effective dose is a tool to optimize and compare radiation technologies and protection procedures. Collective effective dose is not intended as a tool for epidemiological studies and cannot be used to predict a risk. This is explained by the assumptions engaged into the calculation of collective effective dose (e.g., the use of the linear non-threshold model), which introduce great biological and statistical uncertainties. This applies in particular to the estimated number of deaths from cancer, made on the basis

of the collective effective doses due to the minor exposure of large populations that do not make sense and cannot be avoided.

To avoid improper summation, for example, the summation of very low individual doses over long periods for the residents of large geographic regions, it is necessary to impose restrictions on the use of the collective effective dose. It is necessary to specify the range of summable doses and the time required for their summation. The collective effective dose consisting of the sum of individual effective doses in the range of E_1 - E_2 is defined as

$$S(E_1, E_2, \Delta T) = \int_{E_1}^{E_2} E(\frac{dN}{dE})_{\Delta T} dE, \quad (2.5.27)$$

where $(\frac{dN}{dE})_{\Delta T}$ – means the number of individuals exposed to effective dose from E to $E + dE$ over a time period ΔT.

When individual doses range captures the several orders of magnitude, the distribution should be characterized by its separation over several individual dose ranges, each of which covers not more than two or three magnitudes; and then consider population size, the average individual dose, and uncertainty separately for each range. When the collective effective dose would be less than the value inverse to the corresponding risk of damage, the risk assessment should note that the number of excess cases of biological effects is most likely equal to zero.

Thus, to assess the product risk, the results of exposure assessment should be represented as the radionuclides levels taken in through inhalation or oral routs, the levels and duration of exposure for external exposure, the expected equivalent effective dose values for each of the radionuclides and the ways of their intake [Steimer J.L. et al., 2010]. When assessing the exposure, it is important to form a complete exposure scenario including the determination of the frequency, duration, and routes of exposure to radiation factor, the size and nature of the exposed population with the assessment of exposure routes, as well as to establish a level of exposure to the radiation risk factor.

"Dose-response" dependency relation assessment

In accordance with the guidance on risk assessment [US EPA, 1989] the assessment of "dose – response" relation is aimed at quantitative assessment of the radiological information and characteristics of the relationship between dose of contaminant and incidence rate of harmful effects in the exposed population. Health responses are developed due to the accumulation of energy corresponding to the radiation dose in the sensitive tissues. Theoretically, any dose of radiation is potentially capable to produce the development of harmful health effect.

The most serious biological effects of radiation exposure can be grouped into two main categories:

– deterministic effects (harmful tissue reactions), mostly related to the death or malfunction of cells at higher doses of radiation;

– stochastic effects, i.e. cancer and inherited diseases associated with the development or cancer in exposed individuals due to mutations in somatic cells, or with an inherited disease in the offspring of exposed persons due to mutations in the reproductive (functional) cells.

The following biological radiation effects in embryo and fetus as well as non-cancerous diseases are also considered.

The type of effect and the probability of its development fully depends on the dose of ionizing radiation. It is believed that the non-threshold linear model is most appropriate to describe the relationship between exposure to low doses of ionizing radiation and the incidence of solid cancers induced by ionizing radiation. However, although the linear non-threshold model remains a science-based element of a practical system of radiation protection, the information that will confirm the hypothesis underlying this model can hardly be collected [NCRP, 2001].

When making practical conclusions concerning the linear non-threshold model, potential problems were considered associated with information on cellular adaptive response, in the relative increase of spontaneous DNA damages and DNA damages caused by exposure to small doses, as well as in the existence of cellular phenomena of induced genomic instability and bystander effect after irradiation [Publication 99, ICRP, 2005]. It is recognized that these biological factors, along with the possible promotion of neoplastic process with prolonged exposure, and immunological phenomena may affect the radiation risk of cancer, but the currently available uncertainty mechanisms of tumorigenic effects of the above processes are too great for practical judgments. The Commission also notes that since the assessment of the nominal rates of cancer risk are based on direct epidemiological data on the person, any changes associated with the above-mentioned biological mechanisms have already been taken into account in these assessments. The uncertainty of the information on the role of these processes in changes in the risk of cancer will continue until their relationship with the development of cancer in vivo will be proved and until the knowledge of the dose dependence of the cellular mechanisms involved in these processes will appear.

According to some authors, the development of a specific form of "dose – mutational effect" relation depends on the biological system under consideration, the final mutation effect of the radiation quality (LET) and dose rate [Thacker et al., 1992], and the general form of the "dose – mutational effect" relation has a linear-quadratic form at low LET and tends to linearity at LET increase. For low LET radiation, dose rate reduction usually lowers the frequency of induced genetic/chromosomal mutations in somatic and germ-line cells of mammals. The maximum reduction ratio on dose rate is typically equal to 3–4 doses, but may be somewhat higher for chromosomal aberrations in human lymphocytes. Quite stable relationship between RBE and LET for the induction of mutations have also been shown for the maximum RBE levels of about 10–20, which is usually observed in the LET range of 70–200 keV μm^{-1}.

It was found that the higher the dose of radiation, the higher levels of health risks are associated with it; the lower the level of exposure, the less the probability of adverse health responses development. The above mentioned can be explained by the fact that any single flow of ionizing radiation has the potential to cause cellular damage. However, it is believed that if only one ionizing particle passes through the DNA cells, the chances of the DNA damage of these cells are proportionally lower than, if 10, 100, or 1000 ionizing particles have damaged a cell. In this regard, there is no reason to expect more pronounced effects under exposure to low doses due to the physical interaction of radiation and cellular DNA. Based on the results of biological studies, it is suggested that cell damages do not require direct contact between ionizing radiation and the cell. This is explained by the fact that the previously damaged cell interacts with other cells through, e.g., chemical signals. Therefore, there are opinions that health effects will be more severe than it was expected as a result of extrapolation of responses observed at the high doses of radiation exposure even under the conditions of low-dose radiation.

Based on the assessment of the biological data it is considered that the graphical representation of "exposure – response" relation will have a linear non-threshold form both at low and the lowest possible doses and thus the impact will create health risks under these conditions. At the same time, some researchers suggest that the results obtained using the linear non-threshold models exaggerate the level of effects on the part of health when exposed to ionizing radiation. There is a hypothesis that the dose dependence of the cancer induction has superliner component at low doses (i.e "dose – effect" relation has a bimodal form), so the risk forecast at small doses range on the basis of observations made in the range of high doses leads to a substantial underestimate of the true risk. This hypothesis is often cited in connection with the reports of unusual epidemiologic or experimental surveillances.

The relationship between mutation and disease progression is the most simple and predictable for Mendelian diseases [Hoffman D.A. et al., 1989; Suskov I.I. et al., 2006; Zasukhina G.D. et al., 2006; Gaziev A.I., 2013]. In case of the assessment of the health risks associated with exposure to radionuclides, it is possible to use the models developed for chemical contaminants within the parameters of radioactive decay.

The increasing incidence of cancer and mortality occurrence at the increased levels of ionizing radiation is set for many types of cancer both for humans and laboratory animals. Studies involving people exposed to external and internal radiation stated an increase of cancer occurrence proportional to an increase of the ionizing exposure level.

The risk levels for the conditions of exposure to low doses for a long time are determined by the extrapolation of the results obtained by the studies of high doses under acute exposure. The malignant tumors of different localization often appear after radiation exposure, usually in 10–35 years [UNSCEAR 1982, 1988].

Thus, when analyzing the "dose – response" relation with respect to the radiation factor of the product it is advisable to quantify the radiological information and to establish the characteristics of the relation between the radiation contaminant dose and the frequency of harmful stochastic and deterministic effects occurrence in the exposed population.

Risk characterization

The integration of data on the risk levels associated with various contaminants and intake routs is performed at the stage of the risk characterization.

Risk assessments specialists should analyse all the used materials concerning their adequacy to validate the results and the possibility of calculations repeat, assess the reasonableness of the assumptions made during the analysis, the parameters and factors of dose conversion used in the simulation.

The set level of risk using the value of the equivalent dose (Sv) and the corresponding risk factor (risk/Sv) cannot be applied in relation to the general population without regard to factors taking into account gender and age, for each organ and tissue receiving radiation dose. This information can be used to determine the slope factor, which characterizes the degree of increase in the incidence of cancer per unit of a radionuclide intake. Slope factor should be multiplied by the amount of inhaled activity for each of the radionuclides to establish the risk level associated with the inhalation intake of radionuclides in accordance with the *Risk Assessment Guidance for Superfund*.

Risk levels for ingestion conditions are the product of the slope factor for ingestion and ingestion values for each radionuclide.

The calculation of the risk level for the conditions of external influence through the air is carried out by multiplying the relevant slope factors by the concentration of radionuclides in the air (Bq/m^3) and the exposure time.

Integrated Risk Information System (IRIS) contains the database of the values of the slope factors of radionuclides for all the major intake routes, as well as the materials establishing these values.

The sum of the individual radionuclides risks and the ways of their intake is considered as the lifetime risk of the total exposure. At that, the risks summation in different intake routs takes into account the expert opinions, as the intake of maximum radionuclide concentrations through all possible routes to the body of one individual is actual unlikely. Due to the lack of data on mutations in the germ cells due to the exposure to ionizing radiation, all forecasting methods of the health disorders risk level had indirect nature since the mid –1950s [Health Risks from Exposure to Low Levels of Ionizing Radiation, 2006]. The method of double doses is one of such method used from the beginning of the 1970s. The concept of the double dose was formulated in the 1950s. Active method for the risk calculation was used in 1972. The double dose method is used to predict the risk of genetic diseases in children whose parents were exposed to radiation, and is based on naturally occurring genetic diseases [Hoffman D.A., 1989].

The double dose method allows calculating the expected increase in the health responses frequency per a unit of ionizing radiation dose relating to the background levels of morbidity of a certain class of diseases. Double dose (*DD*) is a dose of ionizing radiation, at which the number of mutations will be equal to the number of spontaneous mutations in a single generation, and is expressed as the relation of the mean frequency of spontaneous mutations to mutations induced by ionizing radiation for one set of genes:

DD = the average frequency of spontaneous mutations / the average frequency of mutations induced by ionizing radiation

The ratio 1/*DD* is considered as relative mutation risk (RMR) per a unit of ionizing radiation dose. Thus, the smaller the value of a double dose, the higher the relative mutation risk and vice versa. Until recently, when using the double dose method, the risk was considered as the product of two variables – the background morbidity *P* and 1/*DD*:

$$Risk = P(1/DD), \quad (2.5.28)$$

where *P* – background morbidity;

1/*DD* – mutation risk (RMR) per a unit of ionizing radiation dose.

This equation is based on the equilibrium theory, in accordance with this theory, the gene mutation frequency (frequency of health response) in a population is stable due to the balance between the frequency of spontaneous mutations in each generation and the frequency of their elimination as a result of natural selection. Equilibrium is disturbed when the number of mutations in each generation increases due to radiation exposure. The degree of increase in the mutations frequency and the time necessary to reach a new equilibrium depends on the fraction of mutations induced by ionizing radiation, the intensity of natural selection, the type of genetic diseases, and the number of consecutive generations exposed to radiation. It should be noted that there is equilibrium between the frequency of mutations, and the frequency of their elimination for the generation not subjected to radiation; the value *P* in the equation represents the equilibrium frequency of the disease, and the product of *P* and 1/*DD* is the expected increase in the diseases incidence under the condition of a new equilibrium [The Effects on Populations of Exposures to Low Levels of Ionizing Radiation, 1988]

The establishment of risk for different classes of genetic diseases

Equation (5.2.28) is applicable for autosomal dominant diseases, since the relationship between mutation and disease for this class is simple. For this type of diseases, it is considered that this increase will be expressed as *x* % increase in the incidence rate of this disease in an increase of the mutation frequency by *x* % in each generation under the conditions of a new equilibrium. Until recently, the calculation of risk for any generation after radiation (postradiation) is performed using the reverse conversion of values of the proposed new equilibrium using certain assumptions. If only one generation was exposed to ionizing radiation, a transient increase in the frequency of mutations, which will be followed by a significant reduction to the previous equilibrium values, is observed only in the first generation [Hoffman D.A. et al., 1989].

The method of risk level prediction for diseases associated with X-chromosome is similar to that described for autosomal dominant diseases.

Autosomal recessive diseases requires a risk calculation taking into account the fact that the recessive mutations occur under the heterozygous state, and the disease does not develop in the children of the first generation.

The multifactorial diseases are a complex situation, since the relationship between mutation and disease development is more complex, and the establishment of risk depends on the type of model. According to the results of improvement conducted in recent years, the above-described concept allows a direct assessment of the impact on the increase in the number of mutations for all classes of genetic diseases in any generation exposed to radiation of only one or a several consequent generations. *MC* indicator – the class of disease and the rate of mutation – specific to generation after radiation was introduced in equation:

$$Risk = P(1/DD)MC. \quad (2.5.29)$$

The establishment of the mutation indicator value is performed as follows: if *P* – the prevalence of the disease to an increase in the mutations frequency and ΔP – change in the

value P due to the change in the value m (the frequency of spontaneous mutations) – Δm. Equation (2.5.30) forms the determination of MC value.

$$\frac{\Delta P}{P} = \frac{\Delta m}{m}\frac{\Delta P / P}{\Delta m / m},$$

$$MC = \frac{\Delta P / P}{\Delta m / m}, \qquad (2.5.30)$$

where $\Delta P/P$ – relative change in the morbidity rate, and $\Delta m/m$ – relative change in the mutation frequency.

In other words, MC determines the relative change in the morbidity rate per a unit of the relative change in the frequency of mutations. It should be noted that the MC value is used only in a change in mutation frequency, and that mutation rate does not match the genetic component of diseases and is a numerical expression of the sensitivity of genetic component of the disease to increased mutation frequency. MC value for such diseases will be lower than for diseases fully associated with genetic abnormalities if the disease has only partial genetic nature, and because a genetic component will response to increase in the mutation frequency. MC is not applicable when the disease is associated only with environmental factors. To transfer the cancer risk assessments established for high doses and dose rates, dose and dose rate efficiency factor (DDREF) is introduced for the risks corresponding to low doses and low dose rates. As a result, the cancer risk at low doses and dose rates was assessed by combining these studies in the field of epidemiology, animal experiments, and cell biology as the risk reducing factor known as DDREF. The recommendations as of 1990 state that the value DDREF equal to 2 established based on the "dose – effect" relation obtained in the experiment, the LSS study, and based on the results of probabilistic uncertainty analysis should be used in the field of radiation protection.

It is necessary to carry out averaging over gender in the course of the risk characterization, as some radiation cancers are specific for gender, and for many other cancers, gender is the main modifying factor of the radiation risk [ICRP, 1991*a*].

In addition, the measurement of risk transfer between populations is important. If two populations differ from each other by the prevalence of the known modifying factors of radiation risk, it can be expected that the response to radiation of this populations will be different. However, even if there is no such information, it is difficult to transfer the estimates of radiation cancer risk in certain localizations in the human body from one population to another, if the relevant background levels of cancer morbidity in these populations are different.

Radiation harm is one of the indicators used in the stage of risk characterization. The harm for tissue T is defined as

$$DT = (R_{F,T} + q_T R_{NF;T}) l_T, \qquad (2.5.31)$$

where R_F – the rated risk of lethal disease,

R_{NF} – the rated risk of nonlethal disease,

q – weighting factor (from 0 to 1) reflecting the decline in the quality of life due to a serious disease,

l – the average life time loss due to the disease compared with the normal duration of life expressed as a ratio to the average for all cancers.

The factor of life quality reduction is a lethal function (k) of the disease and the subjective judgment about pain, anguish, and the side effects of treatment. Since the disease data are used, the factors of nominal risk are expressed as:

$$R_I = R_F + R_{NF}. \qquad (2.5.32)$$

The harm is calculated as

$$(k_T R_{I;T} + q_T (1 - k_T) R_{I;T}) l_T = R_{I;T} (k_T + q_T (I - k_T)) l_T . \qquad (2.5.33)$$

Thus, the damage assessment is expressed as

$$R_F + k(1-k)R_F / k)I \text{ , that is equal to } R_F(2-k)I \text{ ,} \quad (2.5.34)$$

where $R_{NF} = (1-k)R_F / k$.

Since cancer patients usually feel the deterioration of their quality of life, it is believed that cancer should be assessed not only by mortality but also by pain, anguish, and any side effects of cancer treatment. q_{min} coefficient used for nonlethal cancers in the assessment of changes in the mortality ratio, qT, is introduced to obtain such a factor assessment. The formula for q_T calculation is given as

$$q_T = q_{min} + k_T(1-q_{min}), \quad (2.5.35)$$

where k_T – mortality ratio;

q_{min} – minimum weight factor for nonlethal cancers.

q_{min} value was set at 0.1 (in most cases the result is not very sensitive to the choice of this value). In fact, q_{min} change affects the calculation of harm in the relation to nonlethal cancers. Therefore, the parameters for highly lethal cancers such as lung and gastric cancer poorly depend on q_{min}, while the parameters concerning nonlethal cancers such as breast or thyroid gland cancer are highly dependent on this value.

However, the amendment on q_{min} is not applied for skin cancer, as radiogenic skin cancer almost always refers to the basal cell type that is usually associated with very small pain, anguish, or the consequences of treatment.

The relative loss of life years is an important component in the calculation of harm. The average number of life years lost due to this cause of death is calculated for each gender and for each composite population averaged by age at the exposure time and the subsequent attained age of the remaining lifetime.

The assessment of risk level acceptability should be considered as the results of the health risk characterization of the radiation products factor, and its classification should be considered to validate decisions on risk management in the case of an unacceptable level. In this case, it is also advisable to present the results of a quantitative assessment of population health risk associated with the exposure of radiation products factor on health.

The assessment of uncertainties

Uncertainty analysis is an important and integral part of the assessment of the radiation health risk of products and allows making more accurate and reliable conclusions on the magnitude of the acceptable risk level, which in turn will form the basis for the development and adoption of the most effective measures to reduce radiation health risks associated with the use of a particular products.

Uncertainties accompany all stages of the assessment of risk associated with exposure to ionizing radiation and include the following features of procedures for radiation health risk assessment.

In accordance with the "Background Information Document" [EPA EIS, 1989], the extrapolation of the data obtained in studies of high doses at lower exposure levels is the main source of uncertainty in determining the risk levels for the low-level conditions of ionizing radiation exposure.

Moreover, the uncertainties can be associated with the processing of data used to determine exposure levels and dose calculation; assumptions made during the exposure assessment phase; quality monitoring; model selection, and its parameters, etc..

The exposure parameters, selection of model type and its parameters can be the sources of uncertainty. Monte Carlo method is more often used to estimate uncertainties in the framework of radiation risk assessment [NCRP, 1984]. The uncertainty associated with the level of confidence that can be attributed to the value of the parameter or model prediction, which is an important factor in the extrapolation procedures. In this regard, the variability of

individual parameters and measurement accuracy is also of great importance. The accuracy of measurements and conclusions will decrease with doses reduction and the increase of system complexity. Variability is associated with quantitative differences between the characteristics of the individual members of the considered population. All these aspects are taken into account in the development of the model and expert judgments rendering.

The lack of certainty or accuracy in dosimetric models is different for the various parameters and circumstances in certain situations. Therefore, it is impossible to give the uncertainty values for all models, despite the fact that the assessment of these uncertainties is an important part of the work on the creation of these models. However, the assessment of uncertainties can be required in special cases; the approaches to its implementation are described in detail in a number of publications [ICRP, 1994, 2005*d*; Goossens et al., 1997; Bolch et al., 2003; CERRIE, 2004; Farfan et al., 2005]. The uncertainties of internal radiation dose assessments including the biokinetics of radionuclides exceed the uncertainty assessments at external radiation. The degree of uncertainty is different for different radionuclides. The statistical uncertainty presented in the form of confidence intervals or statistical probability distributions is the most obvious.

When the assessment based on data of specific exposed population is applied to other populations or other sources of radiation, it introduces additional uncertainty. The differences between the radiation sources can produce uncertainty having a random or systematic error in the assessments of doses for the initial or secondary population.

The transfer of risk assessments between populations sets a particularly difficult problem for the risk assessment for those cancer localities, the background morbidity levels of which are very different between these two populations.

The other major sources of uncertainty include the possible association of exposure to other cancer risk factors including the history of smoking for lung cancer and reproductive history for breast cancer in female. This problem is similar to the problem of risk assessments transfer between populations, in which the interaction can be represented as an uncertain linear combination of the additive and multiplicative models.

Another source of uncertainty is the relative biological effectiveness concerning high-energy photons, the radiation of different quality, including medical x-ray radiation within the energy range of 30–200 keV, electrons, neutrons, protons, and alpha particles. Another aspect of uncertainty is the possible presence of low-dose threshold when assessing the risk of cancer.

Thus, the information and analytical review of the criteria and methodological approaches of public health risk assessment when exposed to radiation risk factor showed that the general assessment scheme does not differ from other hazards and includes the stages of hazard identification, the assessment of "dose – response" relation, exposure assessment and risk characterization.

In the products hazard identification in the case of radiation risk assessment, it is required: to identify the source of ionizing radiation, to determine risk cohorts, set the harmful effects on health.

When analyzing the "dose – response" relation with respect to the radiation factor of the product it is advisable to quantify the radiological information and to establish the characteristics of the relation between the radiation contaminant dose and the frequency of harmful stochastic and deterministic effects occurrence in the exposed population.

The results of exposure assessment should be represented as the radionuclides levels taken in through inhalation or oral routs, the levels and duration of exposure for external exposure, the expected equivalent effective dose values for each of the radionuclides and the ways of their intake. When assessing the exposure, it is important to form a complete exposure scenario including the determination of the frequency, duration, and routes of exposure to radiation factor, the size and nature of the exposed population with the assessment of exposure routes, as well as to establish the level of exposure to the radiation risk factor.

The assessment of risk level acceptability should be considered as the results of the health risk characterization of the radiation products factor, and its classification should be considered to validate decisions on risk management in the case of an unacceptable level.

In this case, it is also advisable to present the results of a quantitative assessment of population health risk associated with the exposure of radiation products factor on health.

Existing methodological approaches to the assessment of the products radiation risk for health after adaptation (for example, in relation to the imported products) can be used in the products risk assessment associated with the impact of various factors on public health.

The analysis of the recommendations of the Codex Alimentarius Commission, FAO, WHO on the safety assessment of radioactively contaminated food products

According to the FAO/WHO, the background levels of radionuclides content in food products vary and depend on many factors, including the type of food and the geographic region where this product was produced.

The most common radionuclides in food are ^{40}K, ^{226}Ra and ^{238}U.

The levels of 40K content, for example, in milk can be equal to about 50 Bq/l; the levels may reach several hundred Bq/kg in meat, bananas and other products rich in potassium. Other naturally occurring radionuclides are determined at lower levels and are the decay products of uranium and thorium.

Food contamination with radionuclides can occur through their contact with the surface of fruits and vegetables or the contact of animal feed and air or rain water and snow [FAO/WHO, 2011].

The control of food radioactive contamination under normal conditions is carried out mainly to prevent radioactive contamination in the case of nuclear accidents leading to the wide distribution of radionuclides; the monitoring of their content is carried out after the event in order to avoid or minimize the development of the harmful responses of health. The Principles of control measures for these two types of events are different.

Since emergencies related to the leakage of radioactive materials are characterized by a greater scale of territorial impact and the affected population, the WHO specialists consider more important to develop guiding documents on the monitoring of the radiation contamination of food in emergencies and conditions based on the principles of risk assessment, however, these guiding documents differ from those used for ordinary conditions [WHO, 1998*b*].

Codex Alimentarius Commission developed the recommended levels of radionuclides content in food products; these recommendations "characterize the maximum level of substance content in food or feed recommended by the Commission and acceptable to the conduct international trade. In case of the excess of the recommended levels the government takes decision on the opportunities and conditions of these products distribution within a particular territory and within its jurisdiction [Fact Sheet, 2011].

Prior to the accident at the Chernobyl NPP in 1986, the Codex Alimentarius had no complete international guidance on the assessment of food contaminated during such events.

The first version of the recommended levels of radionuclides content in food products was adopted by the Codex Alimentarius Commission in 1989. The values of the recommended levels have been developed by the Codex Committee on Food Additives and Contaminants (CCFAC) on the basis of materials prepared jointly with Food and Agriculture Organization (FAO), World Health Organization (WHO) and the International Atomic Energy Agency (IAEA).

The recommended levels of ^{90}Sr, ^{131}I, ^{134}Cs, ^{137}Cs, ^{239}Pu and ^{241}Am content in food products were developed in 1987 and are assumed to be used in international trade as indicative levels for the assessment of the need for control measures [Fact Sheet, 2011].

According to the results of the Commission meeting in 1987, it was decided to use the developed values of the recommended levels of radionuclides content in food in relation to ready-to-use food products, and to develop special requirements for products consumed in small volumes (spices) [Fact Sheet, 2011].

In accordance with the "Guidelines for application after widespread radioactive contamination resulting from a major radiation accident" [WHO, 1988], the value of derived intervention level (DIL) was introduced for food, i.e., the level of radiation factor exposure,

the excess of which requires specific protective measures. The derived intervention level inversely depends on the consumption of foods and the factor considering the dose per intake unit, and directly depends on the value of the reference dose:

$$DIL = \frac{RLD}{md}, \qquad (2.5.36)$$

where *RLD* – reference dose (reference intervention level) (Sv/year);

m – the level of food consumption (kg/year);

d – dose per consumption unit (Sv/Bq).

The analysis of the food intake levels for the population of 140 countries over the world on a number of food groups identified the need for the establishment of the values of intervention levels for representative consumption volumes, which, according to FAO data amounted to 550 kg/year (water consumption is not included) and 200 kg/year for children, a representative level of water flow – 700 l/year (for adults) [WHO, 1998*b*].

The set of radionuclides allocated to the objects of the environment varies depending on conditions and can include both long-lived and short-lived radionuclides. ^{90}Sr, ^{131}I, ^{134}Cs, ^{137}Cs, ^{239}Pu are the most significant radionuclides contaminating food in terms of emergencies according to the WHO documents as of 1988 [WHO, 1998*b*].

Radiation dose in radionuclides intake with food depends on the products intake rate and on such variables as age, metabolic parameters, body weight.

The development of special factor taking into account the dose value per an intake unit is considered necessary in the establishment of the radiation dose for a particular age group.

The recommended equivalents of expected effective or organ (thyroid gland) doses per an intake unit (Sv/Bq) for three age groups are presented in Table 2.45.

Table 2.45

Age-specific dose values per unit of food consumption for different radionuclides (Sv/Bq) [WHO, 1998b]

Radionuclide	Age		
	1 year	10 years	Adults
^{90}Sr	$1.1\cdot10^{-7}$	$4.0\cdot10^{-8}$	$3.6\cdot10^{-8}$
^{131}I	$3.6\cdot10^{-6}$	$1.0\cdot10^{-6}$	$4.4\cdot10^{-7}$
^{134}Cs	$1.2\cdot10^{-8}$	$1.2\cdot10^{-8}$	$2.0\cdot10^{-8}$
^{137}Cs	$1.0\cdot10^{-8}$	$1.0\cdot10^{-8}$	$1.3\cdot10^{-8}$
^{239}Pu	$2.4\cdot10^{-6}$	$1.4\cdot10^{-6}$	$1.3\cdot10^{-6}$

In this case, all the radionuclides based on the value of the "dose per intake unit" factor were divided into two classes: the first – with a high value of the factor (10^{-6} Sv/Bq) (e.g., ^{239}Pu), the second – with a low value of the factor (10^{-8} Sv/Bq) [WHO, 1998*b*].

The establishment of intervention levels for radionuclides was performed taking into account doses and the following input data:

– the *maximum annual equivalent* of the expected effective dose – 5mSv (the maximum equivalent of the expected dose – 50 mSv for a thyroid gland);

– the *normalized hypothetical set of products* based on representative values higher than the average consumption levels of the various types of food in different countries;

– *two dosimetric indicators for radionuclides* (the first for actinides, the second for other radionuclides).

Since the radiation dose from a particular radionuclide for children can greatly exceed the dose established for adults, separate regulatory values have been developed for children on a milk diet.

The regulatory values of intervention levels for seven groups of food and drinking water are presented in Table 2.46.

Table 2.46

Normative values of intervention levels (Bq/kg)

Product	Radionuclides class	
	with the value of the "dose/intake unit" factor 10^{-6} Sv/Bq	with the value of the "dose/intake unit" factor 10^{-8} Sv/Bq
Grains	35	3500
Roots and tubers	50	5000
Vegetables	80	8000
Fruits	70	7000
Meat	100	10000
Milk	45	4500
Fish	350	35000
Drinking water	7	700

Regulatory values developed for the child population based on the expected level of annual milk consumption equal to 275 kg of milk and 275 kg of water, and based on the "dose per intake unit" factor for children are presented in Table 2.47.

The values set for drinking water are applicable both for adults and for children, except for ^{90}Sr, this indicator amounts to 160 Bq/l for children.

Table 2.47

Regulatory intervention levels for the child population (Bq/l)

Radionuclide	Level value
^{90}Sr	160
^{131}I	1600
^{137}Cs	1800
^{239}Pu	7

In case of the contamination of several types of food with several types of isotopes, "specific" intervention levels can be developed according to the formula providing the non-exceedance of a total reference level of radiation dose (5 mSv):

$$\sum_i \sum_f \frac{C(i,f)}{DIL(i,f)} \le 1, \qquad (2.5.37)$$

where $C(i, f)$ – the specific radioactivity of the isotope i in the product f;

$DIL(i, j)$ – the level of isotope i intervention in the product f.

Regulatory levels were used for the moment of consumption and form of a food product in which it is consumed.

The increase in the penetration level of 10 was recommended for products with a high level of consumption (root crops and tubers), thus, the values of intervention levels for radionuclides of the first and second class amounts to 500 and 50,000 Bq/kg, respectively [WHO, 1998*b*].

In accordance with the request of the International Atomic Energy Agency (IAEA) (2002), the list of assessed radionuclides has been expanded and method for radiation doses estimation was improved, including:

– the expansion of the list of radionuclides to 20 (^{3}H, ^{14}C, ^{99}Tc, ^{35}S, ^{60}Co, ^{89}Sr, ^{90}Sr, ^{103}Ru, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U, ^{134}Cs, ^{137}Cs, ^{238}Pu, ^{239}Pu, ^{240}Pu, ^{144}Ce, ^{192}Ir, ^{241}Am) separated in accordance with the value of the dose per intake unit for 4 groups; these radionuclides were chosen as the most important in relation to their intake with food;

– after the revision, the intervention level of food withdrawal became equal to 1 mSv/year (indicator was equal to 5 mSv in accordance with CAC/GL 05-1989 "Practical Principles for Risk Analysis in the Field of Food Safety for Application by Governments");

– the recommended levels for products consumed in small amounts (eg., spices) and having small portion in the diet, were increased by 10 times;

– in accordance with the assumption that 10% of the diet is the imported products, the value of the portion factor of food products import amounts to 0.1.

The revised and currently effective recommended levels of radionuclides content in food products were approved in 2006 in accordance with the «Fact Sheet on Codex Guideline Levels for Radionuclides in Foods Contaminated Following a Nuclear or Radioilogical Emergency" (2011).

Recommended level (Bq/kg) is established according to the following formula

$$GL = IED / (M \cdot ipf \cdot e_{ing}), \quad (2.5.38)$$

where *IED* – intervention dose level for withdrawal (mSv/year);

M – the level of food consumption (kg/year);

IPF – the factor of import food products portion accountance from the zones of radioactive contamination;

e_{ing} – coefficient taking into account received dose (dose per intake unit mSv/Bq) (Table 2.48).

Table 2.48

The coefficients of received dose used to establish the recommended levels of radionuclides content in food

Radionuclide	Coefficient (mSv/Bq)	
	Child population	Adult population
^{238}Pu	$4.0 \cdot 10^{-3}$	$2.3 \cdot 10^{-4}$
^{239}Pu	$4.2 \cdot 10^{-3}$	$2.5 \cdot 10^{-4}$
^{240}Pu	$4.2 \cdot 10^{-3}$	$2.5 \cdot 10^{-4}$
^{241}Am	$3.7 \cdot 10^{-3}$	$2.0 \cdot 10^{-4}$
^{90}Sr	$2.3 \cdot 10^{-4}$	$2.8 \cdot 10^{-5}$
^{106}Ru	$8.4 \cdot 10^{-5}$	$7.0 \cdot 10^{-6}$
^{129}I	$1.8 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$
^{131}I	$1.8 \cdot 10^{-4}$	$2.2 \cdot 10^{-5}$
^{235}U	$3.5 \cdot 10^{-4}$	$4.7 \cdot 10^{-5}$
^{35}S	$7.7 \cdot 10^{-6}$	$7.7 \cdot 10^{-7}$
^{60}Co	$5.4 \cdot 10^{-5}$	$3.4 \cdot 10^{-6}$
^{89}Sr	$3.6 \cdot 10^{-5}$	$2.6 \cdot 10^{-6}$
^{103}Ru	$7.1 \cdot 10^{-6}$	$7.3 \cdot 10^{-7}$
^{134}Cs	$2.6 \cdot 10^{-5}$	$2.0 \cdot 10^{-11}$
^{137}Cs	$2.1 \cdot 10^{-5}$	$1.3 \cdot 10^{-5}$
^{144}Ce	$6.6 \cdot 10^{-5}$	$5.2 \cdot 10^{-6}$
^{192}Ir	$1.3 \cdot 10^{-5}$	$1.4 \cdot 10^{-6}$
^{3}H	$1.2 \cdot 10^{-7}$	$4.2 \cdot 10^{-11}$
^{14}C	$1.4 \cdot 10^{-6}$	$5.8 \cdot 10^{-7}$
^{99}Tc	$1.0 \cdot 10^{-5}$	$6.4 \cdot 10^{-7}$

The following assumptions were made when establishing the recommended levels:

– the value of the intervention dose level for withdrawal – 1 mSv/year;

– the consumption level for adult population – 550 kg/year;

– the level of food and milk consumption by children – 200 kg/year;

– imported products amount to 10% of the human diet, the factor of import food products portion accountance amounts to 0.1.

It is theoretically and practically shown, that the use of recommended levels would not result in the exceedance of the radiation dose at the intake with food 1 mSv.

The values of the recommended levels of radionuclides content in food products are presented in Table 2.49.

Standard levels for radionuclides in food and their values are based on the general principles of radiology and the experience of the existing international and national standards for the control of radionuclides in food.

The levels of human exposure resulting from the consumption of food containing radionuclides at the levels specified in Table 2.49 were evaluated both for children and for adults, and in respect of the permissible dose. The norms of food consumption and food consumption rates are estimated in order to assess the impact on the population and public health risks from the intake of radionuclides with food. It is assumed that the adult population consumes 550 kg of food per year; the consumption of baby food and milk during the first year of life amounts to 200 kg [Luykx F., 1990; US DoHHS; 1998]. The most conservative values of factors specific to radionuclides and different age groups under the conditions of the intake into the body, i.e. the ratio of the chemical forms of radionuclides with the greatest absorption from the gastrointestinal tract and remaining in the tissues of the body are taken in accordance with the publication by the International Atomic Energy Agency (1996).

Table 2.49

The recommended levels of radionuclides content in food products [Codex Stan 193-1995]

Name	Radionuclides	The value of the recommended level, Bq/kg
Baby food	^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Am	1
Baby food	^{90}Sr, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U	100
Baby food	^{103}Ru, ^{35}S, ^{60}Co, ^{89}Sr, ^{134}Cs, ^{137}Cs, ^{144}Ce, ^{192}Ir	1000
Baby food	^{3}H, ^{14}C, ^{99}Tc	1000
Other	^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Am	1
Other	^{90}Sr, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U	100
Other	^{103}Ru, ^{35}S, ^{60}Co, ^{89}Sr, ^{134}Cs, ^{137}Cs, ^{144}Ce, ^{192}Ir	1000
Other	^{3}H, ^{14}C, ^{99}Tc	10000

In addition, a number of documents of the Codex Alimentarius Commission are dedicated to the issue of exposed products assessment, for example, in order to reduce the microbial contamination of food, increase the duration of the storage of perishable products: CODEX STAN 106-1983 «General Standard for Irradiated Foods» (2003) and «Code for Practice for Radiation Processing of Food (CAC/RCP 19-1979)».

The purpose of monitoring of the food exposed to ionizing radiation is to ensure the safety and accuracy of the radiation exposure, the development of the system of specific documentation for this kind of food, as well as ensuring the compliance of such products at its entry into the international market, compliance with radiation processing and labeling standards.

The radiation processing of food products uses:

– ^{60}Co and ^{137}Cs gamma radiation;

– x-ray radiation of technical sources, operating at or below the energy of 5 MeV;

– electrons generated by technical sources operating at or below the energy of 10MeV.

In accordance with the General Standard for Irradiated Foods (CODEX STAN 106-1983, REV. 1-2003), the minimum absorbed dose should be sufficient enough to achieve the technological objectives and should ensure the safety of consumers and should not disturb the structure, functional quality and the organoleptical properties of food products.

The Codex Alimentarius Commission, FAO, WHO on the safety assessment of radioactively contaminated food products has developed a system of recommended levels of radionuclides content, but there is no practice to incorporate the results of radiation exposure assessment into the assessment of public health risk due to various factors of food products.

Thus, the results of the analysis of the recommendations of the Codex Alimentarius Commission, FAO, WHO on the safety assessment of radioactively contaminated food products established:

– the list of radionuclides selected as the most important in relation to their intake with food products consists of 20 substances (^{3}H, ^{14}C, ^{99}Tc, ^{35}S, ^{60}Co, ^{89}Sr, ^{90}Sr, ^{103}Ru, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U, ^{134}Cs, ^{137}Cs, ^{238}Pu, ^{239}Pu, ^{240}Pu, ^{144}Ce, ^{192}Ir, ^{241}Am), these radionuclides are divided in accordance with the value of the dose per intake unit into 4 groups; the interference levels are set in accordance with these values;

– the following is established as criteria for the products radiation risk assessment:

– the recommended levels of radionuclides content in food (the maximum level of the substance content in food recommended by the Commission);

– the level of exposure (dose), the exceedance of which requires specific protective measures (the intervention level of food withdrawal is 1 mSv/year).

– when assessing the radiation risk in accordance with the assumption that 10% of the diet is imported products, the value of the portion factor of food products import of - 0.1 is used.

The use of experience accumulated in the framework of the Codex Alimentarius Commission, FAO, WHO, especially on the recommended levels of radionuclides content in food products, is appropriate to assess the population health risk associated with the consumption of food products, including the integrated assessment of the health risks associated with heterogeneous risk factors of food products for various consumers cohorts.

However, the use of the experience and standards recommended by the Codex Alimentarius Commission requires careful and thorough approach. It is extremely important to take into account the specific characteristics of the background levels of the exposure of the population. It is shown, that the population health risk can be much greater in some cases than the risk of possible consequences the Chernobyl accident for the population of Russia. The currently effective regulations are acceptable to Russia; in addition to the dose criterion these regulations take into account the change in risk with age.

Furthermore, the difficulties of practical implementation of the recommendations of the Codex Alirncntarius should be taken into account in terms of potential accidents at facilities using sources of ionizing radiation. Thus, numerous EU Directives have gradually decreased initial levels comparable with those of Codex Alimentarius starting in 1987 after the Chernobyl accident, especially after the accident at the Fukushima nuclear power plant [Romanovich I.K. et al., 2012].

The analysis of these situations implies that the position of the international community on this issue is not finally established and will require further research and consultations, the frameworks of which require the reapprochement of positions and the specification of the conditions under which each of the established standards and interference levels may and/or should be used.

But, the methods of population health risk assessment associated with radiation hazard factor are in high demand and require the development and improvement under all the existing problems and objectives.

2.6. The assessment of risk associated with exposure to macrosocial factors and lifestyle on the health of the population

In 2005, the former general director of the World Health Organization (WHO) Lee Jong-Wook established the Commission on Social Determinants of Health the main task of which became the determination of the priority directions of activity for global organizations, governments and civil society on the achievement of equitable distribution of health among different social layers and the provision of equal access to the health care. The recognition of the significant influence of social differentiation, the level of the social and economic development of society and the lifestyle of population on the population health determined the actualization of impact on the social determinants of health as the priority of global and national health policy and its consideration as the state management efficacy criterion [WHO Report, 2009].

However, the interest to social factors forming the health of population is not new from the side of scientific society and political authority. The first attempts to determine and characterize the social determinants of health as well as explain scientifically the impact of social factors on the morbidity and mortality were made already in the middle and at the end of XIX century when in 1848 the French scientist J. Guerin having introduced into the scientific turnover the notion of "social medicine" as the subject of this discipline determined the relationship between the physical and mental state of population and legislation as well as other social institutes, relationships between the social factors, health and morbidity; measures on the promotion of health and disease prevention [Reshetnikov A.V., 2000].

In 1980, the UK Health and Social Safety Department published the report "Inequalities in Health" [Inequalities in Health, 1980] which later was named as The Black Report (in honor of its author Douglas Black) the main idea of which was the demonstration of significant social inequality in the country population health as well as the justification of the dominant role of social factors in its formation.

The professional status (data on which are available to a greater extent) is used in this report as the main indicator of social inequality. For the majority of population groups, it also indirectly reflects the other aspects of social inequality (differences in financial resources, housing and education).

The results of study revealed the significant differences in the level of mortality between the professional classes for both sexes and all ages. Thus, at birth and during the first month of life, children from families where the parents are engaged in unskilled labor die two times more often than from families in which the parents are highly skilled; and 4 times more for girls and 5 times more for boys die in the first 11 months of life. During life, the ratio of coefficients changes depending on the age, but in general the tendency to the greater level of mortality as well as morbidity is preserved among the unskilled and low skilled specialties. The report emphasizes that the absence of improvements and in some cases also the deterioration of health for unskilled and low skilled groups of population compared to the high skilled groups during 1960s and in the beginning of 1978 is significant. This relates also to the indicators of infant and child mortality as well as the mortality among men of economically active population and mortality among women.

There are a lot of very different approaches to the explanation of this problem; the report underlines the importance of differences in the material conditions of life. But the majority of factors associated with social inequality in the field of health can be adequately understood in relation to the peculiarities of social and economic environment (for example, low level of safety on roads and in the regions of residence, overpopulation, smoking and alcohol abuse), dependence from social and class differences. The importance of health services especially the preventive services is underlined (for example, the necessity of prenatal care that is evidenced by the global experience). But besides this there are the factors of wider spectrum – factors associated with the social and class structure of society: poverty, adverse working conditions, deprivation.

One more significant conclusion made by the authors of reports is that the early childhood is the period of life during which the provision of proper social support and medical assistance can decrease the existing dependence between the health indicators and belonging to the social class.

The report states that there are significant problems in the systematization of knowledge about the problem of social inequality in relation to health, the difficulty in collection and presentation of required data. The public health monitoring is imperfect; besides that, during the health assessment it is required to account the social conditions.

The report offers the system of measures in the field of social policy on struggling against the inequality in relation to health. It should be noted that these conclusions and recommendations actually were ignored by politicians currently holding the power during the publication of report. Besides that, the circulation of report composed small number of counterparts that is why the access to it was limited to the wide public.

As of today, the degree of the scientific exploration of the influence of social risk factors on health is high from the first sight. The specified issues are considered in the works of such foreign scientists as L. Berkman and L. Syme, K. Horn (1983), M.G. Marmot (1986),

R.G. Wilkinson (1986), B. Link (1995), G. Steinkamp (1999), G. Pappas, M. Susser, W. Watson, K. Hopper, etc. Among the domestic researches the problems of social determinacy are considered by V.P> Petlenko (1979), M.S. Bedny (1984), N.M. Rimashevskaya (1987), R.M. Baevsky (1997), Yu.M. Komarov (1997), L.S. Shilova (1999], A.V. Reshetnikov (2000), I.V. Zhuravleva (2001), I.B. Nazarova (2003), O.A. Kislitsyna (2007), N.L. Rusinova (2007), Yu.P. Lisitsyn (2009) and other scientists.

In general, it is possible to distinguish several main directions of the analysis of the influence of social factors on the individual and population health [Barg A.O., 2010].

The first direction, let us name it as "*entity-oriented*", discloses the content of notion "social risk factors", describes the interrelations and mechanisms of influence of these factors on the population and individual health, studies the contexts of their occurrence. The works related to this approach have theoretical and methodological character using the complex approach to the investigated problem.

The second "*structure-oriented*" direction offers different options for the classification of the social health factors. The works representing this direction, first of all, contain the offers on grouping the factors depending on the level of management, the character of influence, etc. The objective and subjective stability factors (favorable determinants) and risk factors (adverse determinants) controlled and uncontrolled are determined; second, the works contain offers on the classification of the factors themselves.

The third "*subject-oriented*" direction is focused on the separate risk factors revealing either at the level of society in general or its certain subsystems, or at the level of separate individual concerning its behavior, style and conditions of life. Here we can include the works dedicated both to studying the influence of social and economic, social and cultural and other conditions of macrocharacter on the health of population and the investigation of problems of healthy lifestyle, self-protecting behavior and safe life activity.

The fourth "*empirically-oriented*" direction is represented by works revealing the empirical methods for studying the prevalence of social risk factors, susceptibility to risks of separate social groups, offering the results of approbation of these methods at the level of country, region or territory.

The fifth "specially-oriented" direction is reflected in the studies which predominantly have medical and social character and describe the mechanisms of the influence of separate risk factors on the development of certain diseases (for example, the influence of smoking on the development of laryngeal and lungs cancer, chronic bronchitis, etc.; alcohol abuse – on the hepatic and heart diseases; hypodynamia – on the development of cardiovascular diseases, etc.).

Regardless of the abundance of literary sources dedicated to the problem of the influence of social risk factors on health no common theoretical and methodological basis for their analysis was developed by the scientific society. The problems of constructing the complex model of influence of social factors on health are still actual; it is required to justify the mechanisms for the management of the social public health risks and adopt the unified classification of the social determinants of health. Six main problems can be distinguished in the quite wide range of problems.

The first problem is associated with the absence in the scientific society of the common understanding of the essence of social risk factors, the character of their impact on health and the mechanism of their conditionality. The presence of this difficulty is underlined by B. Link in his work, marking the wrongfully increased attention of modern investigators to the nearest risk factors potentially controlled on the personal level at ignoring the fundamental prerequisites of health deterioration having the macrosocial character.

B. Link confirming the presence of stable bond between the social factors and health points on the necessity to contextualize the risk factors, including: 1) the understanding of that namely the circumstances of human life determine his susceptibility to such risk factors as unprotected sexual intercourse, malnutrition, sedentary lifestyle and stressful family life; 2) the determination of social conditions at which the separate risk factors are associated with disease. In other words, it is important to be focused on that at which social conditions the risk factors are leading to disease and if there are any social conditions at which the

individual risk factors have no influence on disease, i.e. on the reasons of one or another human behavior having the macrosocial character or on the "risk of risks" [Link B., Phelan J., 1995]. The main idea of B. Link is in the consideration of social conditions as the fundamental reasons of disease.

G. Steinkamp and K.Horn in their works underline the importance of problem specified by B. Link. The conduct-based approach to the social risk factors analysis prevailing in the modern studies have, on their opinion, the significant disadvantage which is in the ignoring the macrosocial factors (according to B. Link – the risk of risks) not depending from individual but resulting in the one or another deviations in the human behavior. Usually, only the deviations themselves (microlevel) are taken as the basis for analysis which results in that the main fault for them is put on the individual that violates the cause-and-effect relationship in interpreting the results of any studies aimed at the investigation of interrelation of social factors and morbidity. K. Horn put attention on the fact that "the risk behavior" shall be interpreted based on the sense-bearing structures supporting the behavior in which it could be possible to reach a compromise between the subjective interests, needs and resources and contradictory requirements of society.

The second problem is in the ambiguousness of interpretations of the influence of social risk factors on health. Thus, G. Steinkamp focuses on that dependences of health deterioration on the conditions and quality of life, the material welfare of individual and social inequality being proved in many scientific works can have the reverse character. The scientist underlines that, for example, when analyzing the relationship between the social and economic status and morbidity/mortality the empirically proven interrelation between these indicators is a result of inaccurate operationalization and incorrect empirical accounting of independent (social layer) and dependent (morbidity/duration of life) variables. The author says: "Social stratification differences in the health and duration of life can be considered as the result of social promotion of healthy people or as the social fall of patients", explaining that "the social position could be interpreted as a result of health condition but not vice versa" [Steinkamp G, 1999].

Eventually, G. Steinkamp offers the multilevel model for explaining the inequality in diseases and duration of life where he distinguishes three levels: macrolevel (place in the social inequality system), mesolevel (the material and social conditions of production (labor) and reproduction (partners, family, leisure) and microlevel (personality, body)).

The third problem which characterizes the described field of scientific studies is in the absence of the common classification of risk factors and ambiguity of their structure. The approaches to the classification of social risk factors are multiple and various. Thus, M. Whitehead and J. Dulgren represent the social health risk factors in the form of the "layers" of influence starting from the individual level and ending at the level of society in general. The center of presented structure is human with his permanent characteristics such as sex, age, and hereditary factors. Further 4 layers are specified: first layer is the features of character and lifestyle, second layer is the relationships between people, third layer is the conditions of life and work which includes the infrastructure factors, and the fourth layer is the common social and economic conditions, the level of culture, environment, etc. [Dulgren J., Whitehead M., 1992].

In WHO the social determinants of health are understood as the conditions in which the people are born, live, brought up, work and grow old, including the health care systems. These conditions are the consequences of the distribution of material benefits, power and resources on the different levels – global, country, regional and local – determined by the implemented social and economic policy.

This approach is developed in the documents of US National Program "Healthy Population" developed by the Department of Health Protection and Human Services (HHS) since 1979 [Lebedeva-Nesevrya N.A., 2014]. The authors of the Program use two terms – "societal determinants of health" and "social environment". The first is interpreted as the "conditions associated with social, physical and economic environment in which the people are born, live, work and grow old" [Healthy people 2020, 2010]. It is explained that the societal determinants of health are included into the notion of social determinants but do not

exhaust it. The social determinants of health also include the social environment which covers the social and cultural institutes, the patterns of individual and collective behavior, social attitudes and valuables as well as the social groups and social relations. The societal determinants and social environment are connected not only between each other but also with so called physical environment which includes both the natural and artificial environments (buildings and facilities, transport infrastructure, etc.) (Fig. 2.37).

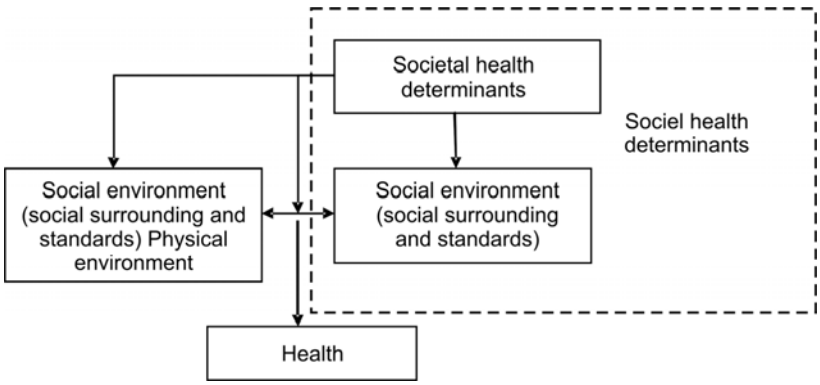


Fig. 2.37. The social determinants of health in the system of the health-forming factors (HHS approach)

M.G. Marmot and R.G. Wilkinson (1986) distinguish such health risk factors as social and economic conditions which include the stress, early childhood, work, unemployment, social support, chemical dependence, nutrition, transport and social alienation.

The famous domestic specialist in the field of social hygiene and public health Yu.P. Lisitsyn (2009) confirming that the health and diseases are determined by the social conditions and social factors includes to them also the activity of health care services and lifestyle; herewith the lifestyle is considered as the most significant factor influencing the human health by 50%. Yu.P. Lisitsyn represents the lifestyle factor as the production, public and political, non-labor and medical activity of human.

Other domestic investigators B.B. Prokhorov, I.V. Gorshkova, D.I. Shmakov and E.V. Tarasova (2007) speaking about the leading role of the social and economic factors in determining the population health conditions include in their number the living conditions; the degree of territory urbanization; the quality of recreational resources; vicious habits; the incomes of population; the development of social assistance for the lower-income groups of population; the availability or absence of good work; the availability and quality of education; the tension of information field in the living environment; the problems of family and morality; migration mobility; the specifics of lifestyle in regions with different natural, social, ethnic and religious peculiarities.

O.Ya. Kislitsyna (2007) offers to subdivide the social risk factors into poverty, social and economic conditions in the early childhood, living conditions, unemployment and work conditions, social capital (family, friends, neighbors – social networks), lifestyle (nutrition, vicious habits, motion activity).

I.B. Nazarova (2003) classifies the social factors into demographic (sex, age, nationality, place of residence), economic (education, income, employment), social and behavioral (alcohol consumption, smoking, physical exercises, the control of weight, confession). The investigator also speaks about the dependence of health on the cultural factors: traditions, upbringing, behavior and lifestyle.

N.L. Rusinova (2007) groups the social health risk factors into three categories: social-structural, social-psychological and behavioral. The social-structural factors include sex, age, education, material situation, marital status and the presence of children in family.

The group of social-psychological factors includes the stress events in life, chronic stressors associated with different life circumstances, personal psychological resources. The preventive physical activity, smoking, alcohol consumption and the correctness of nutrition are studied among the behavioral factors. This study demonstrates the self-assessment of health by respondents under three components: general self-assessment, the assessment of physical well-being and mental health. Special attention is paid to the problem of gender differences in the self-assessment of own health.

The fourth problem which in many ways limits the possibilities for management of social risk factors to develop the adequate measures for their mitigation is in the complex assessment of contribution of the social risk factors into the deterioration of health as well as the difficulties and variety of approaches to the assessment of strength of their influence on health. Thus, the domestic scientists Yu.M. Komarov (1997) and Yu.P. Lisitsyn (2009) detected that the specific weight of lifestyle factors in the health deterioration makes up 49–53% and health care system dysfunctions – 8–10%, the share of other genetic and external environmental factors makes up from 35 to 42%.

The other assessment of the social risk factors contribution into the health deterioration is offered by S.M. Chechelnitskaya, A.A. Mikheeva and V.G, Finagin (2008). Within the work on constructing the expert human health model based on the expert classification of the state of health, the investigators detected that among the classes of factors influencing the health the first place shall be taken by mode (4.0 points under the results of expert evaluations), second – by the biological factors (3.9 points), then with equal coefficients the family and professional environment are placed (3.8 points). S.M. Chechelnitskaya with colleagues having ranged the factors and indicators offers to use them during the health monitoring construction.

The other example of assessment of contribution of one or another factor into the health condition is presented in the work of R.M. Baevsky (1997) who studied the condition of health and morbidity of one of the social groups – administrative and managerial staff of the enterprise. Within the study it was established that this social group is characterized by the adverse health structure (more than 50% of persons in this group have unsatisfactory adaptation to the environmental conditions or breakdown of adaptation); also it was determined that administrative and managerial staff of large industrial enterprise (key personnel) to a greater extent is subjected to the exposure of factors having the adverse influence on the adaptation abilities of human body. Among these factors the maximum specific weight belongs to the psychoemotional stresses, hypodynamia and smoking.

The fifth problem which justifies the complexity of attributing the number of the social determinants of health to the risk factors is in the multivalued character of their influence on health and ability to act both as the risks and anti-risks.

The ambiguity of the relation of social and other risk factors with health is expressed with the health of *V*-shaped or *U*-shaped influence curves. We mean the nonlinearity of disease dependence on the risk factor when in the determined endpoints of the factor values (very high extent of motion activity and very low degree of motion activity) it equally negatively influences on the human body. V.Ya, Yadov [1998] writes: "*V*-shaped relations reflect such dependences as, for example, the relation of mortality with body weight. It was found that the mortality is minimal in the middle of the indicator distribution and persons with excessive or insufficient body weight die more often but from different diseases: fat people – from cardiovascular diseases, slim-jim people – from lung and oncological diseases". M.G. Marmot (1981) provides the other example for confirmation of *V*-shaped relations: the mortality due to the cardiovascular diseases in the excessively drinking people under the analysis of the results of studies are significantly low than in the non-drinking people; however the mortality from other diseases was higher. Also the alcohol consumption has the *U*-shaped interrelation with risk of development of coronary heart disease. A number of investigators believe that the moderate alcohol consumption has the cardio protective action [Prevention of coronary heart disease in clinical practice, 1996]. The U-shaped dependences are detected in the relations of mortality and alcohol consumption, cardiac rate, night sleep duration, etc. The detected universality of these relations leads to the necessity of new

thinking during the healthy lifestyle formation. Its essence is in that the healthy lifestyle recommendations cannot be equal for everybody. They differ in crucial respect, depending on where the population or individual is located on the *U*-shaped curve – to the left or to the right from the minimum mortality point. Herewith, the certain values of indicator on the *U*-shaped curve depend on the region of residence of the population or individual and relation of these values to the certain diseases [Kozlovsky V.A., 2012].

It should be noted that many investigators using the letters *V* or *U* when describing the health condition determination by the risk factors do not make any difference between the types of dependences described by these letters; however it still exists. Regardless of that both *U*-shaped and *V*-shaped distributions means the distribution with high frequencies (or probabilities) for very low and very high values and low frequencies (or probabilities) for moderate values the *V*-shaped character of dependence stipulates the existence of certain absolute minimum, i.e. the single value which is characterized by the smallest probability or frequency. It is better to use the term "*U*-shaped relationship" to explain the relations of the social risk factors and health, because it more accurately characterizes the detected dependences. *V*-shaped relationship is a dynamic structure where one point with minimal risk exists and any deviations from it to the left or to the right mean the increase of disease probability. *U*-shaped relationship provides a wider range of values in which the risk is minimal. For example, if we take the alcohol consumption we cannot say exactly that a person drinking, for example, 100 ml of red dry wine daily is exposed to the minimal risk of cardiovascular diseases (*V*-shaped relationship). Thus, the *U*-shaped relationship provides the possibility to speak that there is a certain range of alcohol consumption within which the human is not only exposed to the risk of health deterioration but also carries out the prevention of cardiovascular diseases. It should be noted that practically there are no studies dedicated to the measurements of the endpoints of values of the social risk factors at which it could be minimal or maximal.

Therefore, one and the same social factor can act in relation to the human health both as the risk and anti-risk factor having the negative influence on the condition of health or, on the contrary, contributing to the increase of resources for the health of human or nation.

Finally, *the sixth problem* which in many ways determines the existence of problems of interpretation of relationships between the social risk factors and health and assessment of contribution of these factors into the development of different diseases is the absence of unified methodology of empirical study of influence of the social risk factors on health.

First, when studying the influence of social risk factors on health the latter is assessed in different ways: both based on the results of medical examinations and during the sociological questionnaires on the basis of the self-assessment by individuals of the condition of their health. The adequate assessment of relationships between the social risk factors and health is possible only at the comparison of the results of those anf other examinations because the results based only on the self-assessment of individual health do not provide the possibility to determine its true condition due to the subjectivity of human thinking as well as there is no possibility to make correct assessment of the social risk factors, their meaning and specific weight of each at the exclusively medical analysis of the human body condition because in such case they just cannot be detected. Second, the existence of those or other risk factors is also assessed with the help of different methods - medical or sociological. This relates, for example, to the action of such factors as the alcohol abuse, smoking and motion activity which can be determined with the help of laboratory analysis, questionnaire or questioning. Third, Russia practically does not carry out the monitoring studies of influence of the social risk factors (specially it relates to the behavioral factors) on the health of population. The majority of studies has local and non-recurrent character and are aimed at the obtainment of the "cut" of the situation but not the monitoring of its dynamics.

The general diagram of methods for the empirical study of the social determinants of health is presented on Fig. 2.38.

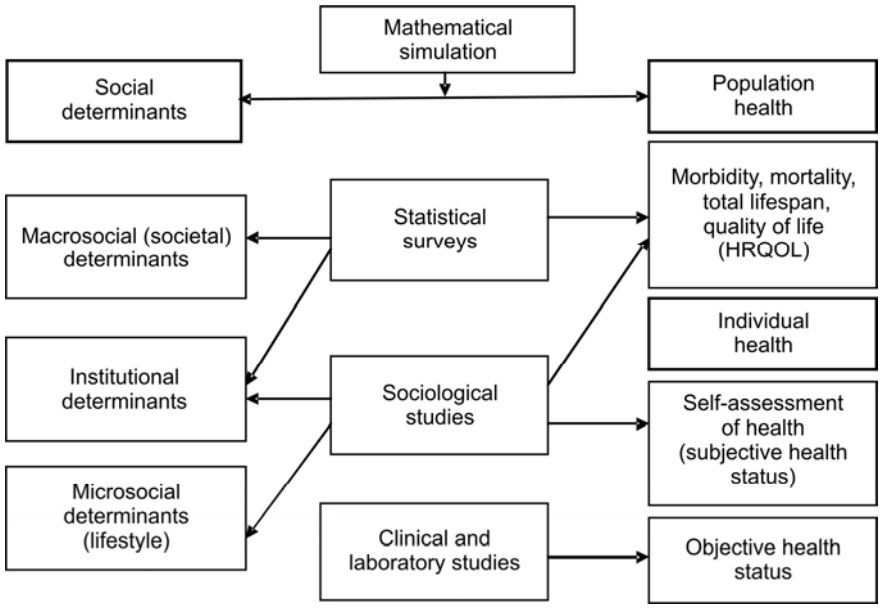


Fig. 2.38. The methods for empirical study of the social determinants of health [Lebedeva-Nesevrya N.A., 2014]

Therefore, the review of scientific works aimed at studying the influence of the social risk factors on the health of population allows for making the following conclusions in relation to the problem exploration degree.

First, regardless of that to the opinion of the majority of scientists the influence of social factors on health has the predominant character which determines the action of other factors no common theoretical and methodological basis was developed by the scientific society yet that complicates the comparison of results obtained by different investigators.

Second, the problem of constructing the complex model of influence of social factors on health, determination of the character of interconnection between different factors and peculiarities of their mutual interaction is still actual.

Third, it is necessary to accept the unified classification of the social health risk factors that will allow for not only reliable assessment of the contribution of each of them to the development of certain diseases but will promote the construction of efficient policy for management of the social risk factors and maximize the effect of taken managerial decisions.

Fourth, the tasks of the human potential development at the level of country, region or territory require the high level of the awareness of persons making the managerial decisions in relation to the health deterioration risk factors that stipulates the necessity of their detection and assessment in the monitoring mode.

Fifth, it is required to develop the measurable indicators of the existence of those or another social risk factors. The social-hygienic, sociological and medical-social monitoring which acts as the basis for making the decisions cannot exist without the analysis of social factors but the absence of unified system of their indicators based on the general classification narrows down the range of possibilities for their use during the public health assessment in the monitoring mode.

The polydeterminacy of human health in the modern world, the complexity and miltifactorial nature of many diseases often makes extremely difficult the demonstration of etiological relationship between the change in the condition of health (for example, the developed disease) and preceding adverse effect of the factor. The variety of potentially harmful external environmental factors with which a human contacts in the urban environment or at production, implementation of self-destructing practices (smoking, alcohol

abuse, sedentary lifestyle, etc.), peculiarities of the action of genetic determinants result as a rule in the impossibility to establish the accurate contribution of the one or another factor into the development of certain disease that decreases the health management potential both at the individual and population levels. In order to solve the specified problems the epidemiology and hygiene since 1970s widely use the risk analysis methodology which is based on the establishment and forecasting of probability for forming the negative effects due to the action of factors of different nature (mainly the external environmental factors).

The risk category regardless of its heuristic value in relation to the analysis of problems of the human health social determinacy is used extremely seldom. The following can be the reason [Zaytseva N.V., Lebedeva-Nesevrya N.A., 2013]. First, the health risk notion itself for the long time was at the periphery of interests being insufficiently developed, debatable and multivalued. Only in the beginning of 1980-s it acquires the social sense. Several decades of productive conceptualization of health risk at the influence of social factors resulted in forming the variety of approaches to its understanding varying from the interpretation of risk close to the natural scientific as the objective phenomenon (but mediated by the social and cultural, social and political and social and economic processes) to the complete negation of the existence of risk "as such" outside its perception as the social subject [Yanitsky O.N., 2003]. Second, the focus of studies for a long time was displaced to the problems of medicine (assessment of its efficacy, functionality of substitutes, analysis of social roles of the doctor and patient, etc,). The range of problems of social conditions and health formation factors, subjective perception and attitude to health, forecasting of changes in health, its protection and prevention of diseases, i.e. the context which stipulates and even seamlessly includes the health risk topics does not received the proper justification. Third, the predominance of "objectivistic" approach to the risk (when the latter is interpreted in the scientific and technical terms, calculated and predicted and its understanding is formalized through the categories of probability, frequency of expected adverse event and seriousness of consequences) as well as the active implementation into the administrative practices of the quantitative health risk assessment procedures (from the environmental contamination) determined the perception of the range of problems of the socially determined health risks as highly specialized.

The study of socially determined health risk is implemented both in the foreign and domestic practice under three key directions which taking into account the subject of analysis can be distinguished as follows: a) studies of the health deterioration risk factors and factors of its stability (anti-risk); b) studies of "objective" health deterioration risks; c) studies of the health risks perception.

The *first direction* represented by the largest number of studies and publications is focused either on the analysis of the social risk factors (often called as the lifestyle factors) of deterioration of individual or public health, or on the study of attitude of different social groups to these factors. Here we can include all works dedicated to the analysis of influence of the social and economic, social and cultural, social and political situation and living conditions on the public health as well as the works on the problems of healthy lifestyle, self-protecting behavior and safe life activity. Special place is taken by the studies of the health risk factors prevalence in the different social groups – among the schoolchildren, students, employees of industrial enterprises, etc. For these works it is typical to use the combinations "behavioral risks", "risky behavior" to define the negative behavioral practices in relation to health implemented by individuals as well as the notions "risk-factorial conditions" and "risk-factorial situation" to describe the contexts of formation and external determinants of these practices.

The main limitation of studies of the social health risk factors is in their predominant fragmentation, narrowness of focus aimed as a rule at the behavioral public health risk factors. Herewith, the health social determinacy model stipulates not only the action of direct behavioral risk factors but also their social contexts. Thus, the low level of the social development of territory and the subsidized character of budget, first of all, limit the possibilities for the social sphere development (in particular, construction, modernization and increase of transport and economic availability of recreational, treatment and resort infrastructure); second, they determine the low level of life for population, increase in the

share of citizens with incomes below the subsistence minimum, growth of unemployment that determines the high level of stress of the social environment Revealing at the level of the certain household, these macroeconomic conditions are expressed in the low level of material welfare and increase of stress in the family mircoclimate that, on the one hand, being the serious stressors already results in the change of health conditions, and on the other hand determines the occurrence of direct (behavioral) health risk factors (such as alcohol abuse or smoking).

The concentration of the investigators attention on the different types of behavior having the significant consequences for health without the understanding of social processes forming the basis of implemented behavioral practices and predominantly descriptive approach to the problem do not allow for disclosing the social mechanism of the public health formation quite in full; besides that, the practical and applied value of research is decreased.

The social health anti-risk factors (anti-risk factors, stability factors) ensuring the resistance of human to the action of risk factors and contributing to the increase of health resources are still under-investigated. Extremely small number of works are dedicated to the analysis of macrosocial health stability factors. As it was mentioned above, the study of M. Brenner established that increase by 1% of the number of unemployed in the country provokes the growth of murders by 5.7%, suicides – by 4.1%, etc. [Brenner M.H., 1979]. Herewith, the mechanism of influence of reduction of the share of unemployed on the risks in the field of health is unclear.

The *second direction* is focused on the quantitative assessment of risk associated either with independent influence of social (social and economic, social and demographic, behavioral, etc.) factors or with the combined influence of social and other (production, external environmental, anthropogenic, etc.) factors on health. It should be noted that within this direction the studies have mainly the interdisciplinary character being based, on the one hand, on the results of empirical sociological studies, and on the other hand – on the results of epidemiologic, medical and other studies. The health risk is interpreted here in the terms of monitored and measured and is determined as the quantitative indicator of hazard and probable damage occurred as a result of some adverse event. The results of such studies are quite popular in the management practice because they allow for not only to forecast the "probability and medical and social significance of possible health disorders at the different scenarios of influence of the analyzed factors but also to establish the precedence and priority of measures on the risk factors management at the individual and collective level". But, using such notions as "acceptable risk", "the value of damage" and "the significance of consequences" which are subjective by their nature, the investigators, as a rule, exclude from the subjective field of analysis the socio-cultural contexts of risks. For example, the acceptable risk means that the level of risk which is acceptable in relation to the risk criteria. Herewith these criteria are established by experts but are not determined by the certain individual exposed to risk or the society in general. When analyzing the risk acceptability it is necessary to take into account the economic benefits for the state or enterprise (i.e. the subject of risk), expenses associated with the risk level reduction, and possibilities for implementing the regulatory measures in order to decrease the potential negative influence of the risk factor. The fact of that for the object of risk (separate individual or social group) the risk acceptability notion depends on the significant number of subjective and objective factors and that it is closely connected with the circumstances and reasons determining the risk perception peculiarities is not always recognized and practically is never taken into account.

The *third direction* of the health risk studies dedicated to the risks perception investigation has the significant theoretical base. The perception of risks is conceptualized in the works of D. Kahneman and A. Tversky (1979), M. Douglas and A. Wildavsky (1982), P. Slovic (1992), J. Tulloch and D. Lupton (2003). The modern social riskology have accumulated enough knowledge about the risks perception factors, about the role of cultures and subcultures as well as the personal experience in its formation, about the peculiarities of perception of risk by different social groups. However, in relation to the health risk analysis these results and achievements are poorly used. Therefore, studying the health risks

perception has some specific features. First, the health risks notion is substituted by the category "risk factors". The attention is focused not on the subjective interpretation by the individual or social group of the level of risk, its acceptability, significance of negative consequences and possible benefits but on the perception of the one or another factor (behavioral, external environmental, etc.) as the hazardous or safe which can cause and causes those or another emotions and behavioral responses. The tools of empirical studies (often conducted in the quantitative tradition using the method of formalized interview or distributive questioning) as a rule contain the close-ended or semi-closed questions offering to assess how the one or another threat (vicious habit, disease, external environmental exposure, etc.) "disturbs", "causes concerns", "horrifies", etc. Also the projective questions offering the respondent to characterize his choice in some hypothetical situation of the influence of factor are widely used. Second, at the intensive use of notions "adequate" or "non-adequate" perception of risk as well as "real probability" [Pautov I.S., 2010] the comparison of "real", "monitored" and "perceptible" risk [Thompson P, 1989] is not performed. The presentation of opinion on the adequacy (correctness) of the perception of risk by the individual or social group is feasible during the implementation of the risk analysis procedure which stipulates the quantitative (semi-quantitative, qualitative) risk assessment and further distribution of information about the results of assessment among the population or persons making the decisions. In such case knowing the risk perception peculiarities allows for making the conclusions about the success of informing about the risk and increases the possibilities to integrate the public opinion into the making of managerial decisions. However, such approach provides the recognition of risk as objectively existing because the category of adequacy itself stipulates the compliance with some reference or standard. When selecting the interpretative paradigm of study and understanding the risk as constructed by the social subject outside which the risk does not exist and cannot be learned, the sense and assignment of opinions on the risk perception adequacy became unclear.

The success of implementation of the interdisciplinary approach to the health risks analysis depends on the possibility to remove a number of contradictions. For example, there are the differences between the approaches to the risk acceptability analysis. The health risk rationing based on the expert opinions which does not take into account the contexts of risk twists the category of "acceptable risk" ("allowable risk") as the one directly depending on the object of risk. Perhaps, we should speak not about the acceptability of risk "in general" but about its social acceptability composed from the "assessments of allowability of the different types of damage provided by the social objects included into the certain risk situation" [Mozgovaya A.V., 2010].

One of the contradictions related to the health risks perception analysis. The sociological studies of this problem are not used in practice and their results are poorly integrated into the managerial processes. Herewith, the risks analysis methodology which is actively used to solve the tasks on the management of public health and quality of living environment provide the support from the side of such studies. For example, the domestic methodical documents regulating the public health risk assessment procedure at the influence of chemical substances contaminating the environment directly indicate the necessity to account the peculiarities of the perception of risk by the different social groups during the implementation of the risk informing procedure.

The risk analysis model used within the system for the management of sanitary and epidemiological situation at the territory can be used as the example of the implementation of interdisciplinary approach to studying the risks for health. The objective approach is accepted here as the basic one (the risk is interpreted as the probability of development of threat to the life or health of human or threat to the life or health of future generations stipulated by the influence of the living environment factors). The mandatory stages of the risk analysis procedure are studying the peculiarities of perception and awareness about the risk understood not as the one-sided process for transferring the information but as the process of interaction and communication.

In general, the integration of sociological approach to the investigation of risk into the public health risk analysis methodology is reflected in the following. The methods of

empirical sociological study are actively implemented at the health risk assessment stage (first element of the risk analysis methodology). In particular, when assessing the exposure representing the risk accounting "unit" the sociological study aimed at the establishment of factors influencing or potentially able to influence on the condition of health of the exposed group is implemented. Depending on the type of the analyzed health risk (associated with the effect of chemical substances contaminating the environment, effect of noise, electromagnetic radiation, radioactivity, etc.) we study the peculiarities of living conditions, labor and rest, food ration and drinking water consumption, specific character of motion activity, susceptibility to stress factors and other social, socio-demographic, socio-economical and behavioral characteristics of the group of exposed persons. The study is carried out through questioning or formalized interview (personal or by phone) of the representatives of groups being the objects of risk. When assessing the risk associated with the influence of lifestyle factors on the health of population the results of sociological study are the starting point for the further risk assessment procedure. The levels of risk factors associated with lifestyle which are specific for the certain individual as well as the prevalence of these factors in the studied aggregate are established during the process of study. The lifestyle factors include the peculiarities of hygienic and medical behavior of respondents, food mode and ration, specific character of motion activity, availability of vicious habits, psychoemotional climate in family, etc. [MP 2.1.10.0033-11]. It is important that many of the listed factors cover the private sphere of the human life and cannot be studied with the help of traditional methods (for example, through the direct questions). Being sensitive by their nature, they require special approach, special formulations of questions and high level of trust from the side of respondents. Most of people consider extremely delicate such topics as the alcohol and drugs abuse. Because the relationship between the sharpness of the topic perception and the level of sincerity of the answers of respondents is proven, the development of methods and tools for studying the behavioral health risk factors becomes especially actual that will allow for decreasing the probability of obtainment of inaccurate information within the health risk assessment procedure.

The risk communication, i.e. the process of interaction, exchange with arguments and opinions between the concerned parties – the manufacturers of risk, its consumers and carriers, separate persons, groups of people and organizations is carried out at the health risk informing stage (second element of the risk analysis methodology). Informing about the risk is not a one-sided but a bidirectional process which is based on the existence and action of inverse relationships ensuring the mutual exchange with data. The informing process efficacy is determined, in particular, by the completeness of accounting of the risk perception peculiarities for different social groups.

Finally, the health risk management also requires the involvement of social methods and tools. For example, the management of risk associated with the influence of behavioral factors (in particular, the alcohol abuse or smoking) on the health of population which stipulates the lifestyle modification for the certain individual or social group requires the accounting of potential possibility of such changes. There is the probability of situation when it is very difficult to transform the established individual lifestyle because it is connected with other aspects of the personal behavior, is structurally conditioned, depends on the social and economic status of individual and is determined by the belonging to the certain social group.

The risk management includes the comparison of risk with allowable levels (which are acceptable and do not require the use of additional measures on its mitigation). The risk acceptability is determined not only by the results of economic analysis but also by a number of social factors, including the risk perception peculiarities for different social groups that again stipulates the active involvement of the methods of empirical sociological study allowing for the determination of the risk acceptability criteria based on its perception. When assessing the risk associated with the influence of external environmental factors, it is feasible to separate the risk manufacturers and consumers for which the acceptability criteria can be principally different. The establishment of the certain level of risk acceptable at this territory and at the given moment requires the accounting of the whole aggregate of techological and economic arguments as well as the opinion of social groups acting as the risk consumers.

The health risks represent the frontier area of knowledge. Being inseparably associated with natural and genetic factors, the peculiarities of the technogenic and socio-economic development of society, depending on the potential or real environmental contamination and specific character of lifestyle of the certain social group, being refracted through the expert evaluations, public opinion and individual perception they require for their explanation the joint efforts of the representatives of liberal and natural sciences. Therefore, namely the interdisciplinarity and orientation to the practical managerial activity shall become the initial methodological principles in the health risks studying.

As it was mentioned above, when explaining the phenomenon of the social environment influence on the human health the investigators use different categories. Such notions as "social determinant", "social risk factor" and "social health context" are used the most often.

To our opinion, the aggregate of different social factors which directly or indirectly influence on the public and individual health represents the social context of the health formation. It is possible to distinguish the macrosocial and microsocial health formation contexts affecting the health, including through the individual human behavior. What is more, according to R. Wilkinson (1986), since the human behavior is always socially determined, it can be changed only if the society will be changed too. The social factors (social micro and macro environment) do not determine directly the probability of the occurrence of adverse event in relation to health, i.e. they are not the direct risk factors but they act as the conditions for their formation.

According to it, it is necessary to provide the definition to the notion of "socially determined health risk".

Socially determined health risk is an objectively existing, potentially observed and perceivable probability of the abnormality (disorder) of individual or population health of certain severity associated with the action of social macro and micro environment occurring under the certain conditions.

The necessity to turn to the category of socially determined risks results from the objective insufficiency of categories "social factors" or "social determinants" in order to explain the human health formation processes in the modern society is stipulated by a number of reasons.

First, the high dynamics of social processes resulting in the impossibility of rapid adaptation and, therefore, the dysfunction of a number of social institutes, the active reorganizing activity of social entities aimed at the transformation, principal reconstruction (E. Giddens) of the social system itself combined with the global integration processes and acceleration of the innovative productions development determine the increase in the riskogenics of environment, including the social, and inclusion of risks into the everyday life when the risk situation becomes permanent (U. Bek), as well as the "risk society" formation.

Second, solving the safety ensuring tasks and increase of reliability in the modern society stipulates the problematization and updating of future as the risk [Behmann G., 2010], understanding of the development of society and its subsystems not as linear and strictly determined but as the probabilistic one.

Third, the management of the health of population, its preservation and strengthening under the conditions of multifactorial dependence of health and high degree of their changeability requires the use of new science-intensive tools allowing for applying the reliable assessment criteria. The heal risk analysis methodology is the one of such tools.

Regardless of understanding the significance of the role of social determinants in the public health formation the scientific studies of the last decades were focused predominantly on the behavioral risk factors associated with the peculiarities of the style and conditions of living of the separate individuals or social groups [March D., Susser E., 2007]. The social contexts of the individual risk factors, i.e. the determinants affecting the population health and form the medical and demographic situation at the territory, were studied very seldom [Macrosocial determinants of public health, 2007]. You might as well say that the conduct-based approach to the social risk factors analysis which dominates in the modern studies has the significant disadvantage, i.e. the ignoring of macrosocial factors [Zaytseva N.V. et al., 2013]. Usually, only the deviations themselves (microlevel) are taken as the basis for

analysis which results in that the main fault for them is put on the individual the cause-and-effect relationship in interpreting the interrelation of social factors and morbidity and mortality is violated [Link B., Phelan J., 1995].

Herewith, the understanding of peculiarities of influence of the macrosocial factors on the medical and demographic situation at the territory, the population health condition as well as the ability to forecast their dynamics is a mandatory condition for the effective human potential management.

The results of assessment of risk associated with the action of macrosocial factors on the health of population can be used: 1) for improving the methods for ensuring the sanitary and epidemiological welfare of population at the territory, including during the development of strategy for the social and economic development of the territory, concepts and programs of the social and economic development of regions and municipal structures; 2) for improving the system of social-hygienic monitoring; 3) for developing the information materials about the sanitary and epidemiological situation at the territory submitted to the state authorities of the Russian Federation, state authorities of the subjects of the Russian Federation, local self-governing authorities and population of the territory; when preparing the annual reports on the condition of health of the territory population, on the social and economic development of the territory, on the sanitary and epidemiological situation at the territory; 4) when developing the complex programs aimed at the preservation and strengthening of the health of population.

The algorithm for assessing the risk associated with the influence of macrosocial factors on the health of population is shown on Fig. 2.39.

The assessment of risk associated with the influence of macrosocial factors on the health of population is carried out in accordance with stages commonly used in the health risk analysis methodology. First stage is the hazard identification: detection of potentially influencing factors, assessment of relationship between the studied factor and the population health indicators, assessment of sufficiency and reliability of available data on the peculiarities of occurrence of macrosocial factors at the territory, and executing the list of priority macrosocial factors which are subject to the further characterization.

The second stage is the assessment of dependence "factor – effect": establishing the quantitative relationship between the values of macrosocial risk factors and the public health condition.

Third stage is the risk characterization: analysis of all obtained data, calculation of risks for the studied population and ranking of risks.

The selection of the indicators of macrosocial factors and health was carried out at the hazard identification stage for inclusion into the risk assessment procedure.

In general the macrosocial risk factors are characterized by two types of qualitative indicators which differ depending on the source of their origin: a) statistical indicators (which are collected and accumulated by the state statistics authorities); b) sociological indicators (which are collected within the sampling sociological studies carried out using the methods of mass questioning, expert questioning, content-analysis of documents or formalized monitoring). Use of sociological indicators is feasible only when the macrosocial factor cannot be described with the help of statistical indicator. For example, it is possible to characterize the degree of the regulatory system development in the field of health (fixation in the strategic documents adopted at the territory, orientation to the public health preservation, availability and quantity of regulatory documents concerning the public health provision and social protection programs for citizens or programs aimed at forming the public healthy lifestyle, etc.) only on the basis of content-analysis of regulatory documents, and the level of social and political tension (trust of authorities, level of protest activity, etc.) can be characterized only through the mass questioning of population.

However, in relation to the sociological indicators, the absence of actual results of sociological studies is a significant problem. Therefore it is feasible to carry out the specially directed sociological study.

When carrying out the sociological study in order to obtain the data on the level and prevalence of the risk macrofactors characterized by the sociological indicators using the mass questioning method, it is necessary to be guided by the following principles: a) selective

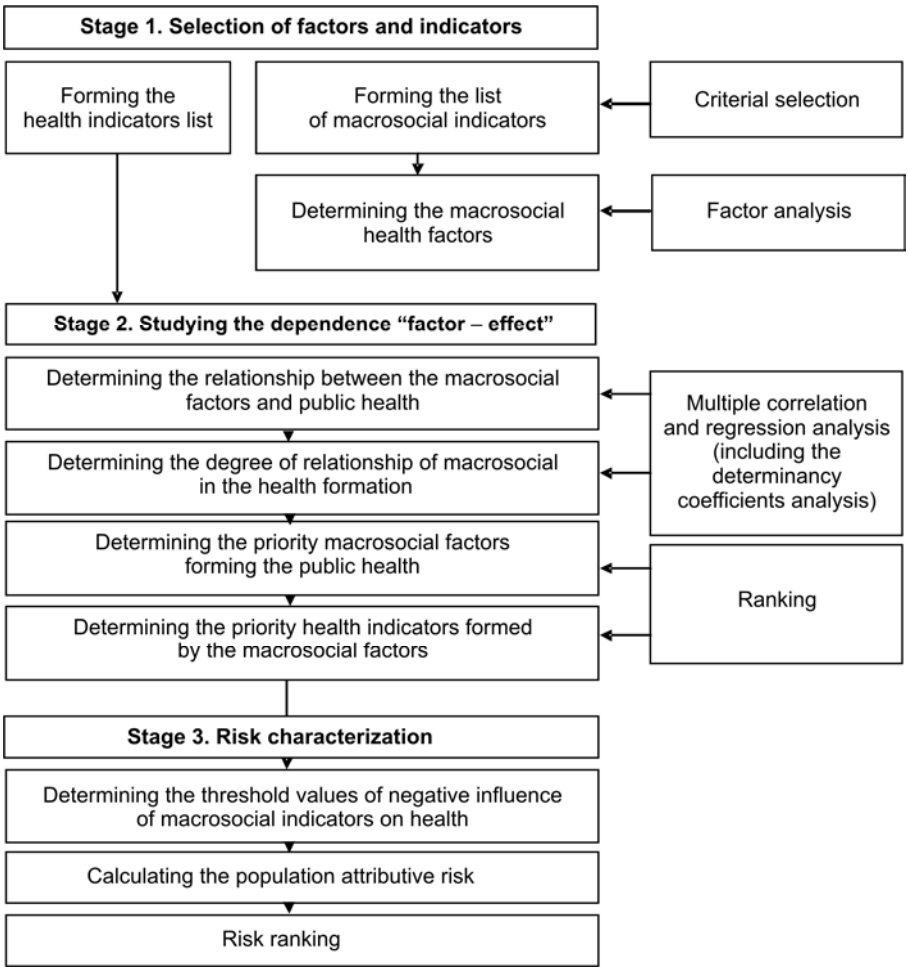


Fig. 2.39. The algorithm of risk assessment associated with the influence of macrosocial factors on the public health [Lebedeva-Nesevrya N.A., 2014]

character of the studied aggregate (not all elements of the general aggregate are examined, for example, not all population of the territory but only a part of it); b) representativeness of selective aggregate (selective aggregate shall reflect the features of general aggregate, and represent its micromodel); c) objective character of the selection of units to the selective aggregate (the elements of sampling shall be selected independently from the will of researcher, for example, using the random selection). When using the expert questioning method, it is necessary to be guided by the following principles: a) the competence of experts ensured by the multi-stage method of their selection; b) formalized questioning (polling) method; c) coordination of expert evaluations through using the majority rule (it is necessary to select that assessment of phenomenon or solution of task which is supported by the majority of experts). The content-analysis of regulatory documents requires the complete covering of regulatory documents adopted at the territory of analyzed objects and qualitative character of obtained information.

Unfortunately, the conduction of special sociological study is often impossible due to the insufficiency of material, human or time resources. The health risk associated with macrosocial factors is assessed only on the basis of statistical indicators.

The sources for forming the list of statistical indicators can be, first, the statistical databases (online bank of medical and sanitary data of the WHO Global Health Observatory,

Central Statistical Database (CSD) of the Federal State Statistics Service, United Interdepartmental Information and Statistical System (UIISS), Database of Indicators of Municipal Structures of the Federal State Statistics Service). Second, the departmental documents of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance determining the list of indicators collected within the system of social and hygienic monitoring [The Social and Hygienic Monitoring Procedure, 2006; On preparing the materials of state report "On the condition of social and epidemiological welfare of population in the Russian Federation", 2013]. Third, the regulatory documents determining the list of indicators for assessing the efficacy of activity of authorities at the different level [Decree of the President of the Russian Federation No. 607 dd. April 28, 2008, No. 1199 dd. August 21, 2012; List of additional indicators, 2012].

For example, the information indicators of the social and hygienic monitoring include, first, the public health indicators, second, the indicators of living environment. The second group consists of indicators characterizing the social and economic condition of territory which can be conveniently divided into four groups: the population welfare level, the level of the territory economic development, the level of development and availability of social infrastructure, and quality of housing and living conditions. However, this list can be extended at the expense of indicators characterizing the labor and rest conditions, the level of the sports and recreational infrastructure development and the social environment safety level. The maximum full list of potentially preferred macrosocial factors at the studied territory will allow for carrying out the deeper assessment of factors possessing the increased hazard and having the highest effect on the public health condition.

Table 2.50 contains some statistical indicators of the public health risk macrosocial factors which can be used in the risk assessment procedure.

The collection of data on the indicators of macrosocial factors can be preceded by the risk group determination and the following can be used as such: a) all population of the territory (macroregion, subject of the Russian Federation, municipal structure, etc.); b) working-age population; c) children's population; d) population of pension age; e) representatives of different social and professional groups (employees engaged in the certain branches of industry, students of secondary and higher educational institutions, etc.).

Besides that, it is feasible to assess the indicators correlation level separately a) inside the group of indicators of factors, b) inside the population health indicators group. For this purpose, it is recommended to use the Spearman's rank correlation coefficient, because its use does not require the prior study of the law of distribution of general totalities for which the dependence is established. In accordance with it, every observation in the table column shall have the corresponding rank (number of element in the ordered sample of observations) having replaced in such way the columns of observations by the columns of ranks.

Table 2.50

Some statistical indicators of the public health risk macrosocial factors

Item No.	Factor	Name of indicator
1	2	3
1	The capital improvement of residential stock	Basic (fixed in the system of social-hygienic monitoring): – specific weight of total area equipped with water supply system in the total area of residential facilities (%); – specific weight of total area equipped with sewerage system in the total area of residential facilities (%); – specific weight of total area equipped with central heating (%); – total area of residential facilities necessary in average per one resident (m^2). Additional: – specific weight of total area equipped with hot water supply (%); – specific weight of total area equipped with gas or floor-standing electric hot plates (%); – specific weight of old and failing housing stock in the total are of the whole housing stock (%)

Continuation of Table 2.50

1	2	3
2	The level of the social and economic development of territory	Basic (fixed in the system of social-hygienic monitoring): – per capita gross product (rubles); – cost of fixed assets under the types of economic activity (thous. rubles); – per capita investment into equity (rubles); – education expenditures (rubles per capita); – health-care expenditures (rubles per capita). Additional: – per capita fiscal capacity (thous. rubles/person); – specific weight of unprofitable enterprises and organizations in their total number (%)
3	Urbanization level	Additional: – specific weight of urban population in the total number of population (%)
4	The living standards of the population	Basic (fixed in the system of social-hygienic monitoring): – monthly per capita population incomes (rubles); – cost of the minimum set of food products (rubles); – size of minimum living wage (rubles); – actual per capita consumption of households (rubles); – average monthly nominal calculated salary of economic employees (rubles).
5	The level of social inequality	Basic (fixed in the system of social-hygienic monitoring): – specific weight of population having the incomes below the minimum living wage per one member of family (%). Additional: – the distribution of population under the level of per capita incomes and the concentration of incomes at the different groups of population: – Gini coefficient
6	The dynamics of social inequality	Additional: – the dynamics of indicator on the distribution of population under the level of per capita incomes and concentration of incomes at the different groups of population
7	The level of unemployment	Additional: – registered unemployment level (%); – duration of unemployment (months); – labor force participation rate (%) (labor force/number of adult population)
8	The development of medical infrastructure	Additional: – the number of hospital beds per 10 thous of population; – the capacity of medical outpatient and polyclinic institutions per 10 thous. of population (visits per shift); – the provision of round-the-clock in-patient departments with beds per 10 thous of population; – the provision of daily patient departments with beds per 10 thous of population
9	The development of social infrastructure	Basic (fixed in the system of social-hygienic monitoring): – the number of daily general education institutions; – the share of covering the children in the age of 1–6 years by the pre-school educational institutions (%); – the number of schools working in 2–3 shifts; – a general length of automobile roads; – the number of automobile hard-surface roads
10	The development of sports infrastructure	Additional: – the level of provision with sports facilities (pcs. / per 10 thous. of population); – the relation of the average cost of visit of the sports and recreation institution to the per capita incomes of population (%)

End of Table 2.50

1	2	3
11	The development of recreation infrastructure	Additional: – the provision of population with recreational institutions (health resorts, recreation centers and vacation houses) (per 10 thous. of population); – the provision of children's population with summer recreational institutions (per 10 thous. of children's population); – the relation of the average cost of health resort or vacation house voucher to the value of per capita incomes of population (%); – the relation of the average cost of children's recreational institutions voucher to the value of per capita incomes of population (%)
12	Crime rate	Additional: – the number of registered crimes (per 100 thous. of population); – the number of registered serious and extremely serious crimes (per 100 thous. of population)
13	The level of safety on the roads	Additional: – the number of registered road traffic accidents (per 100 thous. of population)

Having determined the list of indicators it is necessary to form the data array in the section of selected territories (macroregions, subjects of the Russian Federation, municipal structures within one region, etc.). It is feasible to collect the data in dynamics (for 2 and more periods). The number of indicators and their time coverage shall be equal for all investigated territories. The array can be created in tabular format using the programs Microsoft Office Excel, SPSS for Windows or any other program designed for statistical data processing. The preparation of data is performed prior to their analysis: checking the data consistency allowing for detecting the data beyond the limits of certain range and correction of values going out of the certain range (as a rule, due to the spelling error). The values going out of the certain range cannot be used in analysis; they shall be corrected.

In order to reduce the separate indicators to the more comparable format it is necessary to use the standardization of their values by relating the numerical value of every separate indicator for this territory to the mean value in the array in general:

$$A_{sit} = \frac{A^*_{sit}}{A_{st}}, \qquad (2.6.1)$$

where A^*_{sit} – is a numerical value of separate indicator *s* for territory *i* in year *t*;

A_{st} – is a numerical value of indicator *s* in average for array in year *t*;

A_{sit} – is a standardized value (index) of separate indicator *s* for territory *i* in year *t*.

It should be noted that first of all it is necessary to select the indicators the relationship of which with health responses is proven in the empirical medical-social studies. It is feasible to assign the priority to the indicators studied during the complex dometic and foreign trials on the example of big samplings. For example, the works of J. Peason (2005) using the materials specific for 165 countries of the world justify the relationship between the duration of the life of men and women, infant mortality and gross domestic product per 1 resident taking into account the purchasing power parity (PPP) [Peason J., 2005]. The works of M. Brenner and A. Mooney (1983) prove the relationship between the indicators of the total mortality of population and the level of unemployment. The article of B. Prokhorov (2008) on the example of the federal districts of Russia demonstrates the relationship of expected population lifespan and such macrosocial indicators as the relation of pensions to the minimum living wage value, number of registered crimes, specific weight of unprofitable enterprises and organizations in their total number, etc.

Within the implementation of project "Socially determined risks for the health of population of industrially developed city" (grant of the Russian Humanitarian Science Foundation 12-16-59016-a (p), manager – academician N.V. Zaytseva) based on the materials of the

World Bank Report for 2011 by 155 countries of the world the relationships between the social-economic and medical-demographic indicators were studied.

Five social-economic indicators characterizing the country welfare level and level of life of its citizens were selected for analysis: 1) per capita gross national income (x_1); 2) level of unemployment in % of the working-age population (x_2); 3) share of population with incomes below the minimum living wage (x_3); 4) share of urban population (x_4); 5) number of cars per one thousand of population (x_5). Three social and demographic indicators demonstrated the population health (expected lifespan, total mortality coefficient and infant mortality) [Barg A.O., 2013].

The Spearman's rank correlation coefficients for each pair of indicators were calculated at the first stage that in future allowed for excluding some of them from analysis because the low correlation or absence of it was detected. The analysis of the first stage results demonstrated that the gross national income (GNI) highly correlates with expected lifespan (ELS) (the value of coefficient is equal to 0.857 at the statistical level of significance p<0.005) and with infant mortality (0.882 at p<0.005). The GNI has weak inverse relationship with total mortality coefficient (–0.229 at p = 0.005). The level of unemployment is weakly connected with all medical and demographic indicators accepted for consideration, but the value of indicator for the share of population with incomes below the minimum living wage has medium inverse relationship with ELS (–0.683 at p<0.005) and strong relationship with infant mortality (0.740 at p<0.005).

The contingency of values of indicators for the share of population with incomes below the minimum living wage with the total mortality coefficient is medium, but it is closer to weak (0.321 at p<0.005). The strong relationship between the indicators of the urban population share and ELS (0.735 at p<0.005) as well as the strong inverse relationship between the indicators of the urban population share and infant mortality (–0.702 at p<0.005) is determined. The medium relationship close to weak is detected between the urban population share and total mortality coefficient (–0.322 at p<0.005). The value of indicator for a number of personal cars per one thousand of population is strongly connected with the values of ELS (0.799 at p<0.005) and infant mortality (–0.873 at p<0.005) and it does not have any relationship with the total mortality coefficient.

Thus, the second stage of work which included the building of regression models with one equation considered only those pairs of indicators which had strong or medium-to-strong relationship.

It is established that the ELS value (y_1) to a greater extent depends on such economic indicators as GNI (2.6.2) (the approximation accuracy value is equal to R^2 = 0,660..), the share of population with incomes below the minimum living wage (2.6.3) (R^2 = 0,470), the share of urban population (2.6.4) (R^2 = 0,48) and personal cars (2.6.5) (R^2 = 0,537).

$$y_1 = 5{,}505\ln(x_1) + 22{,}89, \tag{2.6.2}$$

$$y_1 = -0{,}000x_3^2 - 0{,}293x_3 + 76{,}16, \tag{2.6.3}$$

$$y_1 = -2Ex_4^2 + 0{,}329x_4 + 49{,}71, \tag{2.6.4}$$

$$y_1 = 4{,}489\ln(x_5) + 50{,}69. \tag{2.6.5}$$

The infant mortality (y_2) also has significant dependency from GNI (2.6.6) (R^2 = 0,794), share of population with incomes below the minimum living wage (2.6.7) (R^2 = 0,565), share of urban population (2.6.8) (R^2 = 0,468) and number of personal cars (2.6.9) (R^2 = 0,706).

$$y_2 = 4331{,}x_1^{-0{,}65}, \tag{2.6.6}$$

$$y_2 = 1{,}298x_3^{-0{,}953}, \tag{2.6.7}$$

$$y_2 = 145{,}7e^{-0{,}03x_4}, \tag{2.6.8}$$

$$y_2 = 181{,}4x_5^{-0{,}56}. \tag{2.6.9}$$

The data specified demonstrate that the GNI indicators and the number of cars have biggest influence on the ELS and infant mortality, and to a lesser degree – the value of the share of urban population and population with incomes below the minimum living wage.

It is established that the total mortality coefficient does not depend on the macroeconomic indicators selected for this study.

In order to classify the macrosocial indicators and reduce the number of variables it is feasible to apply the factor analysis procedure [Zaytseva N.V. et al., 2013]. The factor analysis was performed using the principal components method during which the initial data array was transformed into the system of general factors not correlating between each other. The classification of macrosocial indicators can be performed on the basis of "factor loadings matrix" which characterizes the relationship (correlations) of initial variables with general factors. The factor is characterized by the group of indicators for which the biggest absolute values of factor loadings were available. The number of factors is determined in accordance with Kaiser's criterion. The factors with own values greater than unity are left for further analysis. The values of orthogonal (not correlating) factors are assigned to each analyzed territory (country, region, municipal structure) as a result of the factor analysis performance. The further analysis procedure includes not the separate macrosocial indicators but the complex macrosocial factors.

The dependence between the macrosocial factors and responses from the side of health is established on the "factor – effect" stage of analysis with the help of correlation and regression analysis. The multiple regression models are built in order to determine the influence of each macrosocial factor included into the analysis separately as well as their joint influence on the simulated health indicator.

The tasks of correlation and regression analysis are as follows: 1) determining the functional relationship between the macrosocial risk factors and health indicators as well as the character of this relationship (i.e. the calculation of mathematical equation for its description); 2) establishing the level of determinacy of the variation of variable characterizing the population health condition, macrosocial risk factors (predictors); 3) forecasting the value of the public health indicators (dependent variable) using the indicators of the macrosocial risk factors (independent variables); 4) determining the contribution of the separate independent variables (indicators of the social risk factors) into the variation of dependent variable (health indicator).

To build the mathematical models, it is possible to assess separately the correlation of indicators of the macrosocial factors and public health indicators, calculate the Spearman's correlation coefficients between the features and check the supposition on the insignificance of the correlation coefficients. If this supposition is rejected, the conclusion on the significant influence of the relevant factors (risk factors) on the responses (health indicators) is made. In addition, if the coefficient is equal to 0.6 and more the conclusion on the availability of the strong relationship between the analyzed components is made. The model shall include only those indicators of risk factors which have close relationship with the studied health indicator. If the strong dependence was detected as a result of analysis of the correlation dependence between the factors these attributes shall not be included simultaneously into the multiple regression model. In addition, it is not recommended to include into one model the indicators characterizing the macrosocial risk factors of direct and indirect effect because they also are interconnected. It is feasible to build several regression models describing separately the relationship between the health and these factors.

The determination indicator R^2 fixing the share of explained health indicator variation at the expense of macrosocial factors considered in the model was calculated for each built mathematical model "macrosocial factor – effect". All the health indicators are ranked under R^2 criterion to determine the health indicators which to the maximum extent depend on the macrosocial factors. The partial determination coefficients are calculated for models which include several macrosocial factors in order to determine the contribution of variation of the separate macrosocial factors into the health indicator variation.

The further calculation of risk associated with the influence of macrosocial factors on the population health is performed. The starting point here is the determination of critical (applicable) values for the influence of macrosocial factors on the health indicators. The

difference between the indicators of morbidity/mortality determined in accordance with established models is established for the current values of macrosocial factors and critical values with allowance for the model determination coefficient and taking into account the severity of negative effect:

$$R_1 = \left[y(x_i) - y(\tilde{x}_i) \right] R^2 g, \tag{2.6.10}$$

where $y(x_i)$ – is a value of morbidity/mortality for the current values of factors;

$y(\tilde{x}_i)$ – is a value of morbidity/mortality for the threshold values of factors;

R^2 – is a determination coefficient;

g – is a severity of negative effect.

The applicable (critical) level of factor ($\hat{x}_i$) can be:

a) the best (the lowest in case of direct influence and the highest in case of reverse influence of macrosocial factor on the morbidity and mortality indicators) value of indicator among the studied territories (for example, the regions of the Russian Federation or the municipal structures of the subject of the Russian Federation);

b) the mean value of indicator on the studied territories;

c) the value determined using the chances relation calculation:

$$\Omega = \frac{\Psi_2}{\Psi_1} = \frac{p_1/(1-p_1)}{p_2/(1-p_2)} = \frac{\frac{m_1}{n_1} \Big/ (1-\frac{m_1}{n_1})}{\frac{m_2}{n_2} \Big/ (1-\frac{m_2}{n_2})}, \tag{2.6.11}$$

where m_1 – is a number of cases with value of factor less than x_i with critical health indicator level;

m_2 – is a number of cases with value of factor more than x_i with critical health indicator level;

n_1 – is a total number of cases with value of factor less than x_i ;

n_2 – is a total number of cases with value of factor more than x_i .

The chances relation is determined by the regression model:

$$\Omega = e^{a_0 + a_1 x}, \tag{2.6.12}$$

where a_0, a_1 – are the regression parameters;

x – is a value of macrosocial factor selected for analysis in the corresponding units of measurement. The point x^* in which the chances ration has the value 1 ($\Omega(x^*) = 1$) is the calculated target value.

The procedure for the assessment of risk associated with the influence of macrosocial factors on the health of population can be supplemented by the classification of the macrosocial health determinants.

This task is solved in two stages. First the groups of territories having the similar indicators for the macrosocial factors prevalence criterion and public health condition are distinguished. The territories are grouped under two grounds: a) public health condition and b) prevalence of the significant types of risk factors for its deterioration. It is feasible to use the cluster analysis in order to solve the grouping tasks.

It should be noted that this study is based on the substantial multidimensionality principle (each territory is represented by the multidimensional vector of observations the size of which is determined by the number of indicators characterizing it in relation to the health condition or the macrosocial factor prevalence). However, in order to solve the local managerial tasks the clusterization can be performed also under the separate indicators of risk factors (having selected, for example, only the indicator "share of population having the

incomes below the minimum living wage per one member of family"). When performing the clusterization, it is necessary to take into account that the variables shall change in the comparable scales. For this the data, unification procedure is implemented.

For classification, it is feasible to use one of the most popular cluster analysis procedures - *k*-means method. This method belongs to the group of iteration reference methods. The advantage of this method is in that during its implementation there is no need to store a quite large matrix of distances or similarities between the objects. The sense of this procedure is in the subsequent clarification at every succeeding iteration of reference points which are set as arithmetical means of observations included into clusters. As a result of it quite compact structures in the geometrical space are determined. Due to that the initial data during the use of procedure are reviewed several times it is possible to compensate the bad selection of initial reference samples which are a zero approximation for the beginning of iterations. The first *k* of observed objects contained in the initial studied data aggregate are used as the initial reference points.

The weak point of used procedure is that the researcher shall set the required number of clusters. It is recommended to use the approach which allows for assessing from the top and from the bottom the number of homogeneous groups in the initial data aggregate to determine the possible number of homogeneous groups in the studied data aggregate. The idea is based on the search of statistically significant local minimums and maximums of variational series composed from the values of the measured distance between the observed objects. Using the *k*-means method for all k values, it is possible to select from the certain interval the optimum breakdown, for example, based on the statistics minimization.

$$\rho = \frac{\bar{r}_{within}}{\bar{R}_{between}}, \qquad (2.6.13)$$

where $\bar{R}_{between} = \frac{1}{C_k^2}\sum_{i=1}^{C_k^2} R_i$ – is an average distance between groups;

R_i – distance between *i* pair of groups;

$C_k^2 = \frac{k!}{2!(k-2)!}$ – number of pairs which can be composed of *k* of different groups;

$\bar{r}_{within} = \frac{1}{n}\sum_{i=1}^{k}\sum_{j=1}^{n_i}(X_{ij} - \bar{X}_i)^T(X_{ij} - \bar{X}_i)$ – average distance inside the group. Here $\bar{X}_i$ – is a reference point of *i* group, X_{ji} – *j* point of observations from *i* group, n_i – number of observed points included into *i* group, and *n* – a number of observations in the initial data aggregate.

The clusterization of territories under the health condition indicators can be performed both separately under the groups of indicators "morbidity", "mortality" and "expected lifespan" (in the end, three options of grouping are obtained) and on the basis of all indicators marking the health condition. Using the second option, it is feasible to exclude from the analysis the population morbidity rates because to a considerable degree they depend on the method of accounting and collection of statistical information.

The result is as follows: a) grouping of territories under the indicators for the prevalence of significant factors where the belonging of territories to different clusters is determined by the degree of expression of certain social factors (the clusterization is carried out separately for each significant factor); b) the list of territories with the health condition indicators which are the worst for the array; c) the list of territories with the biggest prevalence of significant health formation macrosocial factors.

The purpose of the second stage of classification procedure is the establishment of key macrosocial risk factors at the territories with the highest level of the public health deterioration risk under the influence of macrosocial factors. The coupling of the formed groups of territories is performed here in order to determine the territories to the maximum

extent subjected to the public health deterioration risk and establish the groups of social factors having the significant influence on the health condition at these territories.

To determine the territories with the highest level of risk requiring the principal emphasis as well as to identify the priority social risk factors at these territories, it is necessary to implement the coupling of clusters (cross-tabulation) distinguished under the indicators of macrosocial risk factors and health indicators.

The information about the distribution of territories by clusters in the form of columns containing the marker of the territory belonging to clusters (cluster number) is added to the data matrix. Each grouping option has its own matrix column. Further, two grouping options are compared (for example, grouping under the health condition and the indicator of prevalence of the certain significant social risk factor, for example, "high level of unemployment"). The breakdown of the aggregate of territories into groups is performed using the cross-tabulation procedure in accordance with results of clusterization under the selected indicators. The territories with same values of variables – clusterization markers – are included into one group. Herewith, the coupling table is formed the size of which is *rc* (*r* is a number of clusters formed according to the first group of indicators and *c* is a number of clusters formed according to the second group of indicators). Every box of coupling table contains the information about the number of objects included into group determined by the combination of two values (belonging to the one or another cluster formed under the different reasons).

Then, the supposition on the insignificant relationship between two studied groups of indicators is checked. Since the analyzed samplings contain the nominal values (cluster marker), the check of supposition shall be carried out based on the Kramer's statistics calculated using the coupling table. This statistics look as follows

$$V = \sqrt{\frac{\chi^2}{n\ min((r-1),(c-1))}}, \quad \text{where } \chi^2 = \sum_{i=1}^{r}\sum_{j=1}^{c} \frac{\left(n_{ij} - \frac{k_i l_j}{n}\right)^2}{\frac{k_i l_j}{n}}, \qquad (2.6.14)$$

where n – is a volume of analyzed aggregate;

n_{ij} – value located in the line i and column j of the coupling table;

k_i – the sum of the elements of line i and l_j – the sum of the elements of column j of the coupling table.

If this supposition is rejected, it is possible to make a conclusion that such relationship really exists.

The results of the clusters coupling analysis are the information basis for the classification of macrosocial risk factors at the territory. In total, it is possible to distinguish three types of macrosocial risk factors having the different characteristics (Table 2.51).

Table 2.51

The classification of the public health macrosocial risk factors

Characteristics	The types of macrosocial factors		
	A	B	C
Public health condition determination degree (results of correlation analysis)	High	High	High
The degree of the influence of the certain territory on the public health condition (results of cross-tabulation)	High	Medium	Low
Kramer's coefficient value	≥0.7	≥0.5	<0.5
The significance of accounting at making the managerial decisions	Priority	Rather significant	Rather insignificant

If there is a significant relationship (p<0.05) between the clusters distinguished under any of health indicators and any indicator of the macrosocial factors prevalence, then, this risk factor shall be classified using the Table 2.51.

The territories included into the group formed by the combination of values corresponding to the most adverse clusters distinguished both under the health indicators and the indicators of type A macrosocial risk factors prevalence shall be considered as the risk territories. Such territories to the maximum extent are subjected to the public health deterioration risk under the influence of social factors.

The result is as follows: a) the list of territories with maximum level of risk at which the macrosocial factors not only prevail to the maximum extent, but make a significant contribution into the public health condition; b) the list of priority social public health risk factors (A type factors) in relation to which at the risk territories it is necessary, first, to tighten control over the dynamics, and second, to make the managerial decisions aimed at their elimination or compensation.

It is feasible to finish the risk assessment procedure by summarizing the risk information, including the listing of main macrosocial factors which can be taken into account during the risk management process and characteristics of factors decreasing the justification and credibility of the risk assessment results, including the risk assessment uncertainties.

Also it is feasible, using the results of the assessment of risk associated with the influence of macrosocial factors, to prepare the recommendations for authorities on the making of managerial decisions. The recommendations can be structured under the priority of their implementation and under the level of introduction. By the priority the offers can be subdivided into a) urgent, b) priority and c) other. By the level of introduction they are subdivided into a) short-term (the effect from introduction will be obtained within one year) and b) long-term (the effect from introduction will be obtained in few years). The recommendations shall contain the offers potentially influencing on the indicators included into the list for assessing the efficacy of activity of the executive authorities of subjects of the Russian Federation or local self-governing bodies. It is feasible to present the quantitative values of these indicators which can be achieved provided that the submitted recommendations are implemented. It is necessary to demonstrate how the measures on mitigating the certain risk factors influence on a) the population mortality decrease and b) population morbidity decrease (both total and under the separate classes of diseases).

Among the human health risk factors in the modern world the expert of the World Health Organization (WHO) distinguish main ones conditioning about 40% from 57 mln. of deaths annually occurring in the world which lead to the one third of global losses in the years of healthy life. All factors distinguished by WHO as priority ones in some way or other are associated with the lifestyle of people and their individual behavior. In addition, multiple epidemiologic studies demonstrated that namely the peculiarities of prevailing lifestyle associated with excessive nutrition, insufficient physical load and smoking are the key risk factor for the development of cardiovascular diseases and malignant neoplasms.

As opposed to the macrosocial health risk factors, the behavioral factors can be controlled by the human himself, forming his "own risk management policy". And if the influence on the social system in general, increasing the level of the social and economic welfare of country, development of medical, sports and recreation infrastructure, etc. are the elements of the collective risk mitigation strategy, the refusal from the risky lifestyle is the strategy for the individual health risk mitigation.

The assessment of risks associated with the influence of behavioral factors on health is carried out according to the following stages: 1) hazard identification (including the risk factors identification and selection of priority factors for study); 2) assessment of dependence "factor – effect"; 3) risk characterization (Fig. 2.40).

The hazard identification stage provides the detection, collection and analysis of initial information about the behavioral risk factors of individual or social group (population of territory). The main task of the hazard identification stage is a selection of priority indicative risk factors the studying of which allows with sufficient reliability to characterize the levels of the public health condition disorder risks [P 2.1.10.1920-04].

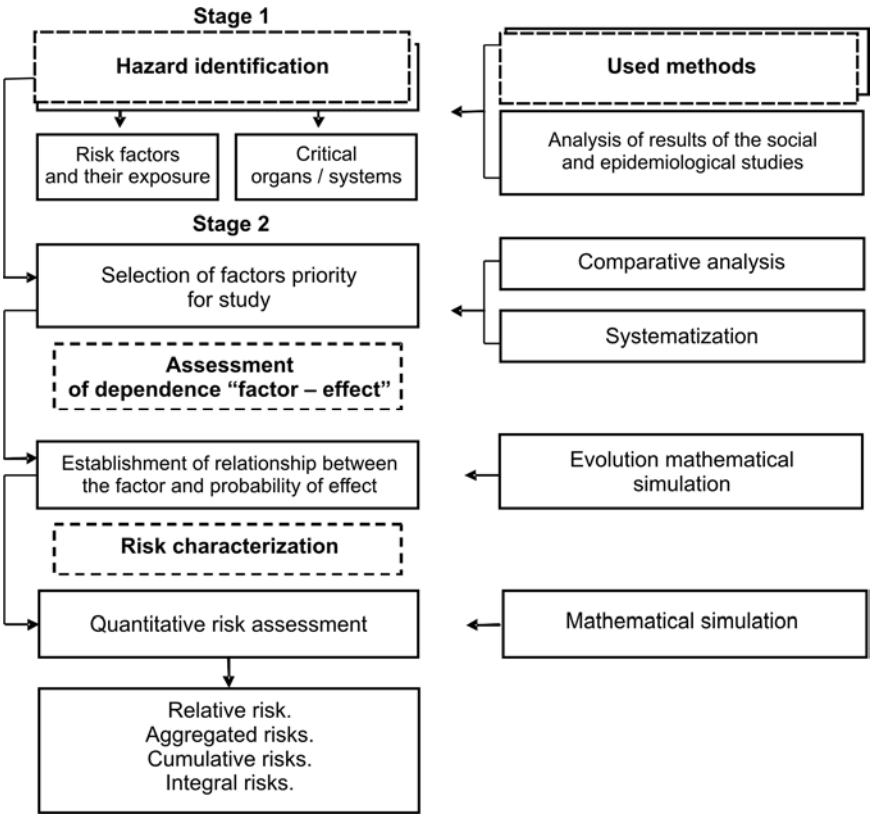


Fig. 2.40. Algorithm for the qualitative assessment of risk associated with the influence of behavioral factors on the health of population

The hazard identification includes two components – behavioral risk factors identification and the selection of priority factors for study. The risk factors identification is performed in order to answer the following questions: a) where the main risk factors are concentrated; b) which of risk factors are the most hazardous for individual (taking into account his social and demographic characteristics, health condition, etc.); c) which of risk factors are the most controllable.

The peculiarities and specific character of the daily activity of individual or social group are the basis for the behavioral risk factors detection. Since it is impossible to obtain complete and reliable information about the risk factors associated with all the aspects of the life activity of individual or social group, it is feasible to collect the information according to the behavioral risk factors structure (Table 2.52).

The criteria for inclusion of factors into the risk assessment procedure are as follows: a) the significance of factor for the occurrence of certain health responses (for example, certain pathologies); b) the ambiguity of the health change nature.

The conduction of sociological study stipulating the use of such methods of questioning as the formalized interview or polling is the main method for the behavioral factors identification.

The questioning itself is preceded by the *operationalization of notions* – procedure for the establishment of relationship between the conceptual framework of study and its methodical tools. The operationalization integrates the problems concerning the formation of notions, technique of measurement and search of indicators. As a matter of fact, the operationalization of notions is a transfer of the content of general notions into the single empirically fixed indicators [Yadov V.A., 2007].

Table 2.52

Behavioral health risk factors [MP 2.1.10.0033-11]

The group of factors	Factors
Irresponsible hygienic behavior	Violation of the sleep-wake schedule. Violation of the work and rest schedule. Nonobservance of the personal hygiene rules. Nonobservance of the domestic hygiene rules. Unsafe sexual behavior
The violations of motion activity	Insufficient motion activity Inadequate motion activity
The failure of nutrition	Unbalanced nutrition. Energetically inadequate nutrition. Eating disorder. Ignoring the safety rules in relation to the food products
Addictive and involuntary conduct	Active smoking (cigarettes, tobacco pipe, shisha). Passive smoking. Alcohol abuse. Use of drugs and non-narcotic psychoactive substances
Irresponsible medical conduct	Untimely visiting a doctor. Unfinished treatment. Self-treatment

The registration of indicators can be carried out on the basis of different methods, techniques and procedures, but with mandatory observance of common rule – extraction of the categories of analysis, units of analysis and units of count. The categories of analysis are the empirical notions established as a result of the theoretical category operationalization and expressing the sense-bearing features of object which can be sociologically measured. The units of analysis are the elements (parts, structures and subsystems) of the studied object which will be measured. The units of count are the quantitative expression of the units of analysis (number of people, their certain actions, statements, opinions, etc.) allowing for fixing the frequency of occurrence of the studied object feature [Tolstova Yu.N., 1998].

The conduction of formalized interview as well as the polling provides the use of *questionnaire* – a form containing the questions marking the one or another health risk factors associated with the lifestyle of respondent.

Usually, the questionnaire consists of three parts: introduction, demographic block and main part. The main task of introduction is to persuade the respondent to take part in the questioning. It shall contain the purpose of conducted questioning and shall demonstrate which benefit the respondent will get from the participation in questioning. In addition, from the introduction it should be understandable who is conducting this questioning and how much time it will be required for answering the raised questions. If the questioning is conducted by mail the introduction can be composed in the form of supporting letter. The demographic block contains the information about respondents: age, sex, belonging to certain social stratum, occupation, marital status, name and address (in case of non-anonymous questioning). In addition, it is necessary to identify the question list itself, i.e to provide it with name, specify the date, time and place of questioning, surname of interviewer (in case of formalized interview). It is not recommended to place the demographic block at the beginning. It is useful to locate the data on the demographic characteristics of respondent in the end of the question list.

When developing the main part of question list the following shall be taken into account: the type of questions (format of responses), the content of questions and their number, the sequence of the presentation of questions in the questionnaire, and the availability of test questions. The reliability of data significantly depends not only from the content of planned information, but also from the structure of the question itself the feasibility of which is stipulated by the certain tasks and conditions of questioning [Yadov V.A., 2007].

The information about the levels of behavioral risk factors specific for the certain individual as well as about the prevalence of these factors in the studied aggregate is the result of the sociological questioning conduction. In case of mass or group questioning the individual profile of risk factors is formed for each respondent.

In a number of cases when the conduction of sociological study is complicated (for example, due to the limitation of resources) it is possible to refer to the statistical data. In particular, such behavioral factors as active smoking, use of alcohol, insufficient motion activity and malnutrition can be characterized based on the indicators collected within the statistical observations (Table 2.53).

The maximally complete list of behavioral risk factors shall be analyzed in order to detect the factors having the increased level of hazard. The leading criterion for selecting the priority factors for study are their critical (criterial) values.

The correct selection of critical values represents the serious methodological problem the existence of which is stipulated by the following factors: 1) the absence (incompleteness) of studies not just establishing the relationship between the risk factor and response from the side of health, but quantitatively parameterizing this relationship, which allows for making the conclusion on the minimum allowable level of behavioral factor not affecting the health; 2) the qualitative nature of factor not allowing for quantitative characterization of its influence on health.

Table 2.53

Some statistical indicators of the behavioral risk factors prevalence

Item No.	Risk factor	The name of indicator	Source
1	Smoking	The retail sales of cigarettes and smokables (pcs. per capita in the age of 15 years and older / year)	Form of FSSO No. 1-TORG "Data on the sales and stocks of goods in the wholesale and retail trade organizations"
2	Alcohol abuse	The retail sales of alcohol drinks and beer in the absolute alcohol (liters per capita / year)	Form of FSSO No. 1-uchet "Accounting of the vloume of retail sales of alcohol products"
3	Hypodynamia	The share of population regularly engaged in physical culture and sports (%). Share of population visiting the physical and recreational clubs, sections and groups (%)	Form of Federal State Statistical Observation (FSSO) No. 1-FK "Data on the physical culture and sports"
4	Nutrition unbalance; the violation of energy balance	The consumption of main food products (per capita / year)	Form of FSSO No. 1-TORG "Data on the sales and stocks of goods in the wholesale and retail trade organizations"

The following can be used as the sources for establishing the critical values of behavioral factors: 1) results obtained during the conduction of large-scale epidemiologic studies; 2) recommendations of global health care organizations; 3) recommendations of national health care bodies and organizations (in case of analysis on the territorial samplings).

For example, when determining the critical value of factor "low level of physical activity" it is feasible to be guided by the WHO recommendations on the physical activity of population [WHO, 2010] establishing the physical activity standard of medium intensity for adults (18 years and older) at the level of 30 minutes per day, 5 days a week, and for children and teenagers – 60 minutes per day.

In relation to such behavioral factor as "alcohol consumption" the solution of issue on the critical value selection can be located in two planes.

First, the reference point can be the results of epidemiologic studies establishing the threshold daily (weekly) doses of alcohol consumption which really negatively affect the health. However, the international scientific discourse does not have the unified point of view in

relation to the "non-hazardous" dose of alcohol - the values vary from 5 to 40 g of pure alcohol per day [Rehm J. et al., 2006]. Herewith, it is important to understand that the role of alcohol in the development of those or another diseases is not similar. For example, M. Marmot in his work [Marmot M.G., 1981] justifies the V-shaped character of relationship between the alcohol and morbidity due to the cardiovascular diseases: for excessively drinking people the morbidity due to the specified reason was significantly less than for non-drinking persons, but the morbidity from all other diseases is, on the contrary, higher. The study of J. Muntwylera and others conducted in 2000 allowed for establishing that the probability of lethal outcome at the consumption from 1 does of alcohol per month and up to 1–2 doses per day occurs more rarely than at complete abstinency [Muntwylera J. et al., 1998].

Second, the international recommended standards in relation to alcohol consumption can be used as the basis for the critical values determination. The World Health Organization (WHO) in the "Guidance on psychological aid at the primary medical assistance institutions" recommends for men to drink not more than 24 g of ethanol per day, for women - not more than 16 g. However, many countries established the national allowable doses of alcohol other than the ones recommended by WHO. Thus, the Australian National Council on the Health and Medicine Studies recommends for men to drink not more than 40 g of pure alcohol per day not exceeding 280 g per week, for women – not more than 20 g per day not exceeding 140 g per day. The recommendations of the National Medical Academy of France establish the allowable level of alcohol consumption for men as 60 g per day and for women – 36 g per day. The Ministry of Health of Spain and Spanish Food Alcohol Research Institute recommends for men and women to drink not more than 30 g of pure alcohol per day.

The most important adverse effects (critical organs and systems) shall be established for each risk factor at the hazard identification stage.

When determining the critical organs and systems it is feasible to be guided by the results of previously conducted social and epidemiologic studies.

For example, in relation to the alcohol abuse it is possible to consider as proven the relationship with the development of such diseases as liver cirrhosis, chronic pancreatitis, breast cancer, prostate cancer, intestine cancer, ischemic heart disease, and diabetes mellitus [Corrao G. et al., 2004]. However, when assessing the risk associated with alcohol abuse it is important to take into account also the medical and social effects – murders, suicides, road traffic accidents (Fig. 2.41).

The works of J. Santamaria established that the share of alcohol factor as the significant reason of attempted suicides makes up from 17 to 22%. It is proved that the drivers drinking the alcohol more often have accidents than those who had zero alcohol content in blood [Compton, R.P. et al., 2002]. The studies of A.J. McLean and others demonstrated that at the content of alcohol in blood at the level of 0.05 g/dl the probability of accident is increased by 1.83 compared to the zero level [McLean A.J., Holubowycz O.T., 1981]. The repeated studies conducted by P. Hurst and others have proved that the risk increases at the lower values of the alcohol content in blood as it was considered before [Hurst P.M. et al., 1994].

The studies of G.Ya. Maslennikova and co-authors demonstrated that at the prevalence of smoking at the level of 63% among men and 9.7% among women the contribution of smoking into mortality from all reasons is 30 and 4%, respectively, and the mortality from the diseases of the circulatory system (DCS) is 29 and 3% [Oganov R.G., Maslennikova G.Ya., 2007]. At that the influence of smoking on the mortality from DCS is quite significant than in the European countries. In 2002 in the Russian Federation 17.1% of the total number of deaths and 13.4% of the total loss of labor capacity were associated with smoking.

The works of V.R. Kuchma and co-authors justify the relationship between the passive smoking of children and teenagers, tension of adaptation mechanisms and decrease of functional abilities and risk of disorders of vegetative regulation of the different organs and systems (Fig. 2.42) [Kuchma V.R. et al., 2008].

It is known that the use of drugs is a significant factor of the mental health deterioration. The risk of coronary insufficiency, bacterial endocarditis and other purulent-septic complications is increased in the users of injectable drugs (Fig. 2.43).

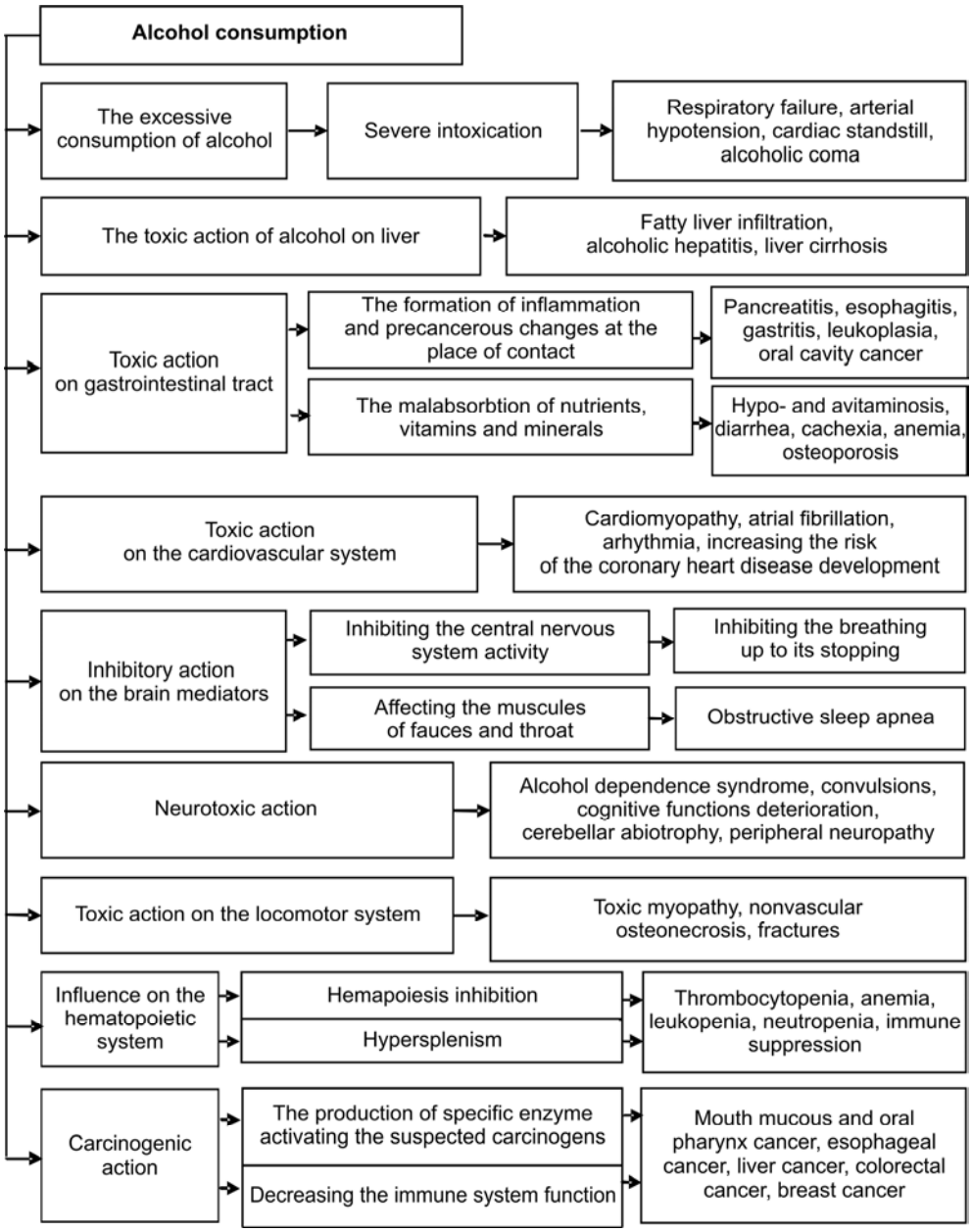


Fig. 2.41. Some effects of the alcohol consumption influence on the human health condition [Elwood J.M. et al., 1984; Keshavarzian A. et al., 1986; Harper C.G. et al., 1986*a*, 1986*b*; Loginov A.S., Blok Yu.E., 1987; Livanov G.A. et al., 2000; Moiseev C.V., 2004; Anderson P., Baumberg B., 2006; Goodsell D., 2006; Moskal A. et al., 2007; Hamajima N. et al., 2002]

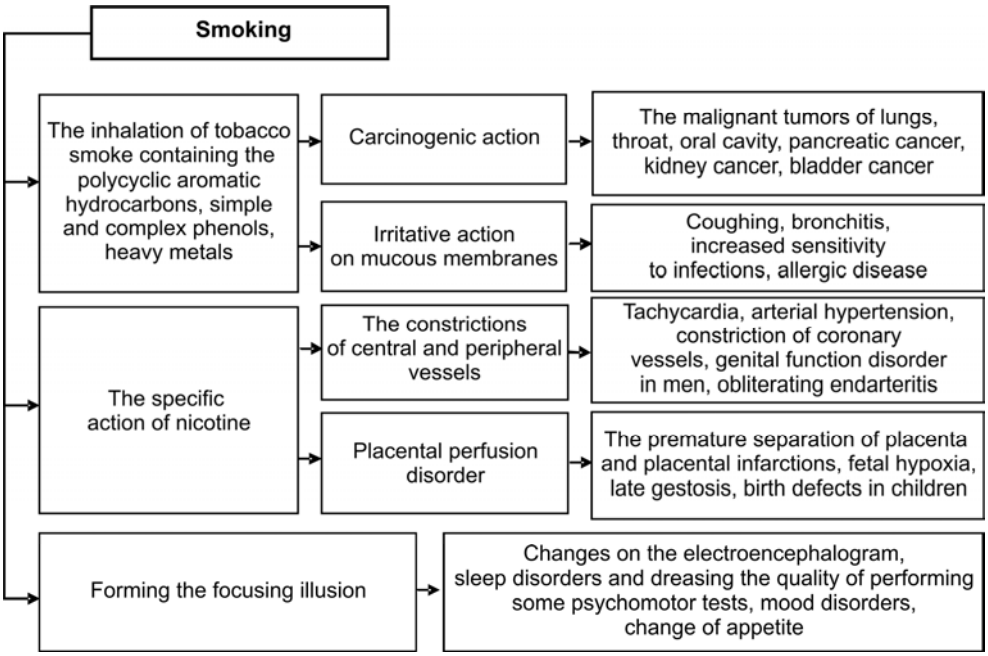


Fig. 2.42. Some effects of the smoking influence on the human health condition [Levshin V.F. et al, 1998; Oganov R.G., Tkachenko G.B., 2001; Schmitz N. Et al., 2003; Schumann A. Et al., 2004; Rehm J. et al., 2006; Vertkin A.L. et al., 2008]

The correct hazard identification, including the credibly established levels of the risk factors action, validly selected criterial values, and objectively detected affected organs and systems, can be the ground for reliable risk assessment, establishment of relationship between the affecting factor and probability for the occurrence of adverse effect.

The second stage of the assessment of risk associated with the influence of behavioral factor on health is the assessment of dependence "factor – response" which represents the quantitative characterization of information about the level of action (expression) for the behavioral risk factors and establishment of relationship between the affecting factor and probability for the occurrence of adverse effect.

The analysis of dependence "factor – response" stipulates the establishment of causation for the harmful effect development at the action of certain factor, detection of the lowest level causing the development of observed effect and determination of the factor increase intensity at increasing the factor action intensity.

The analysis of the results of domestic and foreign epidemiologic studies allows for making a conclusion that the quantitative analysis of dependence "factor – effect" at this stage can be performed at least in relation to four behavioral risk factors – active smoking, alcohol abuse, malnutrition and insufficient motion activity (Fig. 2.44).

The indicator of daily nicotine intake into human body (F^K) is used to assess the dependence "factor – response" in relation to the influence of active smoking on the human health:

$$F^K = \frac{\sum S_i K_i}{n}, \qquad (2.6.15)$$

where Si – is a number of cigarettes (cigars) consumed in day i (pcs.), Ki – is an average content of nicotine in one cigarette (cigar) (mg), n – is a number of days taken for analysis[1].

[1] The recommended period for analysis in the retrospective surveys is 7–14 days.

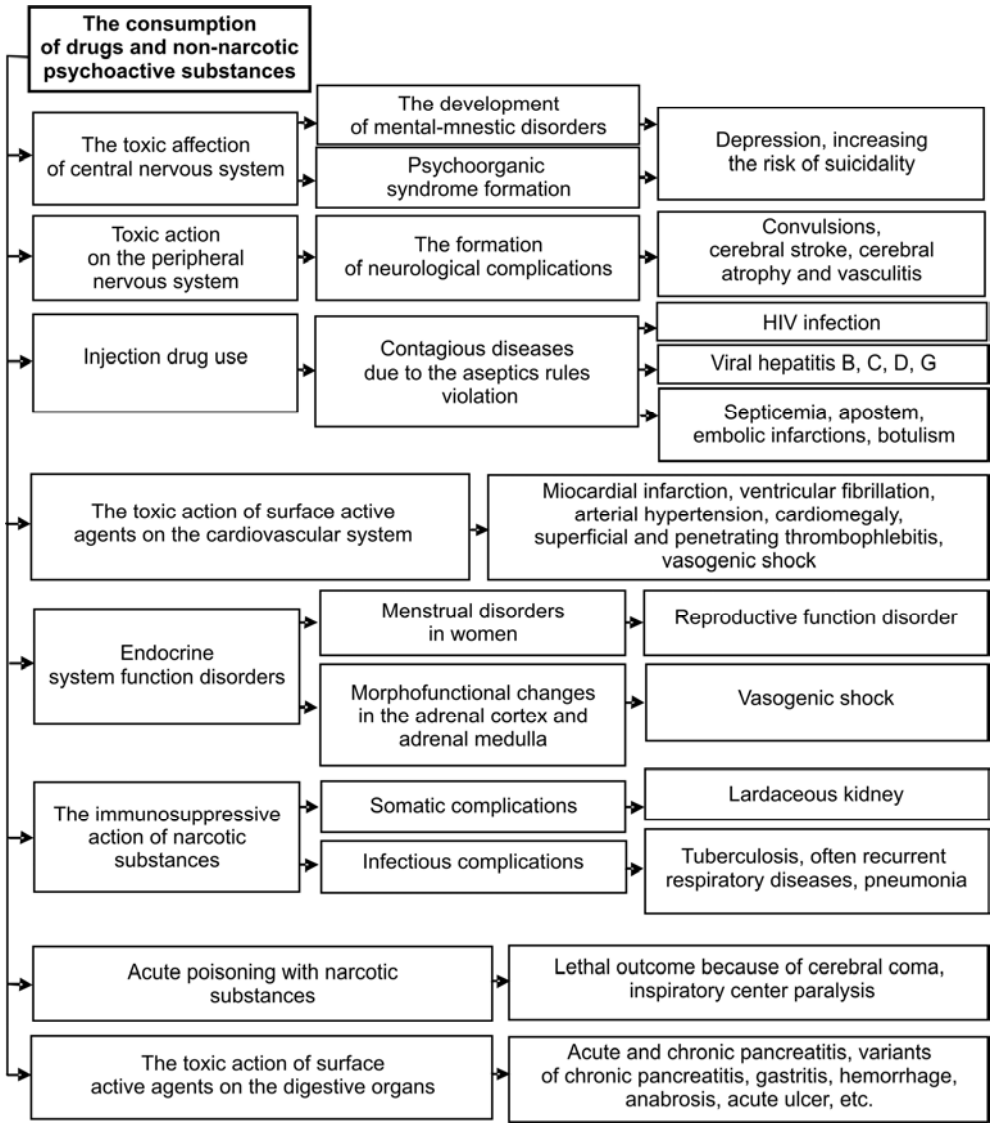


Fig. 2.43. Some effects of the drugs use influence on the human health condition [Traynina E.G., 1984; Cregler L.L., 1986; Matuzok E.G., 1993; Chakko S., Myerburg R.J., 1995; Aleksandrovsky Yu.A., 1996; Dolzhanskaya N.A., 1996; Ling W et. al., 1996; Rokhlina M.L. et al., 1998; Egorov V.F., 1998; Ivanets N.N. et al., 1999; Onishchenko G.G. et al., 2001]

The indicator of daily pure alcohol intake into human body (F^A) is used to assess the dependence "factor - response" in relation to the influence of alcohol abuse on the human health:

$$F^A = \frac{\sum_i \sum_b A_i^b k^b}{n}, \qquad (2.6.16)$$

where A_i^b – is a quantity of alcohol drink of type b consumed on day i (g), k^b – coefficient for transfer of alcohol drink of type b to "pure alcohol", n – is a number of days taken for analysis.

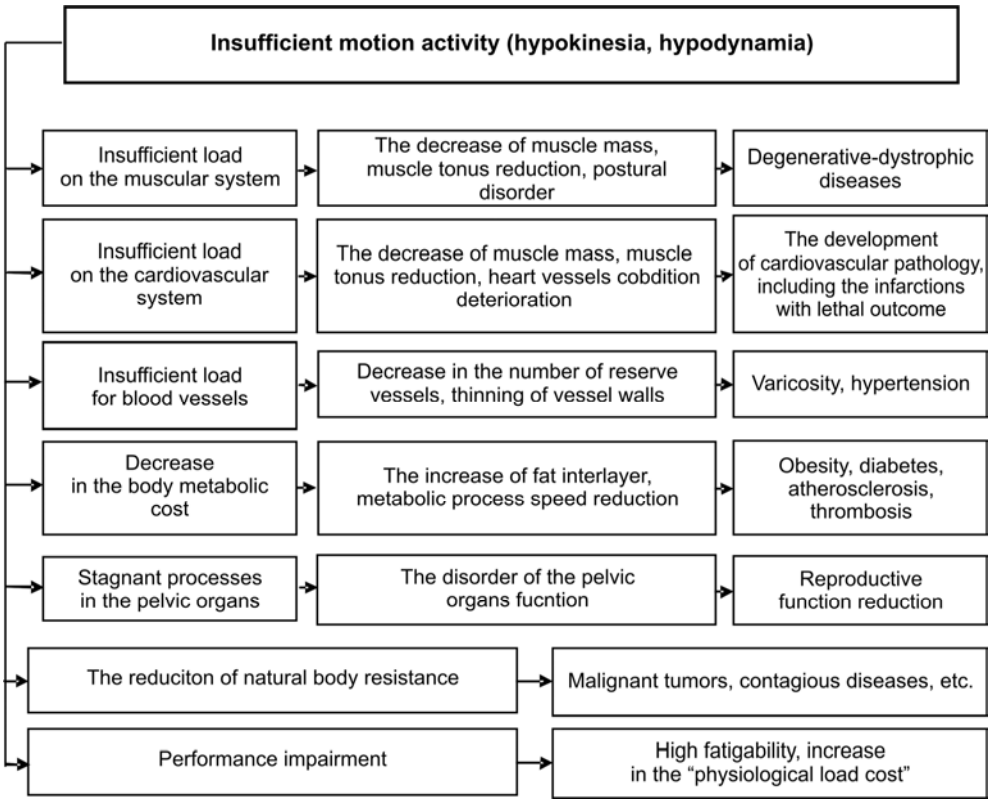


Fig. 2.44. Some effects of the hypodynamia influence on the human health condition [Sirotinin I.N., 1981; Prevention, diagnostics and treatment of Ayerza disease in the Russian Federation, 2000; Arkhipovsky V.L., 2007; Kozlova T.A., 2007; Sheveleva I.N., 2007; Tyurnikov V.M, 2008; Kuznetsova T.Yu. et al., 2009]

To assess the dependence "factor – response" in relation to the malnutrition influence on the human health, it is necessary to calculate the malnutrition integral index (F^P). The initial data for its calculation are as follows: a) frequency of food ingestion during day (N) (normal range for change of values from 1 to 5) and b) share of calories consumed after 6 PM (A) (normal range for change of values from 0 to 100%). To calculate the index, it is necessary to convert the obtained values into the ordinal scale and calculate the indicators $N_{мод}$ (value "3" corresponds to extremely rare food consumption (1 time per day), value "2" – is a rare food consumption (2 times), value "1" – is a normal food consumption (includes the values 3 and more) and $A_{мод}$ (value "3" – more than 70 % of daily ration is consumed after 6 PM, "2" – 50 to70 % of daily ration is consumed after 6 PM, "1" – less than 50 % of daily ration is consumed after 6 PM).

The malnutrition integral index is calculated under formula

$$F^P = \frac{N_{мод} + A_{мод}}{2} \qquad (2.6.17)$$

(the composite indicators are considered as equivalent, the integral indicator value varies from 1 to 3). The critical value is equal to 1.5.

The indicator of duration of weekly physical activity of average intensity (F^D) (min) is used to assess the dependence "factor – response" in relation to the influence of insufficient motion activity on the human health.

The assessment of risk associated with the influence of behavioral factors on the human health can be carried out using the risk evolution simulation as the basic approach. This approach provides a possibility at the set exposure scenarios during the whole life of human to assess the risk for occurrence of disorders of functions of the separate organs and system and to analyze the contribution of separate factors and/or their combinations in the health risk formation.

The dependences "factor – response" obtained on the basis of evolution deterministic models describe the relationship of behavioral factors both with separate and aggregate responses, taking into account the natural body aging processes (Table 2.54).

Table 2.54

Dependences "factor – effect" calculated for the behavioral health risk factors

Effect	Item No.	Dependence
Active smoking		
Lung cancer (per 100 thous.)	1	$P_{t+1} = P_t + \left(0{,}1255P_t + 0{,}00954F^K\right)K$
Oral cavity cancer (per 100 thous.)	2	$P_{t+1} = P_t + \left(0{,}116P_t + 0{,}00138F^K\right)K$
Bladder cancer (per 100 thous.)	3	$P_{t+1} = P_t + \left(0{,}135P_t + 0{,}0018F^K\right)K$
Pancreatic cancer (per 100 thous.)	4	$P_{t+1} = P_t + \left(0{,}12P_t + 0{,}00072F^K\right)K$
Gastric cancer (per 100 thous.)	5	$P_{t+1} = P_t + \left(0{,}139P_t + 0{,}00096F^K\right)K$
Esophageal cancer (per 100 thous.)	6	$P_{t+1} = P_t + \left(0{,}1P_t + 0{,}00156F^K\right)K$
Cervical cancer (per 100 thous.)	7	$P_{t+1} = P_t + \left(0{,}145P_t + 0{,}0015F^K\right)K$
Ischemic heart disease (per 1 thous.)	8	$P_{t+1} = P_t + \left(0{,}199P_t + 0{,}0058F^K\right)K$
Aortic aneurysm[1] ((per 1 thous.)	9	$P_{t+1} = P_t + \left(0{,}1312P_t + 2{,}7\cdot10^{-7}F^K\right)K$
Chronic bronchitis and emphysema (per 1 thous.)	10	$P_{t+1} = P_t + \left(0{,}096P_t + 0{,}0049F^K\right)K$
Brain vessel disease (per 1 thous.)	11	$P_{t+1} = P_t + \left(0{,}162P_t + 0{,}00175F^K\right)K$
Pneumonia (per 1 thous.)	12	$P(t) = \left(1{,}9\cdot10^{-6}(Kt)^4 - 4{,}18\cdot10^{-4}(Kt)^3 + 0{,}0325(Kt)^2 - 1{,}083Kt + 16{,}5\right)\times \left(1 + \left(0{,}19F^K\right)\cdot\left(e^{-Kt\cdot0{,}035} + 0{,}8\right)\right)$
Alcohol abuse		
Liver cirrhosis[1] (per 1 thous.)	13	$P_{t+1} = P_t + \left(0{,}0569P_t + 6{,}6\cdot10^{-7}\left\langle\frac{F^A}{30} - 1\right\rangle\right)K$
Chronic pancreatitis (per 1 thous.)	14	$P_{t+1} = P_t + \left(0{,}172P_t + 0{,}0022\left\langle\frac{F^A}{30} - 1\right\rangle\right)K$
Breast cancer (per 100 thous.)	15	$P_{t+1} = P_t + \left(0{,}184P_t + 0{,}0023\left\langle\frac{F^A}{30} - 1\right\rangle\right)K$

[1] To calculate the "risk of disease" during the first year of life, the risk value is taken as equal to 10^{-6}.

End of Table 2.54

Effect	Item No.	Dependence
Prostate cancer (per 100 thous.)	16	$P_{t+1} = P_t + \left(0{,}164P_t + 0{,}00066\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Ischemic heart disease (per 1 thous.)	17	$P_{t+1} = P_t + \left(0{,}199P_t + 0{,}018\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Ischemic stroke (per 1 thous.)	18	$P_{t+1} = P_t + \left(0{,}13P_t + 0{,}006\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Haemorrhagic stroke (per 1 thous.)	19	$P_{t+1} = P_t + \left(0{,}072P_t + 0{,}00006\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Diabetes mellitus (per 1 thous.)	20	$P_{t+1} = P_t + \left(0{,}0933P_t + 0{,}0014\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Suicide (per 100 thous.)	21	$P_{t+1} = P_t + \left(0{,}0875P_t + 0{,}0115\left\langle \frac{F^A}{30} - 1 \right\rangle\right)K$
Malnutrition		
Gastric cancer (per 100 thous.)	22	$P_{t+1} = P_t + \left(0{,}139P_t + 0{,}0021\left\langle \frac{F^P}{1{,}5} - 1 \right\rangle\right)K$
Ischemic heart disease (per 1 thous.)	23	$P_{t+1} = P_t + \left(0{,}199P_t + 0{,}00054\left\langle \frac{F^P}{1{,}5} - 1 \right\rangle\right)K$

The following designations are accepted in the mathematical models: P_t – the probability of disease at the initial (set) moment of time *t*, per 100 thous. of people; K – time empirical coefficient takan in accordance with Table 2.1. The equations allow for calculating the risk at any set moment of time *t*.

The third stage of risk assessment – the risk characterization – integrates the data obtained at all previous stages of study and it purpose is in the quantitative and qualitative risk assessment, detection and analysis of comparative significance of the existing public health problems.

The calculation of values for the health risk associated with behavioral factor is performed with the help of quantitative methods using the equations (see Table 2.54).

When calculating the individual risk values in relation to the separate health disorders ($R_t^{A/F}$) by solving the equations specified in table 2.54 through the introduction into the relevant equation of the actual or predicted value of factor (F^j) we obtain the probability for the occurrence of *i* disease in the age *j* (P_j^i).

It is feasible to calculate the individual health risk due to the action of behavioral factors taking into account the severity of certain harmful effect (for example, the severity of disease). The severity of diseases g^j in general can be assessed as the relation of disease prevalence to the morality due to this disease. Under the severity assessment results all the diseases can be divided into three groups: minor, severe and medium. If the information is available, it is possible to establish the severity coefficients for each certain nosology, if the information is unavailable, the severity coefficient medium for group is taken. The death severy coefficient is determined as equal to unit value.

Taking into account the disease (health disorder) severity factor, it is possible to calculate the individual risk:

$$R_t^{A/F^i} = P_t^i g^i. \quad (2.6.18)$$

The quantitative characterization of the individual health disorders risk associated with probability of carcinogenic effects development due to the influence of behavioral factors can be performed taking into account the criteria specified in P 2.1.10.1920-04"Guidance on the public health risk assessment at the influence of chemical substances contaminating the environment".

The evolution simulation methods can be used for other types of negative effects associated with the influence of behavioral factors.

When using the evolution simulation for the health risk assessment the additional risk and specific risk index can be calculated. In this case the scale specified in the item 2.2 is used:

– the value which is less than 0.05 can be qualified as the negligible risk practically not affecting the condition of health. The measures on the minor lifestyle correction and selection of more rational self-protecting behavior strategy are recommended.

– the value within the range 0.05–0.35 is qualified as the moderate risk. The measures on the significant local behavior correction in relation to health in some fields of life-sustaining activity are recommended.

– the value within the range 0.35–0.6 is qualified as the high risk. The measures on the principal change of the style and conditions of living concerning, in particular, the complex change of the food mode and ration, complete refusal from vicious habits, etc. are recommended;

– the value which is more than 0.6 is qualified as very high risk. The measures on the urgent change of lifestyle requiring the active external interference are recommended.

The recognition of social contextualization of the behavioral health risk factors leads us to the necessity to develop the methods for determining the social environment contribution into the formation of risks associated with behavioral factors. Because the behavior is not only the social phenomenon but is stipulated also by the psychological and genetic personal qualities, it is probable that only a part of behavioral health risks will be socially determined.

2.7. The assessment of health risk associated with climatic changes

During the last decades the extremely high speed of global warming and climate change raises a lot of concerns. It is established that the human economic activity significantly affects the climate. These changes of climate are multivarious and are manifested in the change of frequency and intensity of climatic abnormalities and extreme weather events. The expected changes of climate will inevitably affect the life of people in all the regions of our planet and in some of them they will become the perceived threats for the population welfare.

Recently the change of climate is considered as one of the leading factors affecting the public health. There is both a direct influence at the expense of increase in the number of days with extremely high and/or low temperatures, floods, storms and typhoons, and indirect, stipulated by the influence of environmental or social and economic factors (increasing the area of arid lands, decreasing the volumes of high-quality drinking water, etc.). The influence of climate changes in cities is combined with adverse effect of contaminated ambient air on the public health.

According to the WHO evaluations annually the climatic changes are the cause of 1 to 10% of deaths among the elder age groups and in the world – more than 150 thous. of additional deaths and 5.5 mln. of years of disability per year. This makes up 0.3% of the total number of lethal outcomes and 0.4% of the total number of disability years, respectively. By 2050 the further increase in the number of lethal outcomes associated with climate warming will be increased approximately by 1–1.5 %. The economic loss from additional mortality as a result of climatic changes in the world varies in a large range – from 6 to 88 bln. dollars per year.

According to the Climatic Doctrine of the Russian Federation the negative consequences of expected changes of climate for the Russian Federation include increasing the public health risk (increase in the level of morbidity and mortality of population). The assessment of risks and losses associated with them is considered as the most important component during the development and planning of measures on the adaptation to the changes of climate. The quantitative risk assessment allows for determining the approximate value of certain consequences (diseases and early death) in different scenarios.

High temperatures, extreme weather events, the propagation of contagious diseases, malnutritions, etc. are considered as the main risk factors associated with climatic changes. The heat and cold "waves" are considered as the one of priority factors of climatic changes affecting the increase in the level of morbidity and mortality of population of the Russian Federation. In these guidelines the population categories which are the most sensitive to the potential effects of these risk factors and for which a risk assessment can be carried out include the elderly people and children.

Main provisions on assessing the health risks associated with the change of climate are harmonized with WHO documents [MP 2.1.10.0057–12].

The meteorological indicators used for assessing the influence of climatic changes on the public health include the daily average and maximum indicators of the ambient air temperature, relative humidity, atmospheric pressure, wind speed and the amount of precipitation.

The source of information on the meteorological data is an interregional territorial hydrometeorology and environment monitoring body (administration) and subordinated state authorities - hydrometeorology and environment monitoring centers.

For the simultaneous assessment of air temperature and humidity it is feasible to use the effective air temperature which is calculated under the formula

$$T_{app} = -2,653 + 0,994(T_{air}) + 0,0153(T_{dewpt})^2, \quad (2.7.1)$$

where T_{app} – is an effective temperature;

T_{air} – is an air temperature;

T_{dewpt} – is a dew point.

The dew point is calculated based on the information about the relative humidity under the formula

$$Td = \frac{b\gamma(T,RH)}{a-\gamma(T,RH)}, \quad (2.7.2)$$

where γ is calculated under the formula

$$\gamma(T,RH) = \frac{aT}{b+T} + \ln(RH/100), \quad (2.7.3)$$

where T – is an air temperature;

RH – is a relative humidity;

a and b – are the constants equal to 17.271 and 237.7, respectively.

The average daily values of temperature and humidity are used to calculate the average daily effective temperature, and their maximum values are used to calculate the maximum effective temperature.

If there is no meteorological station at the studied territory the data of nearest meteorological stations can be used.

The data of meteorological station located in the radius of up to 300 km is used for determining the average daily temperature, the data of meteorological station located in the radius of up to 1200 km is used for determining the average monthly temperature.

The data of meteorological station located in the radius of up to 50 km is used for determining the average daily humidity and daily amount of precipitation, the data of meteorological station located in the radius of up to 400 km is used for determining the average monthly humidity and amount of precipitation.

Under the influence of meteorological factors on the public health, especially at the territories with technogenic contamination it is necessary to assess the modifying effect from the influence of substances contaminating the ambient air (suspended substances, sulfur dioxide, nitrogen dioxide, nitrogen oxide, carbon oxide and other substances included into the monitoring program).

The source of information on the ambient air contamination monitoring is the data of interregional territorial hydrometeorology and environment monitoring body (administration) and subordinated state authorities - hydrometeorology and environment monitoring centers as well as the laboratories of industrial enterprises and organizations. The results of measurements at the observation stations are the initial information about the ambient air contamination.

The most distributed diseases characterized by the sensitivity to climatic factors include:

– respiratory diseases: acute respiratory infections (J00-J22), allergic rhinitis (J30), chronic obstructive pulmonary diseases (J40-J44), bronchial asthma (J45);

– circulatory diseases: diseases characterized by increased blood pressure (I10-I15), ischemic heart disease (I20-I25), conduction and cardiac rhythm disorders (I44-49), cerebrovascular diseases (I60-I69);

– endocrine diseases: diabetes mellitus (E10-14);

– injuries, poisonings and other consequences from the influence of external causes: injuries (S00-T14), frostbites (T33-35), drownings (W69-70), suicides (X60-84);

– mental diseases: alcoholic psychosis (F10);

– intestinal infections: salmonellosis (A02), shigellosis (A03) and other bacterial intestinal infections (A04) and poisonings (A05), viral intestinal infections (A08);

– transmissive diseases: Lyme disease (A69.2), tick-borne viral encephalitis (A84), Aden fever (A90-91), West Nile Fever (A92.3), yellow fever (A95), malaria (B50-54), leishmaniasis (B55), African human trypanosomiasis (B56), Chagas disease (B57), onchocercosis (B73), filariasis (B74).

The groups of population with increased level of risk for which the assessment of influence of climatic changes on the health indicators is conducted include:

– children (0 to17 years old);

– elderly (60 years and older) *и* advanced old age people (75 years and older));

– persons with chronic diseases suffering from respiratory diseases, circulatory diseases, diseases of nervous, urinary and endocrine systems;

– the persons of active working age, including the persons working in the open air;

– indigenous people.

The influence of meteorological factors on health shall be assessed under the following indicators:

– the mortality of population;

– the morbidity of population under appealability;

– the morbidity of population under the hospital admission data;

– the appealability of population for emergency medical services.

The primary document registering the cases of death is the form No. 106/u-8 "Medical certificate of death" and "Death record" issued by the Civil Registry Offices. The collection of initial information about the population mortality for the study is conducted by two methods: copying the data from the form No. 106/u-8 and death record in the Civil Registry Offices on all cases of death in the city (district); based on the existing electronic mortality databases formed in the medical information and analytical centers in the subjects of the Russian Federation or at the territorial body of the Federal State Statistics Service.

The sources of information about the cases of diseases are the "Outpatient ticket" (form 025-6 (7) / u-89) and "Inpatient medical record" (form 003/u). The collection of initial information is conducted through copying or based on the electronic databases of medical and preventive organizations, and territorial compulsory medical insurance funds.

The source of information about the daily cases of contagious diseases is the "Urgent notification on the contagious disease, food, acute occupational poisoning, unusual response on vaccination" (form 058/u) or the log-book for the contagious diseases accounting (form 060/u). The information about the number of diseased per month can be obtained from the

reporting forms "Data on the contagious and parasitic diseases" (form 2) and "Data on the outbreaks of contagious diseases" (form 23–09). Data on the number of cases of contagious diseases are registered by the center for hygiene and epidemiology of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance in the subject of the Russian Federation.

The collection of information about the tick-borne viral encephalitis includes the number of persons affected by the ticks attack ("bitten by ticks"), number of persons having the tick-borne encephalitis, indicators of the amount of ticks ("filling of territory with ticks") and data on infecting the ticks by the virus of tick-borne encephalitis.

The source of information about each case of applying for emergency medical services is the "Emergency call sheet" (form 110/u). Daily data on the appealability for emergency medical services are formed at the first-aid stations or in the departments of emergency medical services.

For the quantitative determination of relationship between the meteorological parameters and public health indicators it is necessary to have the daily data or date grouped by weeks or months on the number of deaths, diseases, hospital admissions and applications for emergency medical services at the studied territory. If the daily data are used in the analysis, the recommended observation period shall be not less than 6 years, and in case of data per month – not less than 20 years.

The source of information about the average annual number of population under the age-sex pattern is a territorial body of the Federal State Statistics Service.

The collection of data for the economic assessment of damage

Economic indicators for calculating the public health damage associated with climate-sensitive diseases include the indicators characterizing the economic losses from the increase of morbidity and mortality level in the groups of risk associated with meteorological factors during the period of existing consequences (the studied period).

The data for the economic assessment of damage shall comply with the requirements of MP 5.1.0029-11 "Guidelines on the economic assessment of public health risks under the influence of the living environment factors".

The sources of data for calculating the economic damage from increase in the population mortality level associated with meteorological conditions are as follows:

– the territorial body of the Federal State Statistics Service which provides the information about the annual gross regional per capita product and average annual salary in the region;

– medical information and analytical centers in the subjects of the Russian Federation and territorial body of the Federal State Statistics Service which provide the data on the average age of persons died within the studied period.

The sources of data for calculating the economic damage from increase in the population mortality level under the appealability, morbidity according to the hospital admission data and appealability of population for emergency medical services associated with meteorological conditions (in relation to the studied climate-sensitive diseases and groups of population with increased risk level) are as follows:

– medical information and analytical centers in the subjects of the Russian Federation or medical and preventive organizations, territorial compulsory medical insurance funds providing the data on the cost of one application in relation to disease, one day of outpatient and inpatient treatment, cost of one call for emergency medical services, average number of days of outpatient and inpatient treatment as well as the average expenses for purchase of pharmaceutical and medical products, rendering of medical services obtained for disease above the state guarantees;

– territorial social insurance funds providing the data on the average size of payment for one day of incapability under the sick leave certificates in relation to diseases, average number of daily work time losses per one case of disease;

– the territorial body of the Federal State Statistics Service which provides the data on the number of employed population (shares of employed in the total number of the studied group of population);

– the territorial tax authorities of the Federal Tax Service which provide the data on the intake of deductions from the corporate income taxes, individual income taxes, unified social tax for the considered period;

– territorial population social protection administrations providing the data on the average annual size of pension coverage due to the illness (disability) and share of disabled pensioners in the total number of the studied group of population.

The meteorological data shall pass the three stage of control: syntactical, semantic and spatial. As a rule, the observations of meteorological parameters at the meteorological stations include eight measurements per day. To assess the influence of air temperature, relative humidity, atmospheric pressure and wind speed on the health, it is necessary to calculate the average daily and maximum daily values.

When assessing the modifying actions of substances contaminating the ambient air, the average daily and maximum daily concentrations are used.

Data on the number of deaths, diseases, hospital admissions, calls for emergency medical services and data on the meteorological variables shall be presented in the same time and geographical resolution.

Data on the health indicators shall be analyzed both in general among the whole population and under the separate age groups, for example, children (0–17 years), working-age population (18–59 years) and elderly people (60 years and older).

In order to carry out the qualitative determination of climate-sensitive diseases it is necessary to have the daily data on the number of diseases (deaths), hospital admissions, calls for emergency medical services under separate classes, categories or nosologic forms of diseases. However, if there are not enough cases or they are not registered daily, it is possible to summarize the cases for one week or month. Therefore, the meteorological factors shall be presented as average and maximum weekly or monthly values for the same time interval.

The small number of cases under the separate categories or nosologic forms of diseases is non-representative and will not allow for detecting the statistically significant relationships. That is why it is feasible to combine the separate categories and nosologic forms into the corresponding classes of diseases in order to increase the number of cases.

If the data on the emergency medical services are analyzed, the calls shall not be represented under the separate categories or nosologic forms of diseases due to the difficulty of the accurate diagnosis verification, and it is feasible to study them always in general under the classes of diseases.

To eliminate the influence of potential factors which can affect the conclusive assessment results, the database shall include the information about the years, months, days of week, holidays, and influenza epidemics. When studying the acute intestinal infections it is necessary to remove the persons suffered in case of group and breakout morbidity from the database.

The logic control of all entered data on the meteorological indicators is conducted. For example, the field "temperature" shall contain the values within the limits corresponding to the seasons. The data quality monitoring can be carried out using the graphical methods. The variable chart construction allows for easy detection of "suspicious" values falling out of the common range, for example, the sign error made when entering the temperature.

The data on the morbidity, hospital admission, calls for emergency medical services and population mortality are monitored. For example, the value of field "date of birth" shall not exceed the value of field "date of death"; the value of each field shall not exceed the database filling out date. Then the compliance of age, date of birth and date of death is checked. The logic control of all the encoded data (such as the cause of death, diseases, etc.) is carried out: they shall contain only the allowable values specified in the reference books.

The databases containing the information about the one or another health indicator and meteorological factors shall be checked for the omitted values. If the information for three days in a row is absent in the database, the average monthly data can be used instead of the omitted values. If the information for one day is absent in the database, the mean value of adjacent days can be used instead of the omitted value. The sensitivity analysis shall be performed after filling out the gaps in the database. If 30% of values for the one or

another meteorological parameter is absent in the database, such variable shall be excluded from analysis.

When assessing the influence of meteorological factors on the number of diseases and hospital admission the Sundays can be excluded if the lags will not be used in the model. In this case the lag means that interval in days (or months) between the change of meteorological indicators (or the ambient air contamination indicators) and change of mortality, morbidity, etc., at which the statistically significant relationship is detected between them. If the model with lag is expected, the mean value from the number of diseases/hospital admissions for Saturday and Monday is used for Sunday.

When detecting the deviating values of the number of cases of the one or another indicators which exceed the limits of three standard deviations, this "deviation" shall be replaced by value complying with two standard deviations.

The methods for assessing the influence of meteorological indicators on the public health condition

The epidemiological analysis of monthly dynamics for the health indicators

The seasonality means the typical variations of the studied health condition indicator during the calendar day or epidemic year expressed by the long-term confinedness of increases and decreases in its level to the certain months stipulated by the influence of periodical (seasonal) factors.

The seasonality index and attributive fraction of seasonal causes are used to study the peculiarities of the monthly dynamics of the public health indicators for the long-term period. Both indicators are calculated for every month for the long-term period based on the intensive indicators of mortality, morbidity, hospital admission and calls for emergency medical services.

To calculate the seasonality index, the intensive indicators are summarized separately for every month for all the years of the analyzed long-term period. The obtained final values are divided by the number of the years of observation which results in the 12 monthly mean values (Y_i). The sum of monthly mean values is divided by 12 to calculate the total mean value (Y_0). The seasonality index is calculated under the formula

$$I = \frac{Y_i}{Y_0} 100\ \%, \qquad (2.7.4)$$

where I – is a seasonality index in %;

Y_i – is the monthly mean values for the long-term period;

Y_0 – is a total mean value.

If the seasonality index value for any month exceeds 100%, it is considered that the seasonal factors were activated in this month.

The attributive fraction of seasonal causes (seasonal influence) shows which percent of cases (diseases, deaths) is stipulated by the seasonal causes. It is calculated under the formula

$$А\Phi = \frac{(Y_i - Y_0)}{Y_0} 100\ \%, \qquad (2.7.5)$$

where АФ – is an attributive fraction in %;

Y_i – is the monthly mean values for the long-term period;

Y_0 – is a total mean value.

Statistical analysis

First the descriptive statistics and building of charts are performed. It is necessary to calculate the arithmetical mean, minimum and maximum values and the standard deviation for every studied variable. It is possible also to calculate the geometrical mean, median,

mode and the certain percentiles (for example, 10th and 90th). These values represent the central tendency and spread of values for the time range variables. The calculations of all required time range characteristics are carried out using some standard statistical package (SAS, SPSS, STATA, Excel).

The charts for all variables shall be built. This will allow for detecting some regularities in the time range behavior: seasonal variations of the air temperature or the ambient air contamination levels; different long-term tendencies in the data. The graphical analysis allows for more accurate selection of mathematical model for assessment of the studied relationship and helps to detect the falling out values which will allow for detecting if they are associated with the input errors or not.

When assessing the ambient air temperature influence on the public health indicators it is necessary to determine the heat and cold waves as well as the threshold values of temperatures above or below which the change in the indicators of mortality, morbidity, population hospital admission and calls for emergency medical services is observed.

The heat wave represents five consecutive days and more during which the average daily temperature exceed the 97th percentile; herewith, at least for three days the average daily temperature shall exceed the 99th percentile. For cold waves the boundaries are determined at the level of the 3rd and 1st percentiles. The wave with duration of five to eight days is called as short. The wave with duration of 9 days and more is called as long.

The threshold air temperature values are determined at the level of the 90th and 10th percentiles of the all temperature values for the studied long-term period. The threshold values are calculated for average daily, maximum, average daily effective and maximum effective temperatures.

One of the analysis options is a time series analysis with the help of which the dependence between the variations of meteorological indicators (atmosphere contamination indicators) and the public health condition indicators is established.

To assess the availability of relationship between the meteorological factors and the number of deaths, diseases, hospital admissions and calls for emergency medical services, the correlation and multivariate regression analysis for discrete dependent variables (Poisson multivariate regression analysis, negative binomial regression analysis) is used.

When carrying out the regression analysis the correction for long-term trends, seasonality, effect of days of week, days-off and holidays, influenza epidemics and other possible factors able to affect the final assessment results is performed. The correction for other meteorological factors is performed to assess the air temperature influence only.

In many cases the air temperature variations result in the change of the number of cases of deaths, diseases, hospital admissions and calls for emergency medical services only in the certain time interval, i.e. lag. Lad 0 means that both variables belong to the same day (month), lag 1 means that the mortality (morbidity, etc.) was analyzed in the day or month following the one to which the meteorological indicator belongs, etc. When assessing the daily data the lag is 1 to 14 days, monthly data – 1–2 months.

The results of assessment of the meteorological factors influence on the public health indicators are the values of relative risks; the indicators of the average percent contribution of meteorological indicators to the morbidity and mortality; the indicators for the growth or decrease of mortality, morbidity, hospital admissions and calls for emergency medical services in percent at increasing or decreasing the values of meteorological parameters (concentrations of air pollutants) by the established growth of indicator (for example, by 1 °C of temperature). The established indicators are provided with confidence intervals of not less than 95%.

The linear and radial diagrams are used for the graphical presentation of the time ranges data. Using the linear diagram it is possible to reflect the daily (monthly) number of deaths, diseases, hospital admissions and calls for emergency medical services as well as the average daily (average monthly) values of air temperature or other meteorological factors (or concentrations of contaminants). Herewith it is feasible to build the linear diagrams with two axes, where the one axis is used for placing the values of dependent variable, and other – for independent variable. The radial diagrams are used for reflecting the monthly health indicators or average monthly values of meteorological factors.

The assessment of the population risk of diseases, deaths, calls for emergency medical services and hospital admissions

When presenting the risk assessment results under the data of epidemiologic studies as the risk ratio - *RR* the population risk ($R_{\text{поп}}$) is calculated under the formula

$$R_{\text{поп}} = Z(RR - 1), \tag{2.7.6}$$

where Z – is an absolute number of deaths, hospital admissions and calls for emergency medical services in the studied population for the same period under the data of long-term observations.

For more complete population risk presentation it is feasible to calculate its value under the upper and lower limit of 95% confidence interval *RR*.

When presenting the risk assessment results under the data of epidemiologic studies as the percent increase or decrease in the number of deaths, diseases, hospital admissions and calls for emergency medical services at the change of temperature by 1 °C the population risk ($R_{\text{поп}}$) is calculated under the formula

$$R_{\text{поп}} = Z \frac{\Delta Z}{100} \Delta t, \tag{2.7.7}$$

where ΔZ – is a percent increase in the number of deaths, diseases, hospital admissions and calls for emergency medical services at the change of temperature by 1 °C;

Δt – is an air temperature deviation above (for heat waves) or below (for cold waves) threshold temperatures, deg °C.

The assessment of economic damage associated with the public health risk at the influence of weather and climatic conditions

The calculation of economic damage for the public health associated with the influence of meteorological conditions is carried out in accordance with MP 5.1.0029-11 "Guidelines on the economic assessment of public health risks under the influence of the living environment factors" [MP 5.1.0029–11].

The economic damage from the public health risks at the adverse influence of meteorological conditions represents the sum of the health harm values occurring due to to the increase in the population mortality and morbidity level (in accordance with section 5 of these guidelines).

The initial data for the economic damage calculation are as follows:

– the population risk of diseases; the number of early deaths, calls for emergency medical services and hospital admissions (additional cases associated with meteorological factors);

– economical indicators for calculating the public health damage as a result of climate-sensitive diseases.

The results for the public health economic damage calculation performed under the studied climate-sensitive diseases among the different groups of population with increased level of risk are used for developing the strategy and measures on the adaptation to the change of climatic conditions and selection of the risk management scenario taking into account the available resources (in terms of value) and possibility of their implementation. In this case the assessments of prevented public health damage performed for the different options (scenarios) for the adaptation measures implementation are used.

To select and assess the strategy and measures on the adaptation to the change of climatic conditions, the methodical approaches specified in MP 5.1.0030-11 "Guidelines on the economic assessment and justification of decisions in the field of the public health risk management under the influence of the living environment factors" [MP 5.1.0030-11].

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3. THE METHODICAL ASPECTS OF THE HEALTH RISKS MANAGEMENT

3.1. The principles and algorithms of the health risks management

In the conditions of continuously changing and complicating world and the growth of technogenic pressing on the public health in order to ensure the sanitary and epidemiological welfare it is necessary to have the assessments for forecasting the negative medical and demographical processes and preventing the conversion of local and individual problems into the regional and common. In this situation the risk assessment methodology practically does not have any equivalents which is confirmed by its wider use in many fields of state management [Dubrovsky V.Zh., Kuzmin E.A., 2010; Yayli E.A., Muzalevsky A.A., 2007; Sheluntsova M.A., 2011; Timashova T., 2012; Vorobyev Yu.L., 2004]. Herewith the risk management methodology and technologies within the structurally complex social and economic systems at the level of states and regions is at the stage of establishment.

The necessity to create the multilevel health risk management system (federation – region – territory – object) is recognized by many researchers [Onishchenko G.G., 2014; Kuzmin S.V. et al., 2010; Zaytseva N.V. et al., 2007; Yakusheva M.Yu., Sergeeva M.V. 2008] and is stipulated by a whole number of problems existing in the country which include:

– increasing the number of hazardous facilities with close to threshold or completely exhausted technical and technological resources that is accompanied by the stable high number of territories and population which for long time are exposed to the significant as well as abnormal technogenic contamination;

– the insufficient efficacy of the state management and regulation concerning ensuring the safety of territories and population (herewith the safety is considered as the absence of unacceptable life and health risk);

– the weakening of the state supervision functions on ensuring the chemical and biological safety as a result of retardation legal and methodical framework from the demands of management in the changing social and economic conditions;

– the insufficient social responsibility of a number of economic entities being the sources of threats and hazards for the health of population during the transfer of state accents from the supervisory business management methods to the selfregulating;

– the absence of principally new approaches to the spatial development of territory and settlements, underestimation of the public health risk indicators and factors;

– the insufficient financing of measures on the mitigation and prevention of the threats and risks;

– the incomplete equivalence of criteria for establishing the permissible loads on the living environment from the real impact;

– in a number of cases – the political priority of economic activity indicators before the safety values.

The effective management of sanitary and epidemiological situation and health risks is in the sufficient minimization or prevention of adverse influence of risk factors on the population and the stable development of society is a result of management. The latter stipulates such levels of medical and demographical indicators which evidence the absence of unacceptable risks formed by the human living environment.

This chapter based on the experience of scientific justifications and methodical basics of the health risks management already accumulated in Russia and abroad considers only some issues concerning the most relevant aspects: risk management principles and algorithms, justification of making the managerial decisions on the risks minimization, including on the basis of economic health risk assessment, the justification of hygienic standards under the health risk criteria (risk-based standards), risk-oriented monitoring and supervision activity, risk management elements on the basis of spatial analysis, medical-preventive health risk management technologies.

In general, the public health risks management is a sequence of actions staying within the classic scheme for management of processes and phenomena and including the stages of planning, implementation and monitoring as well as the management system efficacy analysis as a whole (Fig. 3.1).

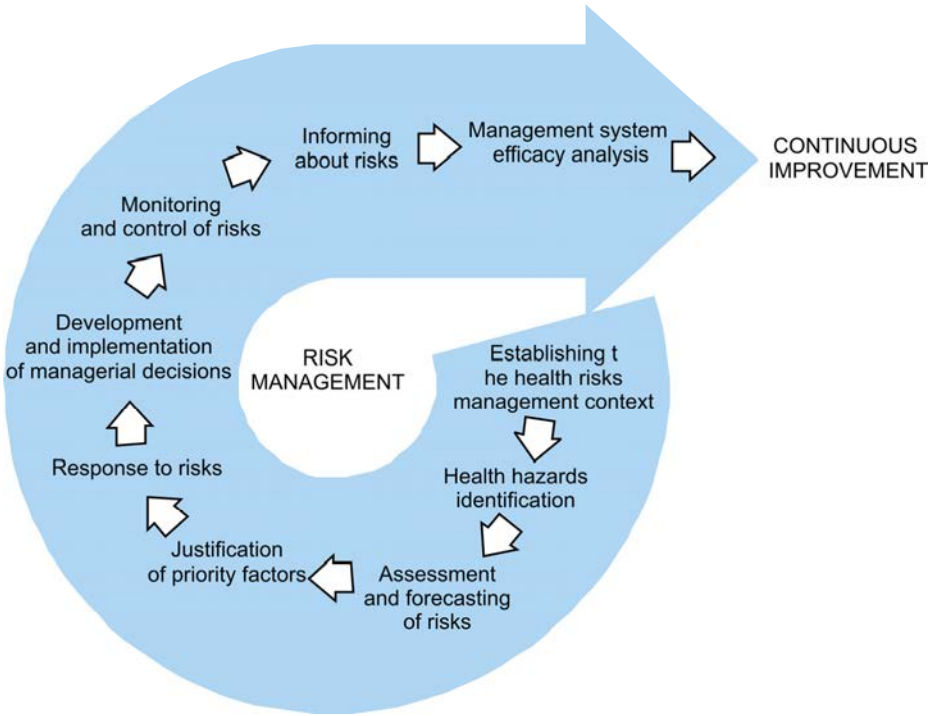

Fig. 3.1. The conceptual model of the public health risks management in the field of ensuring the sanitary and epidemiological welfare of population

Within this scheme

♦ *at the stage of planning the following is performed:*

– a general analysis of the situation within which the process shall be performed,

– management (establishing the risk-management context),

– determining the strategic and tactical goals and objectives of management, determining the criteria for optimizing the system of measures,

– the assessment of the whole aggregate of health risks (through the identification of all the types of hazard),

– prioritizing the risks taking into account the scale and severity of one or another consequences for health, including in the economic context,

– forming the action plans and programs taking into account the economic efficacy of every measure and optimal terms of implementation;

♦ *at the stage of implementation the following is performed:*

– the introduction of developed measures,

– control over the fulfillment of plans and programs,

– the monitoring of the achievement of intermediate (indicative) values;

♦ *at the stage of reporting and management efficacy analysis the following is performed:*

– the assessment of the degree of the achievement of the set goals and objectives,

– residual health risk assessment after the fulfillment of the planned measures (monitoring and control of risks),

– the informing of all concerned parties about the risks,

– management efficacy assessment in general.

The decisions on new strategic and tactical goals and objectives and, respectively, on new action plans and programs taking into account both the accumulated risks and losses of the past periods and newly occurring threats and hazards are made based on the final management system efficacy assessment.

General principles and typical scheme for the health risks management are appropriate for any level – federal, regional, local and objective. The certain algorithms of actions and plans and programs of measures can be developed, implemented and formed on their basis.

The models for the public health risks assessment and management at the level of region or separate problems of sanitary and epidemiological situation are considered by a number of authors [Bykov A.A., Murzin N.V.; 1997; Sokolova L.A., Prokopenko L.V., 2009; Dikonskaya O.V., 2010; Fridman K.B. et al., 2011; Berezin I.I., Suchkov V.VB., 2013] and in the one or another way are implemented in some regions of the country and abroad [Zaryaeva E.V., 2011; Kuzmin S.V. et al, 2011; Mekhantyev I.I. et al., 2012]. Concerning the sanitary and hygienic aspects the issues of the health risks management when exposed to the environmental factors [Gurvich V.B., Kuzmin S.V., Dikonskaya O.V. et al., 2000–2014; Surzhikov V.D., 2006] and labor conditions (Izmerov N.F., Denisov E.I., Prokopenko L.V.) are the most illustrated. The approaches to the radiation risks assessment and management are developed [Tikhonov M.N., Muratov O.E., 2013; Rakitin A.I., Gorsky G.A., 2013; Komarov Yu.A., 2011, 2014].

Thus, the works of Kuzmin S.V. and others (2010, 2011) describe the regional health risks management system within the activity of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance which includes the following sages: a) risk factors identification, the assessment of interrelation between the different risk factors, selection of priority risk factors for management; assessment of reliability and sufficiency of data on the risk factors and their influence of the health of population; b) public health risk assessment with the separation of priority risk territories and groups, the establishment of target acceptable risk level; c) the planning of risk management activity; d) public health risk assessment during the selected scenario implementation, the establishment of the residual risk level; e) risk management activity monitoring; f) the assessment of effects and results of ensuring the sanitary and epidemiological welfare and public health risk management, comparison of obtained results with expected. The work of Yu.A. Komarov (2011) considers the approach to the risks management based on the assessment of risk as the losses in the system "reliability - safety - efficacy", use at the probabilistic analysis of safety of the fuzzy sets theory, Herewith the main outcome of management system is a justification and implementation of minimum sufficient measures on ensuring the safety of facility.

The approaches developed by the laboratory of integrated automated design systems IPMash of the Russian Academy of Sciences [Karasev V.V., 2013] within which a

number of logical and probabilistic risk models with any logical complexity of the event relationships is offered are of great interest. To a greater extent, the models are tested on the examples not associated with the health of population but the scientific direction is prospective also for the tasks of state, municipal and objective management.

The state level of management is oriented, first of all, to the management of risks through the program and target planning that allows for implementing the system of long-, medium- and short-term measures on the achievement of strategic goals through the minimization of the most significant health risks [Kondratiyev-Firsov V.M., 2008]. Herewith the general methodology and algorithm for the health risks management when exposed to the living environment factors at the level of country or region is preserved being supplemented by the elements of system analysis, "expenses – benefits" analysis, etc.

The typical algorithm for the management of risks through the program and target planning system is shown in Fig. 3.2.

Since the risk assessment methodology allows for assessing the risk from the separate hazard factors and sources as well as from their aggregate the decision maker obtains the possibility to assess the structure of risk, carry out the comparative analysis of different risks and distinguish the most significant among them. The latter allows for determining the urgency and priority for implementation of those or another measures and, respectively, the priority and urgency of their financing.

The risk evolution simulation is also aimed at the solution of the same task. The method provides the possibility to assess the risk growth period and qualitative change of its characterization (for example, the transformation of acceptable risk into the unacceptable or moderate risk – into high) and make the justified decision on the possibility to take not the short-term but the medium- and long-term measures. In other cases the risk evolution assessment allows, on the contrary, to forecast the unobvious health risk in the conditions of long-term low-level exposure that allows for taking the measures which could be omitted during the use of other analytical methods.

The number of executive bodies of the country gradually switches to the risk management systems creating and improving own experience of such management organization. Thus, the structure of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance builds a cascade risks management system where each stage is provided with relevant functions and information and analytical data, first of all, with the results of control and supervisory activity and social and hygienic monitoring (see chapter 2 for more detailed information).

The risk management task shall be solved using the most effective method, especially in the budget financing conditions.

Certainly, the risks management system requires the management criteria. The issues concerning the acceptable risk levels are discussed in chapters 1 and 2 of this monograph. The role of economic assessments increases significantly if there are no common criteria for the medical and demographic risks assessment. The latter not only provide the comparative values of losses which probably are inflicted by the factors of different origin but also allows for comparing the efficacy of measures on the risks minimization taking into account both the prevented losses and the expenses for the measures implementation. The role of qualitative economic risk assessment increases significantly when there is a possibility to choose from the aggregate of alternative options of optimum decision ensuring the largest probability of the best result at the lowest expenses and losses.

If the algorithm for making the decisions on the public health risks management in the tasks on ensuring the sanitary and epidemiological welfare has the character common for the management in general, the certain measures are determined by the specific character of the objects of management which include both the sources and factors of risk as well as the population as the risk recipient. Herewith the risk aversion methods as well as the risk diversification and prevention and/or compensation methods are used. At the same time the success and efficacy of management depends significantly on the loading points, selection of the list of measures and making the decisions on the priority and urgency.

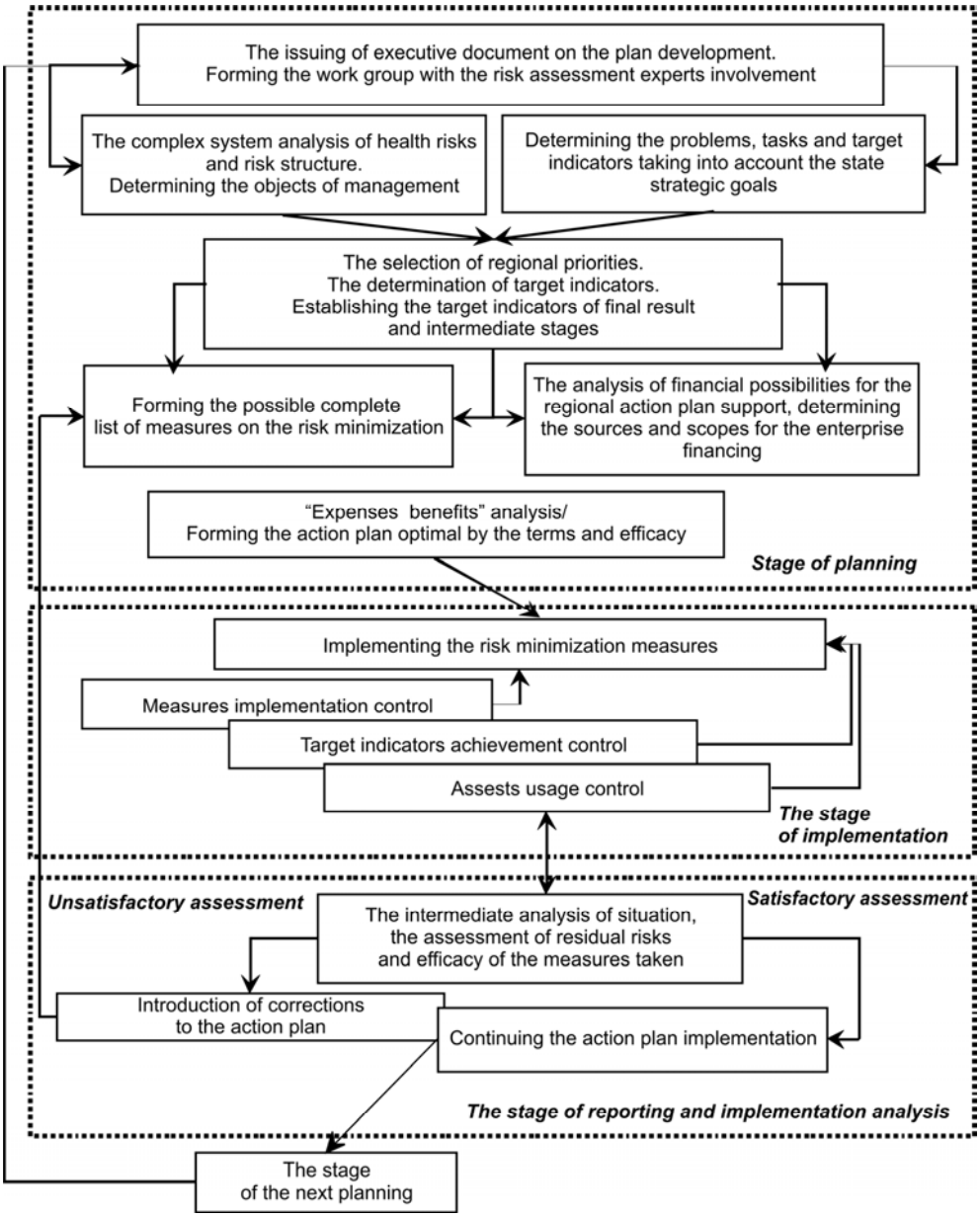

Fig. 3.2. Typical algorithm for the health risks management through the program and target planning

The main types of measures on the health risks management at the level of state are determined by the federal legislative documents. Thus, the Federal Law No. 52-FZ dd. March 30, 1999 "On the sanitary and epidemiological welfare of population" determined the types of measures designed for the management of threats having the sanitary and epidemiological nature at the level of state. The Federal Law "On environment protection" provides the measures on the management of ecological threats.

The Federal Law No. 29-FZ dd. January 2, 2000 "On the quality and safety of food products" determines the measures on the management of safety for food products, materials and items, etc. In virtue of that the notions "threat" and "safety" are very close to the notion "risk" practically all actions established by law can be qualified as the risk management measures, including the health risks. Examples for the comparison of managing actions to the risk management methods classification are specified in Table 3.1.

In general, the state management is essentially aimed at the risks aversion (refusal) and localization of risks that completely meets the strategic goals and objectives of the country. The hygienic standardization and supervision are the main tools for the health risks

Table 3.1

The comparison of managing actions provided by the Russian legislation with the risk management methods classification

Managing actions	Classification as the risk management method	Federal law
State sanitary and epidemiological standardization	Risks aversion (refusal)	No. 52-FZ dd. March 30, 1999 "On the sanitary and epidemiological welfare of population"
The prevention of diseases	The localization of risks (prevention, mitigation of risks)	
State sanitary and epidemiological surveillance	Risks aversion (refusal), localization of risks	
The formation and maintenance of open and public federal threat information resources	Risks aversion (refusal), localization of risks	
The mandatory confirmation of the compliance of products with the sanitary and epidemiological requirements	Risks aversion	
The licensing of activity posing a potential hazard for human	Risks aversion, the acceptance of risks	
The state registration of chemical and biological substances potentially hazardous for human	Risks aversion, the acceptance of risks	
The hygienic education and training of population and healthy lifestyle promotion	Risks aversion (refusal), localization of risks	No. 52-FZ dd. March 30, 1999 "On the sanitary and epidemiological welfare of population"
The development and implementation of the federal and regional target programs on the ambient air protection	Risks aversion (refusal), localization of risks	No. 96-FZ dd. May 4, 1999 "On the ambient air protection"
The submission of claims on the environment harm compensation	The compensation of risks	
Environmental insurance	The transfer of risks	No. 7-FZ dd. January 10, 2002 r. "On the environment protection"
The economic support of entrepreneurial, innovative and other activity aimed at the environment protection	The localization of risks	No. 7-FZ dd. January 10, 2002 r. "On the environment protection"
Bringing to responsibility for violating the legislation of the Russian Federation on ensuring the sanitary and epidemiological welfare of population	The compensation of risks, the localization of risks, the prevention of risks	No. 52-FZ dd. March 30, 1999 "On the sanitary and epidemiological welfare of population"
The state expert review of construction documents	Risks aversion (refusal)	Town planning code

management when ensuring the sanitary and epidemiological welfare of population. Herewith, both can result in the development and implementation of the certain measures on the primary and secondary risks prevention and significant role in the risks management. Such methods of the state surveillance as the licensing of activity posing the potential hazard for human, registration of chemical and biological substances potentially hazardous for human, etc. are aimed at the localization or complete refusal from risks.

Herewith, it is obvious that to consider the management as the risk-oriented it is required to have the methodical support for each type of managing actions from the perspective to include into the decision making system the results of assessment or forecasting of risks. Thus, the hygienic standardization system in order to be considered as the health risks management method shall include the risk assessment elements when establishing the criteria for the permissible exposure limits. Disease prevention measures shall be oriented to the risk groups and have the specific territorial referencing to the most hazardous areas, etc.

The methodical developments in relation to supporting the risk-oriented management systems in the field of ensuring the sanitary and epidemiological welfare and preserving the health of population are carried out by a number of scientific groups. Some approaches are represented in the chapters 2, 3, 6, 8 of this monograph.

Methodical approaches to justifying the measures on the risks minimization

The sets of measures on the public health risks management to a significant extent depend on the decision making level. At the federal and regional levels the risks management is carried out mainly through the legal methods and implementation of the development strategies. In this regard, the selection of directions for improving the state legislative base and strategies for the social and economic development of the country and regions complying with the existing risks is extremely important. It should be noted, that the irrational selection of priorities (first of all, in the economic sphere) is determined by the experts as the highest and the most significant among 36 main strategic risks for the sustainable development of Russia [Strategic risks of Russia, 2005; Vorobyev Yu.L., 2004].

In this regard, the correspondence of forming the action programs and plans on the health risks minimization shall be provided with reliable science-intensive information and analytical support based on the complex dynamic assessment of the objects, areas, territories and factors of risk and data on the actual level of medical and demographical indicators (as a reflection of the whole aggregate of risk factors affecting the population). The latter is implemented through the systems of social-hygienic and ecological monitoring, the collection and processing of statistical data on the demographical and medical-demographical indicators of the public health condition.

At the level of federation and regions the program and target risk management planning can be based both on the expert evaluations and on the results of assessment of relationship between the risk factors and medical and demographical indicators. Herewith the methodical approaches to distinguishing the priority health risk factors are based on summarizing the maximally complete information about all potentially harmful factors which can cause the health disorders in the exposed persons. The collection of data on the number or density of population at the surveyed territory is performed in parallel. The sources of such information can be the data of the local self-governing bodies, bodies of the Civil Registry Offices, compulsory medical insurance fund, etc. The risk assessment allows for determining the contributions of the one or another factor into forming the increased levels of the population mortality and morbidity. The methodical basics of such analysis are specified in the chapter 7 of this monograph.

Namely in relation to the factors, sources and causes forming the largest contributions to the negative medical and demographical processes at the level of federation and regions for the tasks of strategic planning it is feasible to perform the territories classification procedure. The classification can be performed using the different methods, including, for example, the cluster analysis method. This allows for detecting the problems typical for the object of

assessment (region, administrative territory, area, object) and considering within the federal and/or regional target programs the common or unified measures on the risks reduction or prevention (Fig. 3.3).

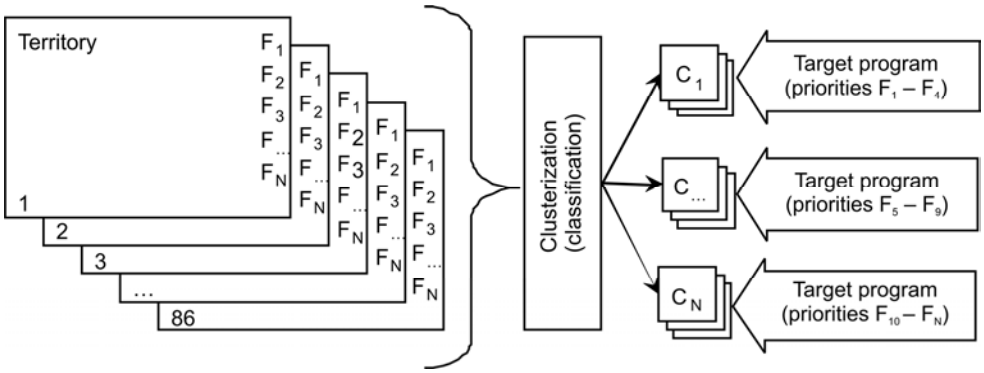

Fig. 3.3. General diagram for justifying the interregional target programs and/or typical action plans

Thus, for example, under the cluster analysis of data from the social and hygienic monitoring of 2009–2013 we distinguished the groups of territories of the country with different indicators of the population mortality, morbidity and lifespan, social-economic and sanitary-hygienic characteristics which is more detailed described in the section 7.1.

The priorities making the largest contribution to the medical and demographical losses and priorities requiring the measures on management were determined and distinguished for every group. Thus, it was established that for a number of regions the achieved level of the social and economic indicators does not have a significant influence on the negative tendencies of the medical and demographical indicators then the sanitary and hygienic parameters of the living environment definitely are the risk factors of increased mortality and morbidity of population. It is obvious that for the regions with these priorities the most important are the target regional programs and action plans on the improvement of quality of drinking water, soils and ambient air. Namely the measures in this direction will probably lead to the most significant results.

For the group of other regions of the country priority are the measures aimed at increasing the social and economic indicators of the life of population. Actions aimed at improving the sanitary and hygienic characteristics can be ineffective against the preserved high levels of the priority risk factors.

The justification of action plans on the management of risks at the level of municipal structures can and shall be supported by the spatial analysis and mapping the risks the methodical approaches to which are specified in chapter 3. This allows for distinguishing the areas with the maximum public health risk.

The priority sources of risk which shall be the object of management are distinguished in the same way. Herewith, the optimum is the risk sources categorization and the differentiation of measures both under their urgency and their content. The categories of objects under the chemical hazard level are specified as an example (Table 3.2).

The risk sources identification and distinguishing the contributions of the separate economic entities to the formation of such risks are carried out for the unacceptable risk areas.

The contribution of factor to the total risk is assessed as the relation of risk formed by the factor *i* to the common risk. But the assessment of contribution from the separate sources of hazard (economic entities) to the formation of common risk at the territory is of greater interest. The assessment of contribution of the economic entity to the risks for population at the territory of settlement (or at the certain area of this settlement) is performed

Table 3.2

The categories of the chemical hazard objects under the risk indicators

The category of object	Criteria	Measures at the object	Measures for population residing within the object activity area
1	2	3	4
Category I Object with very high level of hazard	$10^{-3} < TCR$, $THI>5$ (one index and more), more than 1000 of population	Conduction at the chemical hazard objects of *urgent* measures on decreasing the level of chemical influence on the health of population (sanitary and hygienic, technological, organizational. etc.). Informing the authorities on the situation and dynamics of its changing. Mandatory *continuous* control at the direct source of hazard (installation, tube, process equipment, etc.)	*Emergency* medical-preventive, rehabilitative and health-improving measures on the risk mitigation. Informing of population. Mandatory continuous impact on-line monitoring of situation at the exposure area
II category Object with high level of hazard	$10^{-4} < TCR < 10^{-3}$, $1<THI<5$ (one index and more), more than 100 persons	Conduction at the chemical hazard objects of *operative* measures on decreasing the level of chemical influence on the health of population (sanitary and hygienic, technological, organizational. etc.). Informing the authorities about the situation. Mandatory *continuous* control at the direct source of hazard (installation, tube, process equipment, etc.)	*Operative* medical-preventive, rehabilitative and health-improving measures on the risk mitigation. Informing of population. Systemic observations with increased frequency over the priority risk factors
III category Object with medium level of hazard	$10^{-6} < TCR < 10^{-4}$, $THI = 1$ (one index and more), any population	Conduction at the chemical hazard objects of *planned* measures on decreasing the level of chemical influence on the health of population (sanitary and hygienic, technological, organizational. etc.). *Planned* control at the direct source of hazard (installation, tube, process equipment, etc.)	*Planned* medical-preventive, rehabilitative and health-improving measures on the risk mitigation. *Planned* monitoring of the risk factors under the estended program.
IV category Object with low level of hazard	$TCR < 10^{-6}$, $THI<1$ (every index), any population	Does not require additional measures on decreasing the chemical hazard object influence. *Planned* environmentally friendly, technological, managerial and administrative measures on keeping the facility in the standard condition	Does not require the additional measures on decreasing the risk level. The risk factors are subject to the periodical control under the shortened program for ensuring the anitary and epidemiological welfare of population

based on building the "risk fields" or "risk matrix" which represent the system of points representative for the surveyed territory of the permanent staying of population. The risks formed by every separate source of hazard and total health risks are assessed at the points. Herewith, the different risks (carcinogenic, acute noncarcinogenic, chronic noncarcinogenic) shall be assessed separately because they are formed by the different factors and different sources (3.1.1–3.1.3).

The contribution of object to every parameter of risk at each point (x, y) is expressed in general:

$$\Delta(x;y)^{o} = \left(Risk^{o} / Risk^{TERR}\right)100, \quad (3.1.1)$$

where $\Delta(x; y)^{O}$ – is a contribution of object to every parameter of risk at each point of matrix (cm);

$Risk^{o}$ – a level of risk created by the surveyed hazard object at each point of matrix;

$Risk^{TERR}$ – a total level of risk from all the chemical hazard object (at this territory) at each point of matrix.

The contribution of the chemical hazard object to the carcinogenic risk level at each point (x, y) is expressed in general:

$$\Delta(x;y)^{o} = \left(TCR^{o} / TCR^{TERR}\right)100, \quad (3.1.2)$$

where $\Delta(x; y)^{O}$ – is a contribution of object to the carcinogenic risk level at each point of matrix

TCR^{o} – a level of carcinogenic risk created by the surveyed chemical hazard object at each point of matrix;

TCR^{TERR} – a total level of carcinogenic risk from all the chemical hazard objects (at this territory) at each point of matrix.

The contribution of the chemical hazard object to the acute noncarcinogenic risk level at each point (x, y) can be expressed:

$$\Delta(x;y)^{o}_{ac} = \left(THI^{o}_{ac} / THI^{TERR}_{ac}\right)100, \quad (3.1.3)$$

where $\Delta(x; y)^{o}$– is a contribution of object to the level of acute noncarcinogenic risk at each point of matrix;

THI^{o}_{ac} – a level of acute noncarcinogenic risk created by the surveyed chemical hazard object at each point of matrix;

THI^{TERR}_{ac} – a total level of acute carcinogenic risk from all the chemical hazard objects (at this territory) at each point of matrix.

The contribution of the chemical hazard object to the chronic noncarcinogenic risk level at each point (x, y) can be expressed:

$$\Delta(x;y)^{o}_{cr} = \left(THI^{o}_{cr} / THI^{TERR}_{cr}\right)100, \quad (3.1.4)$$

where $\Delta(x; y)^{o}$– is a contribution of object to the level of chronic noncarcinogenic risk at each point of matrix;

THI^{o}_{cr} – a level of chronic noncarcinogenic risk created by the surveyed chemical hazard object at each point of matrix;

THI^{TERR}_{cr} – a total level of chronic noncarcinogenic risk from all the chemical hazard objects (at this territory) at each point of matrix.

The contribution of object to the total risk indicator can be recognized as insignificant (small) if its value does not exceed 10%; the contribution from 10 to 50% shall be considered as the average contribution of source (enterprise) to the risk indicator at the level of 51–75% shall be recognized as high. If the source forms more than 75% of the total value of all health risks, its contribution shall be recognized as main.

Thus, using the methods of cluster analysis, the spatial assessment of risks and the calculation of the contribution of separate factors and sources to the total health risk at the measures planning stage will distinguish the facts, sources, risk areas and risk groups which shall become the objects of management.

The justification of priority measures at the local level

The selection of measures on minimizing the priority risk factors is determined, as a rule, by experts or using the economic assessments under the method "expenses – benefits" [Brent R. J., 1999; Applied cost-benefit analysis, 1996].

Benefit from decreasing the health disorders risk due to the planned or implemented managerial decisions is the difference between the value of prevented compensated damage associated with health disorders and costs of the managerial decisions implementation (3.1.5).

$$W = U - Z, \tag{3.1.5}$$

where W – is a benefit from the health disorders reduction;

U – is a value of compensated damage;

Z – is a value of costs for the managerial decisions implementation.

The benefits are classified as planned (design) and actual (observed). Planned benefits are calculated based on the planned expenses and actual benefits – on the basis of real expenses. The detailed description of methodical approaches to the economic assessments in the health risk management system is specified in chapter 3.

The main condition required for the calculation of benefits is a conformance of damages and expenses. Often the economic indicators expressed in the units of financial resources are applied for measuring the values used for the calculation of benefits. In addition, it is allowed to use as the units for measurement of benefits the demographical indicators (number of population, demographical load, etc.), social indicators and so on.

In case of difference between the methods for measuring the damages and expenses it is necessary to introduce the special conversion or measures interconnection operator. Usually the line function or conversion factor is used as such operator.

$$\mu(U) = k\mu(Z), \tag{3.1.6}$$

where $\mu(U)$, $\mu(Z)$ – are the measures of damages and expenses, respectively;

k – is a conversion factor.

For example, when using as the damage measuring unit the aggregate number of years of non-staying alive to the pension age and as the expenses measuring unit – the financing for the rehabilitation measures program in rubles the notion of cost for one year of life can be introduced. The absolute and relative benefit characteristics are used as the indicators of benefit from the health disorders risk mitigation.

The absolute benefit shows the exceedance of compensated damages over the expenses and is expressed in the units of damage.

The indicator of relative benefit (or the measure efficacy indicator) characterizes the efficacy of managerial decisions and is expressed either in relation "rubles of benefit per 1 ruble of expenses" or in percent.

$$\tilde{W} = \frac{W}{Z} 100\ \%, \tag{3.1.7}$$

where $\tilde{W}$ – is an absolute benefit indicator expressed in percent.

The field for applying the indicators characterizing the benefits from the health disorders risk mitigation determined by the hazard factors covers the tasks on planning the sanitary and hygienic, medical and preventive measures as well as the other aspects of managerial decisions.

The selection of priority measures based on the "expenses – benefits" analysis allows for considering the efficacy of decisions taken on the risks management, taking into account all the benefits provided by the measure (Fig. 3.4).

It should be noted that the "expenses – benefits" method is extremely required as of now at the local (objective) level. Herewith, the assessment of regulatory influence of legislative and regulatory legal acts as of now does not consider the economic component of the public health losses prevented as a result of the regulatory acts implementation that in a number of cases results in the underestimation of significance and efficacy of the decisions taken.

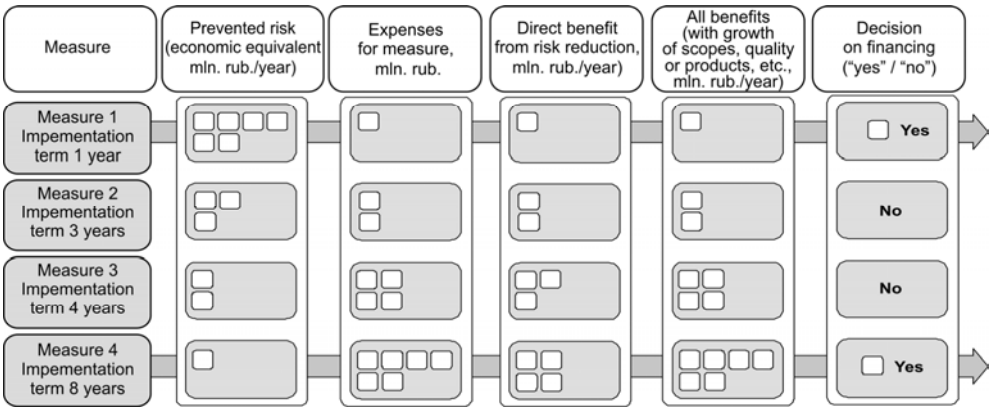

Fig. 3.4. The scheme of assessment "expenses – benefits"

The approaches to the economic methods of management are considered in the following section.

3.2. Methodical approaches to justifying the making of managerial decisions based on the economic health risk assessment

The health risk assessment results are the basis for justifying the managerial decisions and selecting the priority measures on the public health protection. However, the presentation of these results as the probability of negative responses or as additional cases of disease or death cannot be to the full extent the justification of measures on the minimization of risk and mainly the expenses for these measures. In this relation the economic health risk assessment can be determined as the key aspect determining the risks management and assessment of its efficacy.

Herewith the solution of two tasks is required:

– selecting the most effective measure;

– assessing the economic feasibility and efficacy of measures.

In both cases the main criterion will be the prevented risk (damage) for the health of population. However, if when solving the first task, the comparison of efficacy can be performed using the natural indicators the quantitative assessment of economic efficacy and the solution of the second task requires the use of financial indicators of the prevented damage.

The damage as the component of risk during the assessment of the medical and ecological situation can be expressed in natural (disease incidences, lifespan reduction) and cost form (additional expenses for medical services, social security, value of non-obtained national product) [Zaytseva N. V. et al., 2004].

In the last case we can speak about the economic risk the main components of which are the risk of additional expenses or the cost risk and the income non-obtainment risk [Golub A.A., Strukova E.B., 1995; Bykov A.A., Murzin N.V., 1997]. Some authors [Kiselev A.A., Ermakov S.P., 1989; Kuzmin I.I., Shaposhnikov D.A., 1994] recommend the indicators of mortality and lifespan reduction as the health risk level criterion, however, it would be more feasible to use the complex analysis of damage from the morbidity and mortality.

The absence of generally recognized methods for the life cost calculation prevents the accurate assessment. The existing methods for the assessment of this indicator can provide only the approximate value of damage. But it is also feasible to calculate it for analyzing the efficacy of preventive measures, selection from the equivalent options of solutions, etc. [Finkel A.M., 1990; Lindley D.V., 1994; Stern P.C., 1996].

Since the number of employed in the economics is one of the main macroeconomic indicators, its fluctuations to a greater extent affect the other indicators, and economic health risk assessment is based mainly on the economic assessment of reducing the period of economic activity associated with this risk.

Using the cost characterization of effects from the negative influence of the living environment factors on the public health conditions allows for transferring from the natural damage indicators (life-long risk and risk of morbidity) to the cost indicators and providing the comparison of harm for the different age categories of population and types of diseases stipulated by the influence of the living environment factors [MP 5.1.0029-11]. In addition, the economic risk assessment provides the rational planning of preventive measures on the health risk mitigation, justification of the size of premiums at the health risk insurance, justification of the supervisory bodies activity efficacy, including the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance.

When carrying out the monetary health risk assessments the following categories of expenses are calculated. First are the expenses and losses of the diseased (deceased) person himself and his family associated with the loss of health or life; second are the expenses and losses of society due to the health disorders.

The first category of expenses includes the cost assessment of the human life losses and loss of health to determine the sizes of corresponding compensations, including to determine the latter in a judicial procedure. Herewith the value of damage is divided into two parts: the compensation of material losses of injured or his family due to the death or disease and additional compensation for moral damage.

The second category of expenses includes the assessment of the lost benefit in the form of underproduction of the gross domestic product (GDP) due to the premature mortality or loss of earning capacity.

Thus, the damage from morbidity, mortality or disablement consists of the following main components:

- expenses for the provision of medical assistance to people, including the out-patient or in-patient treatment; rehabilitation measures; sanatorium-resort therapy;
- expenses for compensating the temporary or permanent incapacity to work for people lost their health (life);
- additional compensation to the injured (or his family) if this disease or death is demonstratively associated with the influence of contaminated environment, for example, the claims of people suffered from the influence of mercury (Minamata disease);
- lost profit for society due to the permanent and/or incapacity to work due to the disease (death).

When establishing the values of damage it is necessary to take into account both the immediate direct and remote expenses:

- the immediate direct expenses include the expenses for medical services, rehabilitation measures and payment for sickness certificates;
- the remote losses are the additional losses due to the work decrement in the remote period and other residual events after treatment, i.e. the human life quality deterioration as well as such (one of the main) indicator as the number of years (days) of the lost healthy life.

The comparing or summarizing the alternative damages shall be carried out taking into account the discount rates [Revich B.A., Sidorenko V.N., 2006].

The methodical approaches to the economic assessment of damage associated with the influence of risk factors became the subject of many normative and methodical documents and patents. Thus, based on the long-term studies the methodical approaches on the economic assessment of damage associated with ecologically determined morbidity were proposed [Invention patent No. 2136220 dd. September 10, 1999].

The methods are based on the analysis of long-term dependences of the population morbidity indicators and environment parameters (quality of ambient air, masses and toxicity of emissions of pollutants into environment, quality of drinking water, etc.) and distinguishing of that share of morbidity which does not depend from the studied factors of living environment.

Within this method it is proposed to carry out the calculation of economic losses due to the influence of contaminations on the population during the provision of medical assistance as the sum of losses under the separate classes of diseases:

$$У = \sum_{i=1}^{N} У_0, \quad (3.1.2)$$

where in general view $У_{oi}$ (further the index *i* is omitted) is carried out as the calculation of the sum of losses and expenses under the following items:

- expenditures for the different types of treatment (out-patient, in-patient) ($У_л$);
- expenditures from the social insurance funds for the payment of sickness certificates for diseased or persons not performing the productive activity due to the care about the sick members of family ($У_{сс}$);
- the losses of the share of tax intakes to the budget due to the temporary or permanent incapacity to work of employed ($У_{пн}$).

$$У_о = У_л + У_{сс} + У_{пн}. \quad (3.2.2)$$

The expenditures for treatment ($У_л$), rub., include the expenditures for out-patient and in-patient treatment for the calculated class of diseases, taking into account the share of diseases stipulated by the technogenic influence.

It was proposed to calculate the additional economic damage ($У_{сс}$), rub., from the expenditures from the social insurance funds for the payment of period of the temporary incapacity to work associated with the increased level of the population morbidity taking into account the average payment for incapacity to work, the number of daily losses of working hours per one case of disease, the annual average standardized indicators of morbidity in the exposed group.

It is recommended to determine the shares of tax intakes to the budget due to the temporary incapacity to work for employed and persons not performing the productive activity ($У_{пн}$) as the average value of profit (income) tax per one worked man-day.

It is proposed to calculate the value for the share of diseases stipulated by technogenic influence based on the comparison with background or under the results of analysis of statistical models reflecting the epidemiological relationship between the indicators of health and factors of technogenic load; herewith the parameter not depending on it is considered as a background level.

It is proposed to calculate the share of separate factor in the formation of the part of diseases stipulated by its influence as the rated partial correlation coefficient.

One of approaches to assessing the lost years of potential life of population allowing for determining the damage from premature death and years (days) of disease with weighing factor depending on the disease severity is the use of DALY indicator developed by C. Murray [Murray C.J.L., 1995]. This indicator includes the losses due to the premature death which is determined as the difference between the actual age as of the moment of death, expected duration of future life in this age and loss of healthy years of life due to the temporary incapacity to work and disablement. In Russian the first detailed description of this integral indicator is provided in the monograph of V.P. Korchagin (1997).

In this case when assessing the damage due to the death of human the key value (key parameter) is a value of damage related to one lost year of life. The damage from the whole life loss is calculated as the sum for all the lost years of life including the discount.

Both in our country and abroad the most distributed are such terms as "price of human life", "price of human", "cost of human life", "cost of human" which the specialists pertaining to the humanities are assessed as the blasphemous and due to this are criticized both abroad and in our country [Trunov I.L. et al., 2006]. As of now there are different approaches to the life cost assessment, depending on the objectives of this assessment.

One of these methods takes into account such factors as the human education level, condition of his health, age, real income, etc. Based on this data the amount of money which can be earned by this person for the certain period of his future life is calculated. This

methodology is usually applied by the insurance companies which evaluate the sizes of their potential payments to the successors of the deceased. For example, in USA such methods are used by the US Office of Management and Budget and Occupation Health and Safety Administration. The specific human life cost is used when calculating the compensations to potential victims, for example, of industrial incidents.

The Environmental Protection Agency uses the other method. Here the specific cost of human life is used to make a decision on if it is feasible to tighten any ecological requirements (that is inevitably associated with additional expenses and losses) in relation to the human lives preservation It evaluates the cost of the different measures taken which are able to prolong or preserve the human life. Herewith the criteria of age, income, education, health, etc. are not taken into account. In this situation the human life cost is assessed under the cost of preventive measures,

There is the method which is based on finding out the opinion of people which are asked to assess themselves. These methods are subjective and inaccurate but it approximately determines the perception by people of their own life value.

Also there is the method which is based on the calculation of sums which the people agree to pay for the preservation of their own lives. Often it is impossible to determine the value of things able to increase the human safety level by the certain value and cumulative effect.

The life insurance field also has several approaches to assessing the economic equivalent of the human life cost. For example, the method for the human life cost economic assessment developed in the USA and UK in the second half of XX century is based on that the economic equivalent of life of average human of average age is equal to the relation of average per capite available monetary annual income to the average probability of death during year:

$$Э = \frac{Д - П_{об}}{К_{см}} N , \qquad (3.2.3)$$

$$К_{см} = \frac{d_x}{l_x} , \qquad (3.2.4)$$

where Э – is an economic human life assessment;

Д – is an average monetary annual income;

$П_{об}$ – are the average annual mandatory payments;

$К_{см}$ – is a mortality factor;

N – is an average lifespan after age x;

d_x – number of deceased when transferring to the age x+1;

l_x – number of persons reaching the age x (per 1000 of persons).

One more method is based on assessing the exceedance of the salary of employees involved into the hazardous productions over the level of payment for the labor of workers who less jeopard their life and health. Several sampled populations of people exposed to the different level of risk at work are considered within these methods. These methods allow for obtaining the life cost assessment both for the average worker and the worker with increased or decreased level of risk.

The sizes of compensation payments to the families of deceased or persons who lost their health as a result of accidents or disasters also can be considered as the economic equivalent of the human life cost. This can be the state payments or compensations established by the court decision. According to the analysis of the foreign insurers practice the first two methods are the most required.

Table 3.3 contains the results of calculations performed by the experts of "Rosgorstrakh" OJSC under the methods taking into account the consent to pay in order to avoid this risk or consent for compensation of that to percept (suffer) it voluntarily. For some countries, in accordance with these methods, the economic equivalent of life cost by 6 times exceeds the discounted income which the deceased could earn during the rest of life. The calculations were performed for the average annual salary in the country discounted by 20 years.

Table 3.3

The economic equivalent of the average human life taking into account the readiness to pay[1]

Country	Economic equivalent for the life of average human in 2005, mln. dollars
Portugal	1.09
Germany	2.12
France	2.12
Japan	2.24
Great Britain	2.32
Netherlands	2.42
Sweden	2.48
USA	2.63
Luxembourg	5.02

Table 3.4 contains the results of calculations performed by the experts of "Rosgostrakh" OJSC for assessing the economic equivalent of the average human life for some countries based on the methods which is based on determining the cost of life according to the level of income and probability of death.

Table 3.4

The economic equivalent of life for average human for a number of countries calculated taking into account the income and probability of death[2]

Country, year	Economic equivalent for the life of average human, mln. dollars
Portugal, 1999	0.98
Netherlands, 2000	1.23
Sweden, 2000	1.95
Great Britain, 2001	2.12
Germany, 2000	2.41
France, 1997	2.42
USA, 2002	3.19

The calculations performed under the methods based on the analysis of the levels of income of people involved into hazardous productions show that the assessment of compensation payment in case of death of working American in 2000 was about 5 mln. dollars.

Based on such analysis it is possible to determine the approximate borders of the human life cost assessment in the economically developed countries from 1 to 9 mln. dollars.

To compare the conformance of calculations under the above mentioned methods of actual indicators, it is possible to compare them to the data on the compensation payments to the families of people died in different tragedies (Table 3.5).

The results of assessing the life cost in the CIS countries calculated for one person, taking into account the public readiness to pay for the risk prevention are specified in Table 3.6.

According to the table, the cost of life for the average Russia is equal to 195.2 thous. dollars or in ruble equivalent – 5.856 mln. rubles. (1 dollar~30 rubles).

According to the second method, the economic equivalent of the Russian life cost was 118 thous. dollars or 3.54 mln. rubles. Table 3.7 contains the sizes of compensation payments to the families of persons died in the air disasters.

[1] "Rosgorstrakh" OJSC: official web-site. URL: http: //www.rgs.ru.

[2] In the same place.

Table 3.5

The global practice of payments to the families of deceased[1]

Event	Size of paid compensation per one person, mln. dollars
"Columbia" shuttle collapse	3.8
Act of terrorism in New York	1.5–4.5
Collapse of Air France Concorde near Paris	1.5
The death of an American soldier in Iraq	0.5

Table 3.6

Economic equivalent for the life of average human (CIS countries)[2]

Country	Economic equivalent for the life of average human in 2005, thous. dollars
Tajikistan	13.3
Uzbekistan	16.2
Armenia	41.6
Azerbaijan	54.5
Ukraine	64.4
Belarus	110.6
Kazakhstan	135.6
Russia	195.2

Table 3.7

Air disasters in Russia, the number of deceased and the size of payments[3]

Event	The size of paid compensation per one person
The crush of Tu-134, air company "Utair" in Samara	75 thous. dollars (2.250 mln. rubles) (amount promised by "Utair")
The collapse of Tu-154, air company "Pulkovo Airlines" near Donetsk	500–900 thous. rubles
The disaster with Airbus A310, air company "Sibir" (S7) in Irkutsk	162 thous. rubles
The disaster with Boeing-737 in Perm	1.960 mln. rubles. Insurance company "Moscow" paid to the relatives of 56 deceased 109.8 mln. rubles

Thus, when analyzing the specified methods of the life cost assessment it is possible to detect that in each case this value is determined depending on the goal of assessment.

Quite close approach aimed at the accounting of losses associated with the working capacity reduction takes into account the economic activity period reduction.

According to the International Labor Organization recommendations formulated in the resolution of the XIII International Labor Statistics Conference "the economically active population includes all persons of both genders which offer the manpower for manufacturing the economic benefits and services as they are determined in the UN Systems of National Accounts and Balances during the certain reporting period" [Modern International Recommendations on the Labor Statistics, 1994]. The economically active population includes both the persons engaged in economy and unemployed.

[1] "Rosgorstrakh" OJSC: official web-site. URL: http: //www.rgs.ru.
[2] In the same place.
[3] In the same place.

In Russia the age brackets of economic activity are determined as 15–72 years, i.e. they are wider than the working age brackets (16–54/59 years)[1]. However, it is feasible to consider as the period of economic activity in Russia the age period from 16 to 55/60 years inclusive, because after the pension age the majority of population does not demonstrate the economic activity that in turn can affect the reliability of results. The reasons of reducing the economic activity period associated with the public health risk shall include the morbidity with temporary and permanent incapacity to work as well as death.

When evaluating the peculiarities of the cost assessment of the economic activity period reduction the following is distinguished:

a) the influence of many factors on the duration of period and a number of cases of incapacity to work;

b) the differences in the economic significance of the disablement period (from the statistically negligible to the significant);

c) the influence of the disablement period duration on the many subjects of economic relations;

d) the limitations imposed by the available statistical material and peculiarities of statistical observation;

e) the availability of deposed effect (especially at the long-term disablement period, death or assessment of the disablement period in future).

The peculiarities stated above impose the following limitations and tolerances on the population economic activity period reduction assessment:

1) the calculations are performed based on the official open data of statistics bodies;

2) only the working population is taken into account that provides the possibility to consider the reduction of the "economic activity period" by the "temporary incapacity period";

3) the incapacity period does not involve the labor resources outside the limits of considered territory;

4) the volumes of manufactured product of each worker in one industry are equal;

5) the money flows discounting is used to assess the deposed effect or the incapacity period duration.

The cost (economic) indicators characterizing the health risk include the following categories:

a) the indicators of change in the manufactured product in economy (from households to global economy);

b) the indicators of change in the cash flows in the budget system (through changing the tax intakes from the individuals and economic agents);

c) the change in the cash flows of extrabudgetary funds (through the intake and deductions to the extrabudgetary funds).

The existing methods for economic assessment of the losses for the life and health of population are also based on the cost assessment of incapacity period (taking into account the influence of the economic activity period value on the main social and economic indicators (gross domestic product for country and gross regional product for region)).

The determination of cost for the underproduced product is considered as the one of key positions in the economic assessment of risk to the health of working-age population. The manufactured product can be considered in economy using the following indicators: release and gross value added (GVA), gross domestic product at the level of country and gross regional product at the level of region (at the level of municipalities such indicator is not calculated; that is why it is allowed to use the corrected release of products).

When determining the cost expression of product manufactured by 1 specific human (gross value added – GVA) per year it is necessary to take into account the following factors [Zaytseva N.V. et al., 2010*b*]:

[1] Federal State Statistics Service: official web-site. URL: http: //www.gks.ru.

a) the level of added value under the different sectors of economy differs significantly, from 27%[1] to release ("production and distribution of electric power, gas and water") to 84% ("extraction of minerals");

b) the contribution of sectors into the total volume of gross product at the territory is different, from negligible values ("fishing and fish farming", "household keeping services") to 30–35% ("manufactures");

c) the number of employed under sectors is distributed irregularly, from the statistically negligible values ("fishing and fish farming", "household keeping services") to 22% ("manufactures").

The peculiarities of the gross regional product formation stated above result in that the contribution of 1 person employed in one sector to the total volume of the gross regional product per year will significantly differ from the contribution of 1 person employed in the other sector (the temporary incapacity to work of employed in different sector will have different influence on the gross regional product). For example, the statistical data for the Perm Territory show that the contribution of employed in the sector "household keeping services" is statistically negligible (partially it is explained by the peculiarities of sector and peculiarities of statistical observation); at the same time the contribution of employed in the sector "extraction of minerals" is about 4 mln. rubles.

At the summarized assessments of losses associated with the health risk, it is feasible to distinguish the uncertainties the sources of which are the assumptions that during the incapacity period the labor resources outside the considered territory are not involved as well as the volumes of manufactured product of each worker in one sector are equal.

When calculating the changes of cash flows under the levels of the budgetary system of the Russian Federation associated with health it is feasible to take into account the changes of intakes under the value added tax (VAT), corporate profit tax (CP), individual income tax (IIT) because namely these taxes are statistically significant and available for the correct calculations as well as namely in these cases the incapacity periods affect the taxable basis. If it is possible and required to carry out the more complete calculations it is feasible to take into account the other taxes and tax regimes.

For the budgetary system the changes of cash flows (incomes and expenses) for extrabudgetary funds (Pension Fund of the Russian Federation, Social Insurance Fund, Compulsory Medical Insurance Fund) also will be significant.

The calculations on assessing the changes of cash flows in a number of cases can be obtained only upon the special requests. First, it concerns the expenses of extrabudgetary funds because the incomes can be calculated if the statistics on the salary of employed population and rates of deductions to the extrabudgetary funds (Tax Code of the Russian Federation) are available. As opposed to the previous considered indicators (cash flows), the calculation of effect under this direction can be performed also for the separate cases and days (depending on the provided information)

The methods of the economic public health and life assessment based on the cost assessment of the incapacity period reduction when implementing the risks for the life and health of population and allowing for taking into account the risk prevention effects at the levels of the budget system of the Russian Federation [Zaytseva N.V. et al., 2012*c*] are proposed for the tasks on justifying the decisions on the planning of measures for the public health risk mitigation at the level of regions, territories and separate objects, assessment of economic efficacy of these decisions, optimization of investment and current expenses for the public health risk mitigation.

These methods for determining the cost of the human economic activity period uses the main approaches in the theory of assessment: cost, comparative and income, including using the cash flow discounting methods. Directly, the cost assessment of the economic incapacity period provides the assessment of the following effects under the groups of economic agents:

a) the change of the manufactured product in the economy (gross regional product);

[1] Design data for the Perm Territory.

b) the change of cash flows under the budgets of the budgetary system of the Russian Federation (through the changes of tax intakes). When considering the budget effect it is necessary to take into account the taxes, included into the cost of goods and services;

c) the change of cash flows under the extrabudgetary funds of the Russian Federation (through the changes of intakes to the extrabudgetary funds and their expenses associated with the health risk).

As of now the "Methodology for calculating the economic losses from mortality, morbidity and incapacitation of population" is applicable (Order of the Ministry of Economic Development of the Russian Federation, the Ministry of Health and Social development of the Russian Federation, the Ministry of Finance of the Russian Federation, Federal State Statistics Service No. 192/323н/45н/113 dd. April 10, 2012) is applicable, but the proposed methodology allows for performing the calculations of economic losses from the population mortality only from the point of view "human - labor resource", on the one hand, and does not consider the issues on assessing the prevented losses, on the other hand.

At the same time, if the data on the prevented cases of mortality/morbidity are available, there is the possibility to assess the prevented economic losses based on the estimated data that in turn provides the required tools for making the managerial decisions.

The decrease of morbidity, decrease of mortality and the increase of birth rate can be reduced to two components of economic effect expressed in value terms:

a) increase in the number of manufactured product and tax intakes to the budgets of all levels;

b) the increase of consumer demand in the economy. Thus, the economic effect obtained due to the implemented measures is reinvested again; the growth of the incomes of population means the increase in the level of domestic purchasing power that becomes the additional factor of economic development, creation of work places and increase of tax intakes.

Herewith, for the maximum complete accounting of the efficacy of measures (actions) on the risk minimization it is feasible to take into account also the effects possessing the stability and revealing within the long term (deposed effects).

The deposed effect of measures on the public health risk mitigation has the following features [Goleva O.I., 2012]:

1. As a rule, the deposed effect is characterized not only by the later manifestation in time, but also by the long duration. The more distant the effect is in time, the harder it is to fulfill its forecasting. For the purposes of assessment it is possible to establish the prognostic and post-forecast period (with different level of data detailing). In this sense the forecasting is required not only for the indicators of morbidity, mortality, etc. but also for the macroeconomic indicators (to assess the manufactured product and tax intakes).

2. When assessing the changes of manufactured product for accounting the used (non-used) raw materials (consumption) it is feasible to assess the manufactured product through the added value.

3. The deposed effect can be accumulated, i.e. can be the consequence of several sequentially implemented measures. The implementation of new measures contributes to the growth of efficacy under one or several other measures. When comparing such measures it is feasible to take into account the effect and efficacy of measures together with complementary in order to consider the synergistic effect from their simultaneous or consecutive implementation.

4. The effect from scale is possible (the reduction of costs per one unit of effect when increasing the scales of measure). It is necessary to take into account both the positive and negative effect from scale.

5. The effects can be both universal, occurring during the implementation of any measure, and specific, stipulated by the certain types of measures and the peculiarities of regions, the groups of population, etc.

6. The sectoral specific character of production and the age-sex specific character of consumption influence on the aggregate effect which not always can be obtained by the simple summation.

7. The implementation of measure (project) aimed at the public health risk mitigation can contain the real options (the possibility to implement any other, may be highly effective, measures (projects)). Respectively, it is necessary to consider the necessity to use the real options method in the cost assessment of effect from the considered measures.

8. The assessment of effects from measures aimed at the public life and health risk mitigation is affected also by the peculiarities of statistical observation (including the available forms of statistical observation, unwillingness to record the facts of diseases in the separate sectors of economy and groups of population, availability of shadow economy).

9. The cost assessment of deposed effect requires the mandatory accounting of the temporary value of money, i.e. the discounting of future cash flows, and for this it will be more correctly to use the social discounting rate.

When assessing the efficacy of measures aimed at the public life and health risk mitigation the important aspect is the analysis of expenses for the implementation of measures. The expenses for measures on the public health risk mitigation can differ under the sources, frequency of implementation, etc., but all of them shall be accounted when calculating the efficacy of measures taking into account the time for their implementation.

Depending on the source of investment the expenses can be made by:

– the federal budget of the Russian Federation;
– the budget of subject of the Russian Federation;
– the budget of municipal structure;
– the profit-making and non-profit-making organizations;
– collectively.

The structure of the risk mitigation expenses is presented as follows:

a) capital expenditures;
b) current expenditures:
– material expenses;
– labor costs;
– allocations for social needs;
– depreciation of fixed assets;
– other expenses.

The formation of effects under the measures aimed at the public health risk mitigation is affected by the type of implemented measure (independent, mutually exclusive, complementary) that shall be taken into account during the assessment of its efficacy.

The independent measures are the measures the decisions on which are taken independently and the results do not affect each other.

The mutually exclusive measures are the measures the decision on the implementation of which excludes the necessity to implement the other measure. When comparing the measures the assessment of effect and efficacy is carried out for each one with further comparison of results.

The complementary (mutually supplemented) measures are the types of measures connected by the complementary relations: the implementation of new measure contributes to the growth of efficacy under one or several other measures. When comparing such measures it is feasible to take into account the effect and efficacy of measures together with complementary in order to consider the synergistic effect from their simultaneous or consecutive implementation.

The assessment of future expenses and results when determining the efficacy of measure is performed within the calculation period the duration of which (calculation horizon) is accepted taking into account:

– the duration of the public health risk mitigation measures;
– the expected term for manifestation of effect from the public health mitigation measure;
– the achievement of established characteristics (the level of morbidity, etc.);
– the requirements of investing party (state authorities and local self-governing bodies, corporate structures).

The calculation horizon is measured by the number of calculation steps. The calculation step when determining the efficacy indicators within the calculation period can be the month, quarter or year. Taking into account the peculiarities of measures on the public health risk mitigation and the peculiarities of effects the duration of which not always can be clearly determined the planning horizon shall и sufficient for the comparative efficacy.

Since the compared indicators of expenses and expected effect relate to the different moments of time the key issue is the problem of their compatibility which taking into account the time value of money theory is solved through the cash flows discounting in order to bring them to the one time point (as a rule, to the beginning of expenses).

In order to compare the performed expenses and occurring effects during the different periods of time the tool standard for such calculations (discounting) is used.

Discounting is the bringing of all future cash flows to the one moment of time. The discounting is called as the basis for calculating the value of money taking into account the time factor if the time lags are available. The discounting is called as the bringing to the moment of time in past. The bringing to the moment in future is called as increment.

The increment to the certain moment in future is performed by multiplying the past cash flows by the increment coefficient $k_s = (1 + r)^n$. The discounting is performed through multiplying the future cash flows by the discounting coefficient $k_d = \frac{1}{(1+r)^n}$, where r – is a discounting rate; n – is a number of periods.

The different options of distribution in time for the effects and expenses for the public health risk mitigation measures are schematically presented in Fig. 3.5–3.8.

Taking into account that the value of money for the different subjects of economic relations can be different, the discounting rate is calculated depending on the source of financing of measure and the nature of expected effect. From the economic point of view the discounting rate is a rate of return for the invested capital required by investor. In other words, using the discounting rate it is possible to determine the amount which the investor will have to pay today for the right to obtain the expected effect in future. That is why the making of key decisions depends on the discounting rate value, including during the selection of the public health risk mitigation measures.

The commercial discounting rate is a value characterizing the alternative option of capital investment for the obtainment of profit. If it is spoken about the public sector of economy it is required to use the other approach which takes into account the social specificity. Since the budget sector resources are formed mainly at the expense of taxpayers' funds the issue on their effective use by the state is raised.

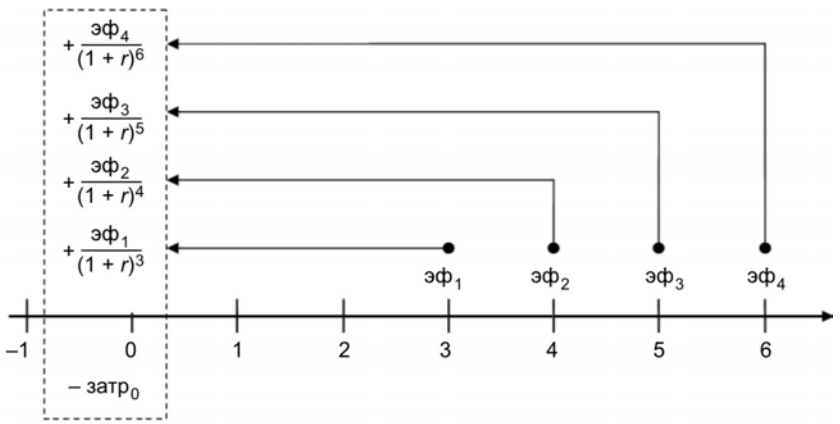

Fig. 3.5. The scheme for bringing the cash flows (effects and expenses) to the initial (zero) moment of time at the lump-sum costs of measures

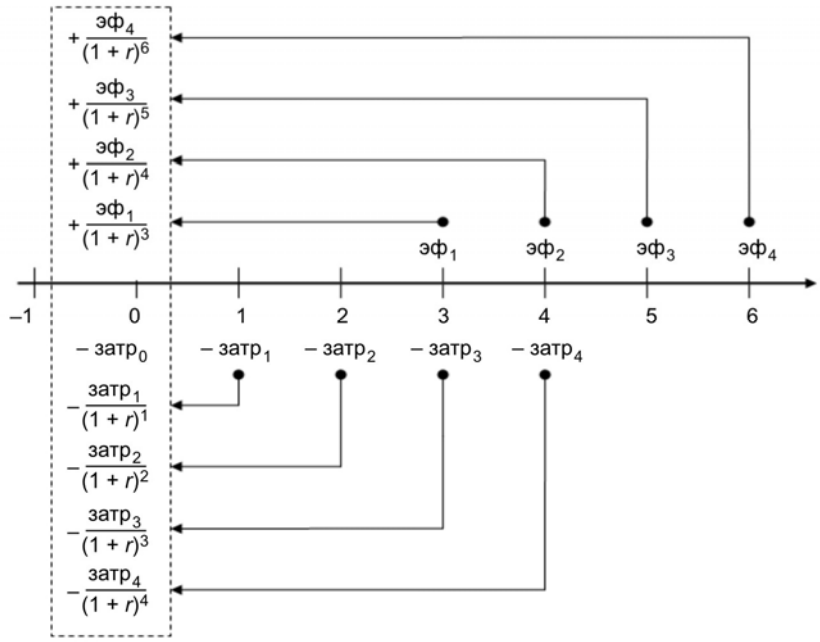

Fig. 3.6. The scheme for bringing the cash flows (effects and expenses) to the initial (zero) moment of time at the recurring costs of measures

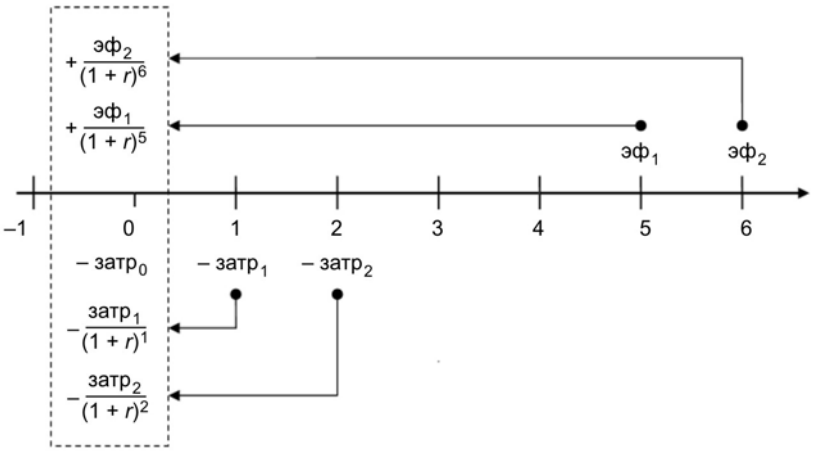

Fig. 3.7. The scheme for bringing the cash flows (effects and expenses) to the initial (zero) moment of time at the deposed effect

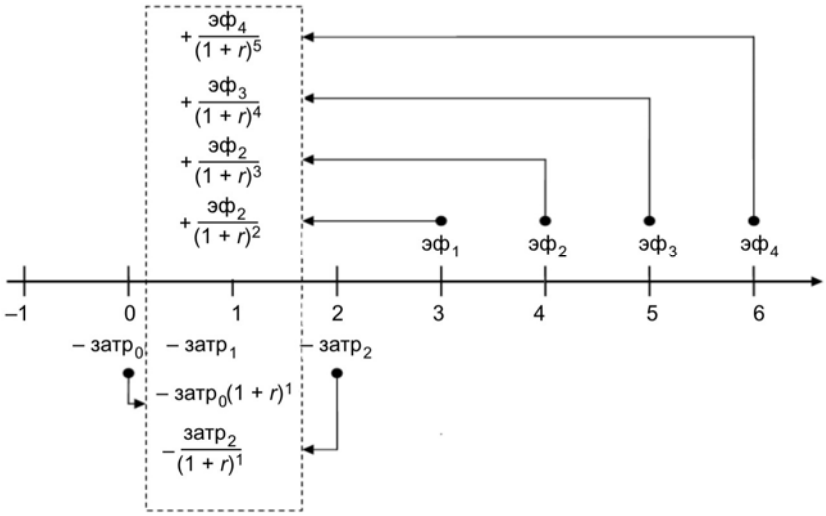

Fig. 3.8. The scheme for bringing the cash flows (effects and expenses) to the moment of time in future (for example, to compare with other possible measures) at the recurring costs of measures and deposed effects

The commercial discounting rate (and the approaches to its building) is not appropriate in this case because it reflects the alternatives of private capital, while the budget funds are the "public" capital. In this case the so called social discounting rate is used. The social discounting rate is the alternative possibilities for society to use the resources either between two periods of time or between the different options of investment.

As of now there are several main approaches to the social discounting rate determination which with different level of success were used in the majority of developed countries:

1. The social opportunity cost of capital, SOC. To use such approach, it is necessary to determine the profitability of the best alternative project from the private sector the implementation of which have to be rejected.

2. The social rate of time preference, SRTP. The approach demonstrates the readiness of society to refuse from the consumption in this period for the benefit of consumption in future.

3. The shadow price of capital, SPC. It allows for assessing the efficacy from the use of capital in the public sector.

4. The approach based on the expert evaluations where the social discounting rate value is determined individually by experts.

Now let us consider each approach in detail and determine their basic benefits and drawbacks for the practical application for the purposes of study.

The social opportunity cost of capital, SOC

The studies in the field of applying the approach based on the social opportunity cost of capital were carried out by the foreign scientists [Baumol J. William, 1968; Marglin S., 1963] during the second half of XX century and are continued till now. This approach acts as the alternative to the time preference approach.

The alternative cost of capital acts in this approach as the "rate of delivery from the best alternative with similar risk which had to be rejected as a result of the certain project implementation" [Kohyama H., 2006]. That is to say, the rate of delivery from this project shall be greater or at least equal to the rate of delivery from the alternative project.

The scientific literature raises the issue on the premium for risk when using this approach because the private investments are more risky than the public. In this case the

social discounting rate shall be corrected by this value the measurement of which is a quite complicated process.

The studies dedicated to this approach provide the approximate SOC values for EU countries – 5–7%.

The practice of the use of this approach causes the single difficulty associated with the search for alternatives. That is to say, the determination of project from the private sector complicates the selection and increases the subjectivity of approach. In addition, this significantly extends the information base on the profitability of projects in the private sector required for calculation.

Several methods (models) were proposed to solve the established problem. The sense of these models is brought to the assumption that because the state does not issue the shares and pay taxes the cost of borrowing for the state acts as the social discounting rate, i.e. the rate on the long-term government stocks the repayment date of which is equal to the date of social project. Some scientists recommend using this approach when assessing the social discounting rate because it shows the alternative for the state funds investment compared to the private sector that certainly serves as the real reference point.

The article of A.M. Emelyanov (2007) specifies the calculation of SOC for Russia and therefore – for its regions. Thus, the average earning capacity under the government short-term bods-federal loan bonds (2000–2007) is taken as the value of rate – 4.5%.

It should be noted, that the obtained value can differ greatly from values obtained with the help of other approaches.

The social rate of time preference, SRTP

The social discounting rate in the context of this approach is considered as the rate on which the society can refuse from consumption in this period for the benefit of consumption in future. It is also called as the "consumer rate of interest (CRI)". It can be determined under formula

$$SRTP = \delta + L + \mu g \,, \tag{3.2.5}$$

where δ – is a net rate of time preferences;

L – is a level of risk for life;

μ – is a flexibility of the threshold usefulness of consumption;

g – per capita growth of consumption.

This approach is the most popular at the foreign scientists because it reflects the general logics of deposed consumption in time, taking into account the interests of society as the main customer and consumer of public benefits.

The level of risk to the health of individual is the most important indicator in the considered studies. Two approaches to its determination are distinguished in the global practice:

1) the level of mortality in the country;

2) the relation of the number of deceased from external causes to the average annual number of population.

The existence of approaches to the determination of this indicator allows varying its value during its use for the different types of tasks.

In addition, the SRTP approach provides the minimum of statistical information which can be easily found in the open sources as well as the comparatively low labor intensity.

The shadow price of capital, SPC

The beginning of this approach results from the prerequisite of equality between SRTP and SOC in the conditions of the perfect capital market. That is to say, the rates shall be equal. But in practice, as a rule, this equality is not performed that is why a number of scientists recommend applying the assessment coordination procedure:

$$SDR = \alpha SOC + (1-\alpha)SRTP \ , \qquad (3.2.6)$$

where SDR – is a social discounting rate;

α – is a share of resources sent for investment;

(1 – α) – is a share of resources sent for the current consumption.

That is to say, we obtain the social discounting rate as the weighted sum of SOC and SRTP. This method was called as the "consumer equivalent method". According to this method, SRTP is corrected by the shadow price of capital (SPC); after that the weights reflecting the shares of consumption and investment in economy are assigned to the corrected and non-corrected SRTP values. Therefore, the SDR formula is looking as follows:

$$SDR = SRTP \cdot SPC\,\omega_I + SRTP\,\omega_C \ , \qquad (3.2.7)$$

where SRTP – is a social rate of time preferences;

SPC – is a shadow price of capital;

W_I – is a share of investment to the fixed capital in economy;

W_C – is a share of consumption in economy.

The main advantage of this method is the absence of necessity to assess the SOC. Many economists consider this method as the best because it solves the problems on the SOC and SRTP inequality. Nevertheless, this approach is labor-intensive and it use stipulates the availability of statistical materials for the long period of time. The SPC value assessment represents one more difficulty.

So, for the purposes of this study the most feasible will be to use the time preferences approach (SRTP). The advantages of this approach:

1) it reflects the specific character of project (as the risk levels);

2) the availability of initial statistical information;

3) low labor intensity.

$$SRTP = \delta + L + \mu g \ , \qquad (3.2.8)$$

where δ – is a net rate of time preferences;

L – is a level of risk for life;

μ – is a flexibility of the threshold usefulness of consumption;

g – per capita growth of consumption.

According to the utilitarian approach, the net rate of time preferences is equal to 0. This means that all generations will be in the same conditions during the consumption of benefits.

The assessment of flexibility of the threshold usefulness of consumption is described in the article of M.A. Sheluntsova (2010). The flexibility determination is performed under the method of Kula E (e = 1.67).

When assessing the per capita growth of consumption for Russia and its separate regions the difficulty occurs due to quite high value of indicator not comparable to the other developing countries. That is why it is feasible to use the gross regional product growth rate as the per capita growth of consumption.

When considering the temporary value of money for the purposes of economic assessment of the efficacy of measures aimed at the public life and health risks mitigation, planning and forecasting of effects from such measures the following periods are distinguished: forecast and post-forecast.

To assess the efficacy of measures on the public life and health risks mitigation, it is necessary to distinguish the forecast and post-forecast periods (Fig. 3.9) where $эф_i$ – is an economic effect on the section i-м of the forecast period; $ЭФ_n$ – is an economic effect in the post-forecast period; $затр_0$ – are the expenses for the measure implementation.

The forecast horizon of planning is characterized by the significant detailing of effects from the measures aimed at the health risks mitigation and, as a rule, it makes up from one year to several years (depending on the sources of risk and the effects manifestation intensity).

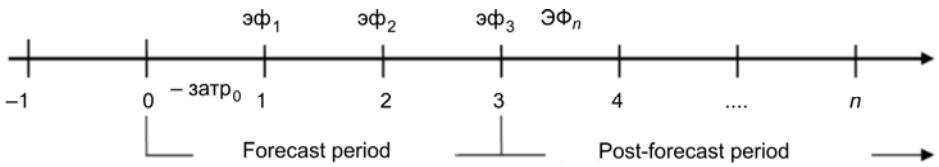

Fig. 3.9. Forecast and post-forecast period in the assessment of the efficacy of measures on the life and health risk mitigation

The post-forecast period is distinguished only at the availability of effects not subjected to the standard assessments and requiring large expert evaluations as well as at the availability of effects for several generations. The post-forecast period can make up from several years to infinity

The practice of economic assessments, including the risk management field, often uses the approaches stipulating the "expenses – benefits" analysis and the analysis of economic efficacy.

The cost-benefit analysis is a method for calculating and assessing the public costs and common social benefits associated with any economic project. The cost-benefit analysis is usually applied by the state authorities during the assessment of investment to the large-scale state projects in order to determine the growth of welfare and net social benefit which will be obtained by the whole country from the implementation of this projects.

The main principles of the cost-benefit analysis are in four key positions:

- the accounting of costs and benefits. All costs and benefits shall be calculated and ranked in accordance with degree of their deviation from the main goal of project; more distant costs and benefits can be not considered;
- the assessment of costs and benefits. During their assessment it is necessary to pay attention to the possible changes of relative prices but not to the total level of prices; the total level of prices applicable in the initial period shall be taken as the basic one. There are special problems of establishing the prices for intangible assets:
- the determination of the rate of interest under which the costs and expenses shall be discounted;
- significant limitations. This group includes legal, administraive and budgetary limitations as well as the limitations associated with the redistribution of income.

Basically, the cost-benefit analysis is focused on the economic efficacy of project and provided that the benefits will exceed the costs recommends its implementation, without taking into account the one who obtains the benefit and who bears the costs [Yakobson L.I., 1996; Greenberg D.H. et al., 2006].

The economic efficacy is an indicator determined by the relation between the economic effect (result) and costs created this effect (result). In other words, the less is the scope of costs and the biggest is the activity result value the higher will be the efficacy. The economic efficacy indicators quite often are used to compare the risk management measures in order to select the priorities for financing [Golub A.A., Strukova E.B., 1995].

The assessment of the efficacy of measures aimed at the public life and health risk mitigation when exposed to the living environment factors provides the accounting of peculiarities of indicators used in this study. The peculiarity of these measures is that the effect from them is assessed first in the form of natural indicators (mitigating the risk of morbidity, mortality, etc.). The use of the whole variety of indicators complicates the making of decisions on the implementation of measures, their selection and planning, and the necessity to take into account the economic efficacy of measures aimed at the health risk mitigation imposes its own limitations on the selection of the list of indicators for the assessment of their priority.

It is possible to assess the value of one unit of the prevented public health risk from two positions:

- in terms of aggregate effect (calculated through the gross domestic product);
- in terms of budgetary effect (change of tax intakes).

Therefore, it is possible to distinguish the following effects:

1) aggregate (for the Russian Federation);

2) budgetary (for the levels of budgetary system in aggregate and separately).

The general sequence of actions on the assessment of the efficacy of measures on the risk mitigation taking into account the deposed effect is presented in Fig. 3.10 [Zaytseva N.V. et al., 2011*c*].

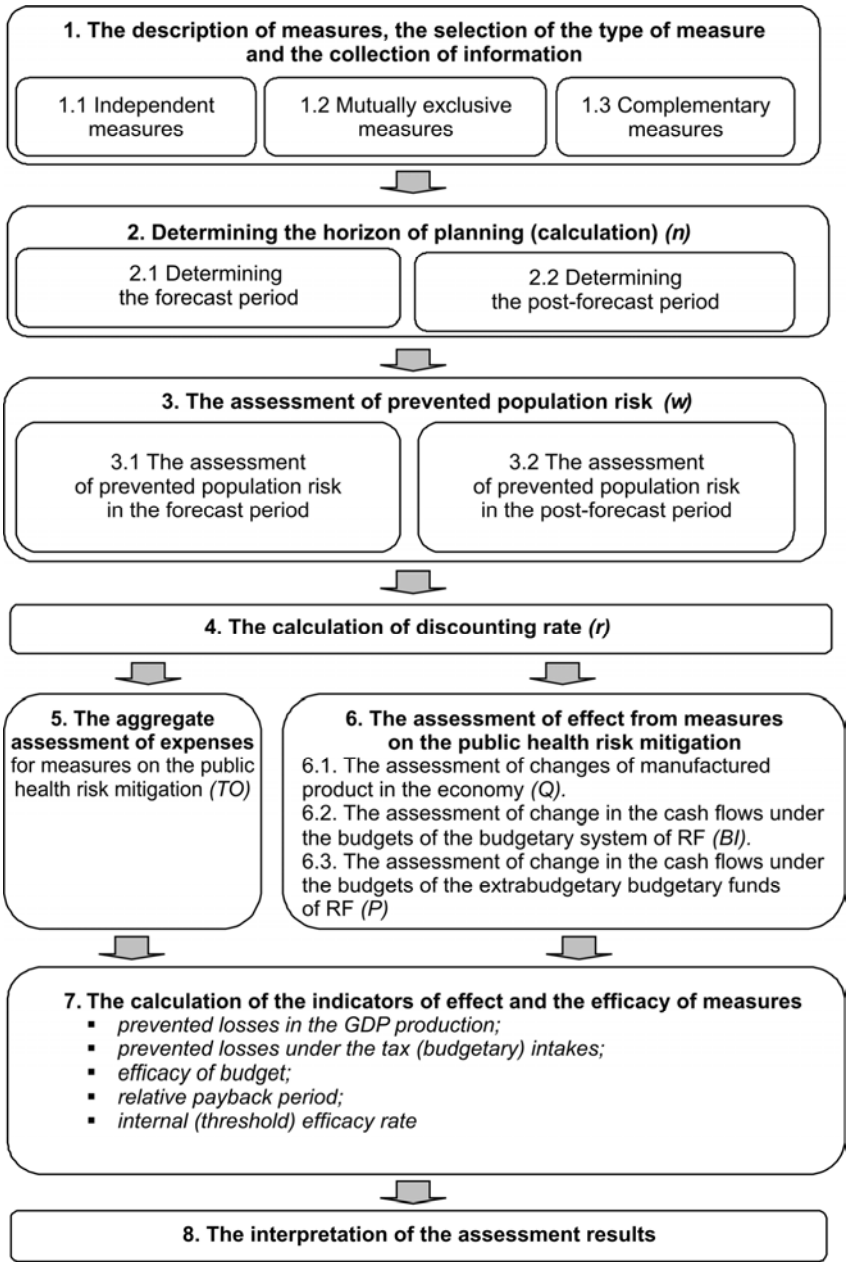

Fig. 3.10. The sequence of actions during the assessment of the efficacy of measures on the risk mitigation taking into account the deposed effect

In order to make a decision on the feasibility of the implementation of measures on the public health risk mitigation it is necessary to use the indicators characterizing the net effect (the difference between the obtained effect and expired costs).

The prevented losses in the gross domestic product production – the indicator characterizes the sum of prevented losses associated with mortality, incapacitation and morbidity of population calculated as a part of the gross domestic product of the country. Before recognizing the risk mitigation measures as economically effective it is necessary to have the positive aggregate net effect of project. The project (measure) with bigger value of this indicator is considered as the more effective.

The prevented losses under the tax (budgetary) intakes – the indicator characterizes the exceedance of budgetary intakes of money (saving) over the cumulative costs taking into account the discounting of all the cash flows. The possibility to calculate the net budgetary effect both under all the levels of budgetary system in aggregate and separately is provided: for the federal, regional and local budgets. Before recognizing the risk mitigation measures as economically effective it is necessary to have the positive aggregate net effect of project. The project (measure) with bigger value of this indicator is considered as the more effective.

Taking into account the public health risk mitigation measures the following indicators of efficacy for the risk mitigation measures are distinguished.

Budgetary efficacy – demonstrates the budgetary economic effect per one unit of costs taking into account the discounting. The possibility to calculate the budgetary efficacy both under all the levels of budgetary system in aggregate and separately is provide for the federal, regional and local budgets. This indicator answers the question: "How much will each unit of costs bring into the budget?" The project (measure) with bigger value of this indicator is considered as the more effective. The minimum value of this indicator can be established by the participant performing the costs as the one criterion of assessment.

Relative payback period – it is the duration of period from the initial moment to the moment when the positive effect from measures will be equal to the funds invested to the risk mitigation measures, taking into account the discounting. The measure with smaller payback period at the other equal conditions is considered as more effective. The maximum payback period can be established by the participant performing the costs as the one criterion of assessment.

Domestic (threshold) efficacy rate – the indicator is a social discounting rate at which the aggregate inflow is equal to the aggregate outflow of funds. The risk mitigation measures can be considered as effective if the domestic aggregate efficacy rate is more than the discounting rate.

The important moment for assessing the efficacy of the risk mitigation measures as well as any other project is the coordination of obtained results which sometimes can be contradictory (first, the absolute and relative). In such case the most significant from the proposed indicators as well as the establishment of different threshold values of indicators can become the basis for the making of decisions. It is preferable to use the net aggregate effect.

The main criteria of priority of financing of those or other measures are the classical economic criteria:

- the achievement of established effect at the minimum costs;
- the achievement of established effect at the fixed costs.

But it should be noted that the peculiarities of considered projects and their social directions can stipulate the deviation from the specified criteria (urgent necessity to implement the measures, necessity to implement the measures at the remote and underpopulated territories, etc.).

When determining the type (types) of measures the following criteria are used:

– for independent measures (aimed at the different goals) the decisions are taken independently from each other and the limitation can be imposed only by the limited financial resources;

– for mutually exclusive measures the decisions are taken based on the above mentioned criteria (achievement of established effect at the minimum costs, achievement of established effect at the fixed costs) in order to select the one of the considered measures;

– for mutually supplements (complementary) measures the possible synergetic effect based on the considered standard approaches is taken into account.

3.3. Methodical approaches to the justification of hygienic regulations under the health risk criteria (risk-based regulations)

The entry of the Russian Federation to the World Trade Organization, its participation in the Customs Union within the Eurasian Economic Community makes the issues on the approximation of sanitary law and, in particular, the harmonization of the sanitary and hygienic regulations for the quality of both the environment and products with international standards the ones of the most priority.

As of now the development of standard indicators of the living environment objects quality stipulates the mandatory use of the public health risk assessment methodology [Canadian Environmental Quality Guidance, 2007; EU, 2000; CAC/GL 30-1999; CAC/GL 62-2007].

When justifying the regulations under the health risk criteria (risk-based standards) it is feasible to use the following main principles:

– the priority of safety and preservation of health over any other life quality elements;

– the concept of non-zero (acceptable) risk;

– the transparency of assessment and description of uncertainties;

– the stages of the health risk assessment procedure – basing the study on the hazard identification, quantitative assessment of dependence "exposure – effect (response)", exposure assessment;

– the use of all relevant information with the priority of results of the epidemiologic studies;

– the accounting of peculiarities of the rated risk indicators and recipients;

– the revision of regulations according to the obtainment of new scientific data.

According to the health risk assessment stages the development of the quality standards under the risk assessment criteria includes the fulfillment of the following stages: Hazard Identification, Dose – Response Assessment, Exposure Assessment and Risk Characterization. The principal algorithm for justifying the hygienic regulations under the health risk criteria is presented in Fig. 3.11.

For the hygienic regulations justification tasks these stages are characterized by a number of peculiarities.

In this case, the hazard factors establishment is not performed at the hazard identification stage because the risk-based regulations development is carried out for the certain risk factors. The main attention at this stage is paid to the analysis of available data on the physical and chemical, biological and other characteristics of the studied factor, the sources of its manifestation and the actual levels in the living environment. Also it is necessary to study the availability of hygienic regulations and standards in the global practice, determine the probable effects from the influence of factor, first, the ones which were used for the establishment of standards (critical organs and systems), investigate if the health risk criteria were used during it. The separate issue is the identification of the most sensitive groups. They can differ depending on the social and economic situation, life style and national peculiarities of behavior. For these groups it is feasible to establish the possible public health disorders in accordance with principal exposure scenarios.

The decision on the necessity to carry out the further risk-based regulations justification is taken under the hazard identification results. If the global practice already has the hygienic standards established based on the risk assessment using the

acceptable risk criteria meeting the requirements adopted in the Russian Federation and taking into account in full the peculiarities of risk groups based on the adequate scientific basis it is possible to offer to adopt the existing standard as the domestic harmonized hygienic regulation.

At the same stage it is necessary to determine if there is a necessity to carry out the additional toxicological or epidemiologic studies. This decision can be clarified according to the performance of the following stages for justifying the hygienic regulations under the risk criteria.

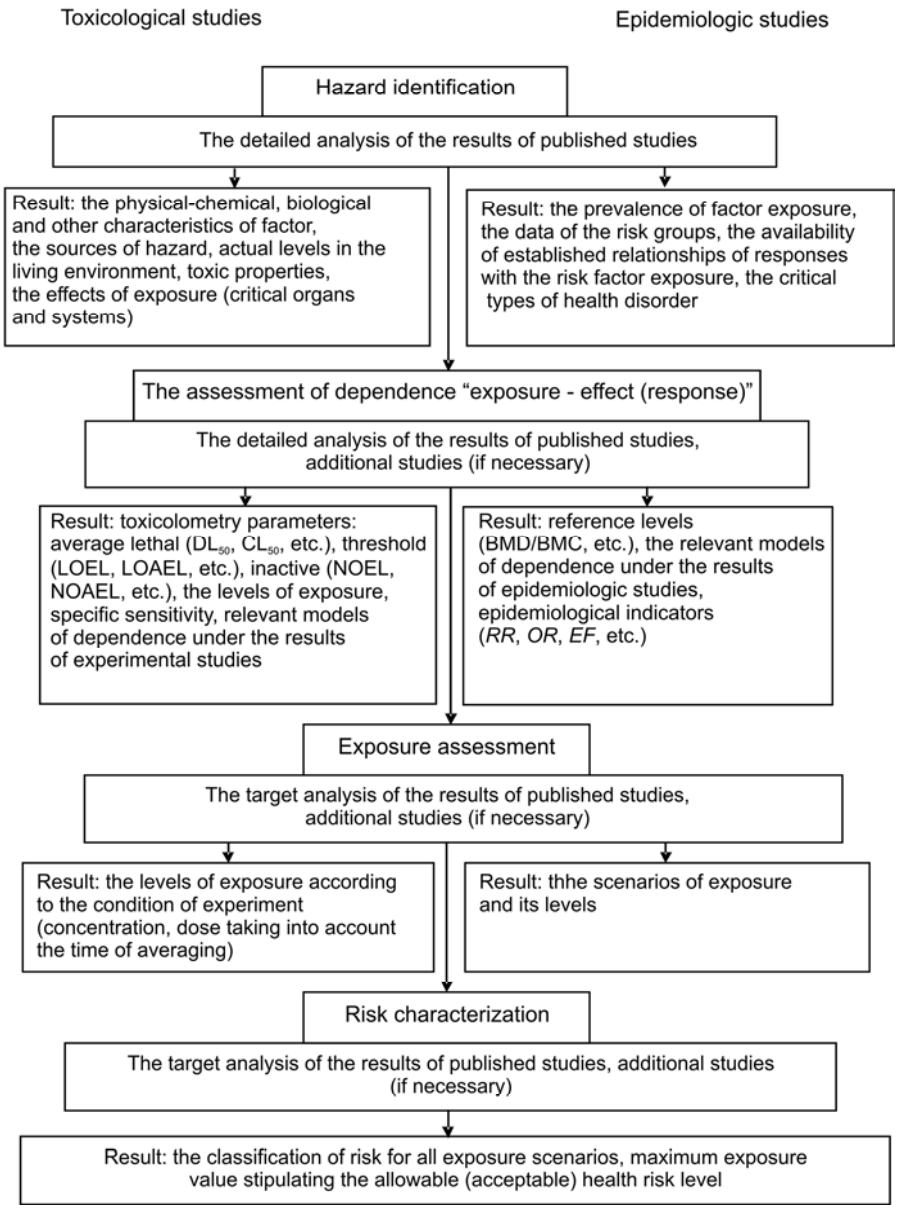

Fig. 3.11. The principal algorithm for justifying the hygienic regulations under the health risk criteria

The peculiarities of stage "Dose – Response Assessment" for the chemical factors and the characteristics of hazard (Hazard Characterization) for the microbiological factors are the establishment in the toxicological or epidemiologic studies of inactive and/or threshold levels of exposure for the factors with established threshold type of exposure. Often as the inactive levels are considered the values characterizing the absence of harmful effect (NOAEL) and the use for this purposes of the maximum levels of exposure not causing any effects (NOEL) is now the subject of discussion [EU, 2000; Hansson S.O., 2002; Lewis R.W. et al., 2002; Valcke M., 2009]. The minimum active levels of exposure, LOAEL, and the benchmark levels of exposure (BMD, BMC) are often used as the threshold exposure levels during the justification of hygienic regulations under the risk criteria. The value of 1–10% characterizing the increase in the probability for the harmful effect development by 1–10%, compared to the background or parallel control, is usually selected as the benchmark effect (BME). The benchmark dose/concentration corresponds to the upper 95% confidence boundary of that level of exposure which is associated with BME [MocMP 2.1.9.004-03].

The Dose – Response Assessment, besides the threshold levels identification includes the assessment of some toxicological parameters (DL_{50}, CL_{50}, etc..) which in future will be applied when determining the assurance coefficients used during the justification of regulations.

The important component of stage for assessing the dependence "exposure – effect (response)" is the analysis and, if necessary, the development of mathematical models quantitatively describing these dependences. These models are used to determine the level of exposure ensuring the risk not exceeding the permissible level. These models shall to the maximum extent describe quantitatively the dependence of critical effects (responses) on the rated factor.

The development of a number of exposure scenarios in accordance with which it is assessed is carried out at the exposure assessment stage for the risk-based regulations justification. As a rule, the detailed scenarios providing the maximum possible level of exposure standard and real, are formed. The scenario of standard (typical) exposure provides the use of rated (recommended) values for the consumption of water, food products, staying in the open air, in premise, etc. The real exposure scenario shall use the same parameters established in the studies, and sometimes with the use of forecast values. For example, recently Russia increases the consumption of meat products, therefore, the maximum permissible levels for the content of chemical substances in them shall be established taking into account the consumption of these products in perspective. It is feasible to consider the exposure formation peculiarities for the most sensitive groups of population in the scenarios providing the standard and actual level of exposure. For example, the diet of pregnant and nursing women differs from the standard, the elderly people spend more time inside the house, etc.

The exposure assessment for the hygienic regulations justification under the health risk criteria is carried out by the direct and indirect methods; herewith the most required are the methods aimed at the exposure markers investigation [Valcke M. Et al., 2009; Onishchenko G.G. et al., 2011].

The main task of the risk characterization stage during the risk-based regulations justification is the establishment of exposure levels at which the health risk level will be permissible. For this purpose based on the risk assessment uncertainty analysis it is necessary to establish the assurance coefficients/modifying factors by the value of which the threshold or inactive exposure levels shall be divided. These factors take into account the scopes of studies, the types of animals in the toxicological studies, the design of epidemiologic studies and a number of toxicological indicators. The uncertainty factor value is established taking into account the possible influence of some factors on the reliability of assessment. When selecting the values of the uncertainty factor components it is recommended to take into account the extrapolation from the one threshold level to another (from LOAEL to NOAEL), interspecific and intraspecific extrapolation, the propagation of data obtained in the conditions of

relatively short exposure, to the longer exposures, influence on the developing body, extrapolation from the one way of intake to another, transfer from the minimum to the complete database, etc. [Onishchenko G.G. et al., 2002].

The risk characterization is performed gradually for the scenarios considered at the exposure assessment stage, using the parameters and models selected during the assessment of dependence "exposure – effect (response)". If the maximum possible level of exposure does not result in the unacceptable health risk, there is no need to consider the other scenarios.

The permissible risk level determination is an essential question during the risk-based regulations establishment. As of now, the probability of death or severe disease $1 \cdot 10^{-4}$ is recommended as such level. For less severe effects it is feasible to use the less severe values, in accordance with their severity.

The levels of risk factors in the living environment objects or products ensuring the maximum exposure value stipulating the permissible (acceptable) health risk level are established as a result of the risk characterization stage performance. These values are considered as the risk-based regulations.

Both in the hygienic standardization and in the health risk analysis methodology the priority is given to the standards established on the basis of epidemiologic studies. In this relation it is feasible to carry out the establishment of harmonized maximum permissible concentrations under the health risk criteria using the harmonized methodology in accordance with which the justification of the benchmark concentrations of risk factors shall be conducted based on the results of epidemiological analysis using the internationally recognized methods, for example, the Benchmark Dose Technical Guidance [US EPA, 2012].

The justification of the hygienic regulations of the living environment objects quality under the health risk criteria is one of the key elements of harmonization with standards adopted in the global practice. The development of quality standards under the risk assessment criteria in accordance with, for example, Canadian Environmental Quality Guidance, Canadian Council of Ministers of the Environment [Canadian Environmental Quality Guidance, 2007] is conducted taking into account the following principles: the use of standards shall not create the risk for the health of population; the development of standards shall be performed for the real scenario of exposure; the critical effect from the side of health shall be established taking into account the most sensitive group of population; the developed standards shall be justified and real for implementation, including all the risk assessment procedure stages.

As a result of the hygienic regulations harmonization with their justification under the risk criteria the regulations applicable in our country can be preserved without changes, corrected with change of the time of averaging, and the development of new regulation using the foreign standards justification experience can be recommended. In this case it is necessary to carry out the comparative analysis of the sources of information (taking into account the reliability of data, availability of the expert evaluation, citedness), the quality of conducted studies (adequacy of the objects of observation, sufficient volume of sampling, duration of experiment, etc.) and the results of study (comparability and reproducibility of obtained data). The result is the establishment of value for the harmonized maximum permissible concentration and critical effects associated with the established level and duration of exposure of the studied compound.

According to the internationally recognized health risk assessment methodology within the preliminary hazard identification it is necessary to select the factor for which the risk-based regulation establishment will be carried out in accordance with a number of criteria.

The following is proposed as the criteria for determining the priority risk factors for which it is necessary to establish the hygienic regulations under the health risk criteria:

– the availability of differences in the values of standards used in the Russian Federation and abroad;

– the results of ranking of risk factors under the degree of hazard for the human health;

– the availability of priority pollutants in the international and national lists;

– the data on the prevalence in the living environment.

Thus, it is feasible to use the following as the criteria for determining the priority ambient air pollutants at the chronic inhalation exposure:

1) the availability for the substances of regulations on the permissible content in the ambient air abroad and in the Russian Federation;

2) the differences in the rated levels of maximum permissible concentrations applied in the Russian Federation and the foreign standards;

3) the results of comparative health effect assessment;

4) the availability of priority pollutants in the international and national lists;

5) the availability of extremely hazardous effects (for example, carcinogenic) for the health of human;

6) the chemical substance prevalence assessment;

7) the exclusion criterion is the absence of chemical substance in the programs for sampling at the ambient air observation stations [Atiskova N.G. et al., 2013].

It is feasible to use the proposed criteria of determining the priority risk factors for forming the list of hygienic regulations on the content of chemical substances in the ambient air for the chronic exposure conditions priority for the development of harmonized regulations using the public health risk criteria.

The list of hygienic regulations and standards on the content of chemical substances in the ambient air for the chronic exposure conditions in accordance with assessment under the first criteria is presented in the Table 3.8 [ГН 2.1.6.1338-03; ATSDR, 2013; IRIS, 1970; OEHHA, 2007].

The identification of substances and their mixtures under the Chemical Abstracts Service (CAS) classification by their names taking into account the trade names of analogs demonstrated that from 390 chemical substances for which the ГН 2.1.6.1338-03 regulates the average daily maximum permissible concentrations the regulations in the foreign databases are available for 387 substances. The comparison of rated values for 48 chemical substances for which there are the rated indicators both in the Russian Federation and databases of the Agency for Toxic Substances & Diseases Registry (ATSDR), USA, the Integrated Risk Information System (IRIS), USA, and the Office of Environmental Health Hazard Assessment (OEHHA), USA, demonstrated that the difference in the rated values is observed for all the substances.

It is important to distinguish the pollutants priority for the harmonization and standardization under the health risk criteria taking into account the weight coefficients, the presence of the substance in the international and national lists of priority pollutants, the availability of carcinogenic effect for human health and the chemical substance prevalence.

Table 3.8

The hygienic regulations and standards for the content of chemical substances in the ambient air for the chronic exposure conditions

The name of harmful substance	CAS	The hygienic regulation of the Russian Federation ($MPC_{c.c}$, mg/m^3)	Permissible concentration in the ambient air for the chronic inhalation exposure conditions			
			The name of harmful substance	ATSDR (*MRL*), mg/m^3	IRIS (*RFC*), mg/m^3	CalEPA (*REL*), mg/m^3
1	2	3	4	5	6	7
Acrylic acid	79-10-7	0.04	Acrylic Acid	–	0.001	–
Acrylonitrile	107-13-1	0.03	Acrylonitrile		0,002	0.005
Ammonia	7664-41-7	0.04	Ammonia	0.07	0.1	0.2
Aniline	62-53-3	0.03	Aniline	–	0.001	–
Arsine	7784-42-1	0.002	Arsine	–	0.00005	–
Acetaldehyde	75-07-0	–	Acetaldehyde	–	0.009	0.14
Benzene	71-43-2	0.1	Benzene	0.0097	0.03	0.06
Bromobenzene	108-86-1	0.03	Bromobenzene	–	0.06	–
1,3-Butadiene	106-99-0	1.0	1,3-Butadiene	–	0.002	0.02

Continuation of Table 3.8

1	2	3	4	5	6	7
Vinylbenzene (styrene)	100-42-5	0.002	Styrene	0.86	1.0	0.9
Hexane	110-54-3	–	n-Hexane	2.14	0.7	7.0
Hexachloroethane	67-72-1	–	Hexachloroethane	–	0.03	–
Hydrogen chloride	7647-01-0	0.1	Hydrogen chloride	–	0.02	0.009
Maleic anhydride	108-31-6	0.05	Maleic anhydride	–	–	0.0007
Hydrogen fluoride	7664-39-3	0.005	Hydrogen fluoride	0.014	–	0.014
Hydrogen cyanide	74-90-8	0.01	Hydrogen cyanide	–	0.0008	0.009
Hydrogenbromide	10035-10-6	0.1	Hydrogenbromide	–	0.025	–
N,N-Dimethylformamide	68-12-2	–	N,N-Dimethylfor-mamide	–	0.03	0.08
Dioxins (in terms of 2, 3, 7, 8 – tetrachlorodibenzo-1,4-dioxine)	1746-01-6	0.5 pg/m^3	Chlorinated dioxins	–	–	0.00000004
Dichloromethane	75-09-2	–	Dichloromethane (Methylene Chloride)	0.3ppm	0.6	0.4
Difluoro-chloromethane	75-45-6	10	Chlorodi-fluoromethane	–	50.0	–
1,2-Dichloro-propane	78-87-5	0.18	1,2-Dichloropropane	–	0.004	–
1,3-Dichloro-propene	542-75-6	0.01	1,3-Dichloro-propene	0.03	0.02	–
1,2-Dichloroethane	1300-21-6	1.0	1,2-Dichloroethane	2.45	–	0.4
1,3-Isobenzofurandion	85-44-9	0.02	Phthalic anhydride	–	–	20.0
Isopropylbenzene	98-82-8	–	Cumene	–	0.4	–
Cadmium dichloride (in terms of cadmium)	–	0.0003	Cadmium & compounds	0.00001	–	0.00002
Cobalt	7440-48-4	0.0004	Cobalt and inorganic compounds, as Co	0.0001	–	–
Cresol (mixture of isomers о-, м-, п-)	1319-77-3	–	Cresol mixtures	–	–	0.6
Xylene (mixture of isomers о-, м-, п-)	1330-20-7	–	Xylenes	0.22	0.1	0.7
Manganese and its compounds (in terms of manganese (IY) oxide)	–	0.001	Manganese & manganese compounds	0.0003	0.00005	0.00009
Methanol	67-56-1	0.5	Methanol	–		4.0
Propylene oxide	75-56-9	–	Propylene oxide	–	0.03	0.03
Methyl-2-methylprop-2-enoate	80-62-6	0.01	Methyl methacrylate	–	0.7	–
4-Methylpentan-2-one	108-10-1	–	Methyl isobutyl ketone (MIBK)	–	3.0	–
2-Metoxy-2-methylpropane	1634-04-4	–	Methyl –T-Butyl ether	0.7ppm	3.0	8.0
Arsenic, inorganic compounds (in terms of arsenic)	–	0.003	Arsenic and inorganic compounds, as As	–	–	0.000015
Naphthalene	91-20-3	–	Naphthalene	0.004	0.003	0.009
Nickel	7440-02-0	0.001	Nickel,asNi	0.00009		0.000014

Continuation of Table 3.8

1	2	3	4	5	6	7
Nickel oxide (in terms of nickel)	1313-99-1	0.001	Nickel oxide	–	–	0.00002
Nitrobenzene	98-95-3	-	Nitrobenzene	–	0.009	–
Ethylene oxide	75-21-8	0.03	Ethylene oxide	–	–	0.03
Acetone	67-64-1	–	Acetone	13 ppm	–	–
Isopropanol	67-63-0	–	Isopropanol	–	–	7.0
Prop-2-en-1-al (acrolein)	107-02-8	0.01	Acrolein	–	0.00002	0.00035
Propylene	115-07-1	–	Propylene	–	–	3.0
Propionaldehyde	123-38-6	–	Propionaldehyde	–	0.008	–
Mercury	–	0.0003	Mercury, elemental. As Hg	0.0002	0.0003	0.00003
Selenium dioxide (in terms of selenium)	–	0.5 μg/m^3	Selenium and compounds, as Se	–	–	0.02
Hydrogen (hydrogen sulfide)	7783-06-4	–	Hydrogen sulfide	–	0.002	0.01
Carbon disulfide	75-15-0	0.005	Carbon disulfide	0.42	0.7	0.8
Sulfuric acid	7664-93-9	0.1	Sulfuric acid	–	–	0.001
diantimony rioxide (in terms of antimony)	–	0.02	Antimony	–	0.0002	–
Tetrahydrofuran	109-99-9	–	Tetrahydrofuran	–	2.0	–
Tetrachloromethane (carbon tetrachloride)	56-23-5	0.7	Carbon tetrachloride	0.19	0.1	0.04
Tetrachloro-ethylene	127-18-4	0.06	Tetrachloroethylene	0.25	0.04	0.035
Toluene	108-88-3	–	Toluene	0.3	5.0	0.3
Tribromomethane (bromoform)	75-25-2	0.05	Bromoform	0.05	0.005	–
Trichloromethane (chloroform)	67-66-3	0.03	Chloroform	0.09	–	0.3
1,2,3-Trichloropropane	96-18-4	0.005	1,2,3-Trichloropropane	–	0.0003	–
1,1,1 – Trichloroethane	71-55-6	0.2	1,1,1 – Trichloroethane (Methyl chloroform)	–	5.0	1.0
Trichloroethylene	79-01-6	1.0	Trichloroethylene	0.002	0.002	0.6
Triethylamine	121-44-8	–	Triethylamine	–	0.007	0.2
1-phenyl-2-chloroethanone	532-27-4	–	2-Chloro-acetophenone	–	0.00003	–
Phenol	108-95-2	0.003	Phenol	–	–	0.2
Formaldehyde	50-00-0	0.003	Formaldehyde	0.009	–	0.009
Phosphine	7803-51-2	0.001	Phosphine		0.0003	0.0008
Inorganic poorly soluble fluorides – (aluminium fluoride, calcium fluoride, natrium hexafluoroaluminate)	–	0.03	Fluorine	–	–	0.013
Inorganic highly soluble fluorides – (natrium fluoride, natrium hexafluoride)	–	0.01		–	–	

End of Table 3.8

1	2	3	4	5	6	7
Chlorine	7782-50-5	0.03	Chlorine	0.001	–	0.0002
Chlorobenzene	108-90-7	–	Chlorobenzene	–	–	1.0
2-chlorobuta-1,3-diene	126-99-8	0.002	Chloroprene	–	0.02	–
Chloroethane (ethyl chloride)	75-00-3	0.2	Ethyl chloride	–	1.0	30.0
Vinyl chloride	75-01-4	0.01	Vinyl chloride	–	0.1	–
(Methyl Chloride) oxirane	106-89-8	–	Epichlorohydrin	–	0.001	0.003
Chromium (VI)	–	0.0015	Chromium (VI)	0.000005	0.000008 (aerosols) 0,0001 (particles)	0.0002
Cyclohexane	110-82-7	–	Cyclohexane	–	6.0	–
Ethyl benzene	100-41-4	–	Ethyl benzene	0.26	1.0	2.0
Vinyl acetate	108-05-4	–	Vinyl acetate	–	0.2	2.0

It is feasible to carry out the comparative assessment of health effect with the use of weight coefficients of carcinogenic and noncarcinogenic effects [P.2.1.10.1920-04]. The highest weight hazard quotient shall be taken into account for substances having the carcinogenic and noncarcinogenic effects. For substances not having the reference concentration it is possible to use the average daily maximum permissible concentration for ranking.

According to the criteria "The vaailability of substance in the international and national lists of priority pollutants" when selecting the substance for the priority harmonization it is necessary to consider such lists of pollutants as:

1) the informational letter of the Ministry of Health of the Russian Federation "On the list of priority substances contained in the environment and their influence on the population" No. 11/109-111 dd. August 7, 1997 (Russia);

2) National Ambient Air Quality Standards (NAAQS) U.S. Environmental Protect Agency;

3) National standards for criteria air pollutants in Australia;

4) Criteria Air Contaminants and Related Pollutants. The Government of Canada;

5) Air Quality Standards, European Commission [WHO, 2000], etc.

Under the results of comparison of the priority pollutant lists in USA, Australia, EU, Canada and Russia it was established that 22 substances from the selected are included into the lists of priority ambient air pollutants.

According to the database of US EPA 29 substances have the carcinogenic properties:

A group (human carcinogen) – 6 substances;

B1 group (probable human carcinogen (limited evidence for human)) – 5 substances;

B2 group (probable human carcinogen (sufficient evidence for animals and insufficient evidence or absence of data for human)) – 12 substances.

C group (possible human carcinogens) – 6 substances.

To assess the prevalence of the chemical substances influence, it is feasible to use the data of State reports "On the state of sanitary and epidemiological welfare of population in the Russian Federation". Thus, according to these sources the biggest number of population of the Russian Federation resided at the territories with high level of the ambient air contamination with formaldehyde, benzopyrene, ethylbenzene, nitrogen dioxide, lead and its inorganic compounds, copper oxide (II), sulfur dioxide [State report, 2012, 2013].

The criterion for exclusion from the list is based on the data of the Federal Information Fund of the Social-Hygienic Monitoring (FIF SHM).

The point rating system is proposed for assessing the chemical pollutants priority for the harmonization and standardization under the health risk criteria. It takes into account the weight health effect coefficient (at the weight coefficient equal to 100 – 1 point; 1000 – 2 points;

10000 – 3 points; 100000 – 4 points; 1000000 – 5 points); the availability of carcinogenic effect under the US EPA classification (one point for the presence of substance in the lists of carcinogens of A, B1 and B2 groups); the availability of substances in the lists of priority pollutants in different countries (assessment for each substance was performed taking into account the sum of points for the presence in every of 6 lists of priority pollutants); the prevalence of influence of the chemical substance on the population of the Russian Federation (2 points for the presence in the list of prevailing substances).

The list of chemical substances priority for the development of hygienic regulations under the health risk criteria and harmonization is proposed based on the above mentioned criteria (Table 3.9).

Table 3.9

The list of chemical substances priority for the development of hygienic regulations under the health risk criteria and harmonization of regulations on the content in the ambient air for the conditions of chronic inhalation exposure

Item No.	The name of substance	Item No.	The name of substance
1	Benzapyrene	16	Dioxins
2	Formaldehyde	17	Nickel
3	Mercury	18	Chloroethanol (vinyl chloride)
4	Carbon disulfide	19	Poorly soluble inorganic fluorides
5	Ammonia	20	Tetrachloromethane
6	Nitrogen dioxide	21	1,3-Butadiene
7	Chlorine	22	Cobalt
8	Sulfur dioxide	23	Ethenylbenzene (styrene)
9	Benzene	24	Carbon
10	Cadmium	25	Prop-2-ennitrile (acrylonitrile)
11	Arsenic, inorganic compounds	26	Trichloromethane (chloroform)
12	Lead	27	Methanol
13	Manganese and its compounds	28	Nitric acid
14	Nitrogen oxide (II)	29	Cupric oxide
15	Sulfuric acid /under molecule H2SO4/	30	Hydrochloride (hydrochloric acid)

The Russian Federation under the health risk criteria performed with a different degree of detailing the justification of harmonized average annual maximum permissible concentrations for a number of substances, including nickel, manganese, copper, fluorides, methanol, trichloromethane, included into the list of chemical substances priority for the development of hygienic regulations on the content in the ambient air.

Under the results of comparison of the priority pollutant lists in USA, Australia, EU, Canada and Russia it was established that 22 substances from the selected are included into the lists of priority ambient air pollutants.

The more detailed establishment of hygienic regulations under the health risk criteria is shown on examples in the chapter 7.

The experience of the justification of hygienic regulations under the health risk criteria in the Russian Federation demonstrated that during the development of risk-based standards it is possible to use a number of methodical approaches, depending on the type of hygienic regulations and objects for which they are established.

Thus, at the hazard identification stage during the establishment of the risk-based regulations of the living environment it is feasible to determine the priority factors requiring the standardization. One of the methods for their identification in relation to the ambient air chemical contamination factors is specified above. In addition, for the external environmental

risk factors the actual is the assessment of real conditions of their influence on the health of population.

When implemented the stage for the assessment of dependence "exposure – effect (response)" to justify the risk-based standards of the living environment objects quality the most feasible is the use of the quantitative risk assessment methods proposed for the carcinogenic risk in the manual P.2.1.10.1920-04, for noncarcinogenic risk – in the guidelines MP 2.1.10.0062-12. In addition, in case of developing the regulations with long-term period of averaging, for example, of average annual maximum permissible concentrations of chemical substances in the ambient air it is methodically feasible to use the risk evolution simulation allowing for assessing the risk in the conditions of the established, including the variable, exposure, during the long time period, up to the whole expected lifespan.

At the exposure assessment stage when developing the hygienic regulations under the acceptable risk criteria the traditional exposure assessment methods can be supplemented by the methods of mathematical simulation of its levels at the separate points. The method for the calculation of concentrations of harmful substances in the ambient air with approximation under the results of field measurements is well recommended [May I.V. et al., 2013].

The risk characterization when justifying the risk-based regulations of the living environment is performed as the assessment of compliance of the considered regulation with the provision of safety (absence of unacceptable individual risk) for health. The upper bound of level *de minimus* is often used as the acceptable risk, or when using the risk evolution simulation - the upper bound of the specified risk index characterizing the negligible risk.

When using the uncertainty factors during the development of hygienic regulations under the risk criteria practically always it is necessary to take into account the modifying coefficients characterizing the interspecific extrapolation (for toxicological studies), intraspecific extrapolation and transfer of the results of study from the high levels of exposure to low.

It should be noted, that the use of the specified methodical approaches in the justification of average annual maximum permissible concentrations of metals in the ambient air allowed for obtaining the results comparable to the reference concentrations of these substances recommended by the U.S. Environmental Protection Agency (USEPA). This shows that the regulations justified under the risk criteria can be used in future as the reference levels for the health risk assessment.

The justification of risk-based regulations for products acquires the special meaning, both the hygienic and economic and political.

In this field it is possible to offer the whole range of methodical approaches based on the internationally recognized risk assessment principles tested in the Russian Federation. In relation to the food products they include:

– the quantitative assessment of carcinogenic and noncarcinogenic risk when justifying the hygienic regulations on the content of nitrates in the food products of vegetable origin;

– the risk assessment based on the mathematical models of influence of the tetracycline antibiotics on the intestinal microflora balance built under the results of *in vitro* tests, with the assessment of the population risk of morbidity associated with this disbalancement;

– the assessment of the health disorders risk evolution at the variable exposure of ractopamine taken with dairy and meat products, including in the target groups (pregnant and nursing women);

– the assessment of risk using the methodical scheme for the microbiological risk assessment recommended by the Codex Alimentarius, taking into account the peculiarities of the food products consumption by the population of the Russian Federation.

More detailed information about the results of the use of methodical approaches to the justification of a number of hygienic regulations under the health risk criteria is presented in the chapter 4.

In general, it is possible to make a conclusion that the methodical approaches to the risk-based standards justification can differ depending on the type of hygienic regulations requiring the justification under the acceptable risk criteria and objects for which

these regulations are established. It is possible to distinguish several common characteristic features:

– compliance with basic health risk assessment principles during the justification of risk-based standards (priority of safety, non-zero risk concept, transparency of assessment, stages of assessment, relevance of information, etc,);

– the use of modern adequate methodical approaches to the processing of information at the stages of exposure assessment and assessment of dependence "exposure – effect (response)";

– the mandatory consideration of exposure scenarios for the target and the most sensitive groups of risk recipients;

– the use of the whole aggregate of available data from the information obtained in the *in vitro* tests to the results of epidemiologic studies;

– the comparison of the risk assessment results using the data from different sources;

– consideration as the priorities of hygienic standards, health risk assessment during the justification of which was performed on the basis of epidemiologic studies;

– the mandatory justification of the set of modifying factors (uncertainty coefficients) and their values.

The use of described methodical approaches for the justification under the health risk criteria of both newly developed and existing hygienic regulations is a prospective direction for the provision of sanitary and epidemiological welfare of population creating the basics for the harmonization of regulatory and legal base of the Russian Federation taking into account the priorites of the social and economic development of the state.

3.4. The elements of health risk management on the basis of spatial analysis

The public health risks mitigation through the system of spatial decisions is a widely used risk management method. Herewith, the spatial decisions can be of different level – from the federal when the risk assessment unit are the significant territories (up to the subjects of federation) to the local when the risks as assessed at the territories limited by the influence of one or several sources of hazard.

The tasks of the large-scale territorial assessment of risks are considered, as a rule, within the regional spatial planning schemes. Since, in accordance with Town Planning Code of the Russian Federation (chapter 3 article 9), the territorial planning means the determination and documenting of the territory intended use according to the aggregate of social, economic, ecological and other factors, the public health aspects shall be mandatory considered. The final objective of planning is the provision of the sustainable development of territories that includes also the medical and demographical component at the level of the Russian Federation, subjects of the Russian Federation and municipal structures.

In the market economy conditions the territorial planning performs the communicative functions and is focused on the complex and optimal solving of the current forecasted social and economic tasks having the geographical aspect. Herewith the spatial organization of territory is directly associated with strategic decisions of the corresponding level and, as a rule, is a component of program for the social and economic development of the country or region [Bertollini R., Martuzzi M., 1999]. According to some authors, only the strategy for development of the Russian Federation under the innovative scenario can provide the significant improvement of the social and economic position of the country in general and its separate regions, and the spatial organization of the country shall play the most important role in the development and implementation of such strategy [Vilner M.Ya., 2009; Sokolov S.Ya., 2010].

By virtue of the fact that the nation health preservation and the increasing of human potential at the level of the Russian Federation are included into the list of strategic priorities

of the country, the use of methodology for the human health life and health risk assessment and management in the tasks of spatial development and urban planning is logical and potentially effective [Bobkova T.E., 2011].

Herewith it should be noted that the classic medical and geographical analysis is used quite widely in practice [Malkhazova S.M., 2001; Prokhorov B.B, 2005; Saurina O.S. et al., 2010; Mapping the chemical environment…, 2011; Alekseev E.V., 2011; Shvets A.B., Chudinova L.S, 2014]. Thus, for example, Saurina O.S. et al. performed the typological classification of Orel region under the sickliness and morbidity of population with different nosoforms. The maps for distribution and tendencies of morbidity of the population of region are executed. The methods and computer technology for the creation of medical and geographical maps are proposed. The same studies are conducted for Voronezh region [Kurpolan S.A., 2004], Perm Territory [May I.V., Balashov S.Yu., 2011], Sverdlovsk region [Vinokurov Yu.I. et al., 2010], etc. However the mapping of levels of the medical and geographical indicators does not answer the question on the causation of the indicators differentiation and does not allow for assessing the relationship between the indicators of mortality, morbidity, disablement and other indicators and factors for their determination. In this relation mapping the health risk assessment results has the significant advantages over the spatial analysis of the health indicators only.

The analysis of peculiarities of the spatial health risk distribution when exposed to the external environment factors is required during the detection of both problematic and the most prospective, attractive for investment, sectors of economy and corresponding functional and planning areas – "the poles of growth". The assessment of the spatial distribution of existing and future health risks and potential losses associated with these risks (first of all, in the form of losses of labor potential) allows for more accurate planning of the basic territory development parameters. Such parameters include: the number of population (including of the working-age) of urban and rural settlements – in general and under the separate territories; the levels of mortality and morbidity; the indicators directly associated with demographical parameters: the scopes of new housing construction and the reconstruction of existing stock; demands for the development of social sphere, including the health care, etc.

The zoning as the most distributed territory differentiation method allows for separating the areas with the highest health hazard and, on the contrary, the most favorable territories that can and shall be taken into account when forming the schemes of settlement, the complex planning assessment of territory and the justification of conditions and requirements on the use of territory [Kurolap S.A., 2004; Wong C.S.C. et al., 2006, et al.].

The main methods for the health risk management using the spatial planning tools are the refusal from risks or their mitigation through:

– the removal of existing hazardous independent objects and forms from the territory of the permanent residence of population;

– exclusion at the stage of design of the location of independent objects hazardous for the life and health in the vicinity of residential construction;

– the removal of residential construction from the exposure areas of the functioning hazardous objects;

– the optimization of the transport schemes of cities taking into account the influence on the health of population;

– the limitation of staying of people in the areas with increased level of risk;

– the maximum concentration of objects with increased level of hazard at the certain territories with clear functional intended use and removal of these areas from the places of permanent residence or staying of population.

The management is implemented through the functional zoning of territories, the introduction of limitations for the use of territories for the civil construction purposes, including through the organization of sanitary protective zones, sanitary discontinuities, etc.

The general algorithm for using the methods of spatial assessment in the health risk management tasks is shown in Fig. 3.12.

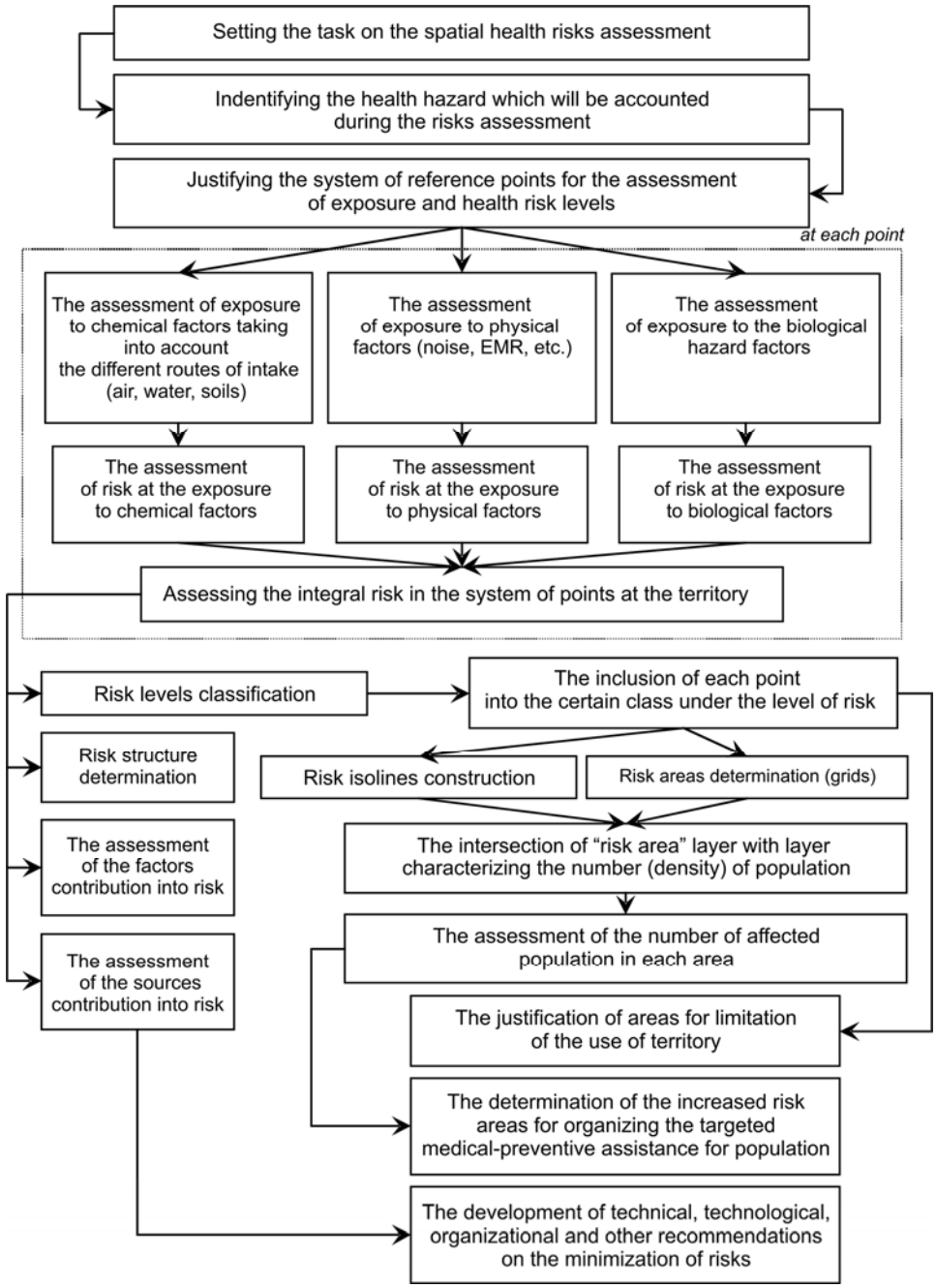

Fig. 3.12. The general algorithm for using the methods for assessing the spatial distribution of risks in the management areas

The main task at the stage of information support for making the decision is the assessment and forecast of risks distribution at the territory and the assessment of the number of affected population. A number of hygienic studies performed the analysis of the territorial distribution of health risks [Swartjies F.A., 1999; Campbell M.J., 2001; Yankovich E.P. et al, 2011; Avaliani S.L. et al., 2012; Vasilyev A.V. et al., 2013, etc.]. Mainly, it is the assessment associated with the ambient air contamination based on the results of the calculation of the diffusion of impurities or the results of field measurements. The essentially weaker the literature reflects the spatial aspects of health risks associated with the quality of drinking water supply, noise, EMR

Practically, there are no data on the territorial distribution of the integral health risks.

Moreover, the methodical support of the integral risks assessment, including on the basis of evolution simulation, provides wide possibilities for the spatial analysis of the sanitary and epidemiological situation at the territories and making of adequate managerial decisions on the management of risks. The task is simplified by the wide distribution and permanent improvement of software and hardware for the spatial analysis supporting, first of all, of computer geographic information systems (GIS). The latter are designed for storage, processing and visualization of the spatially distributed data [Chistobaev A.I. et al., 2010; Svetlichnaya A.D., 2012, etc.]. Main GIS currently used in the decision making system at the level of state authorities of the Russian Federation, subjects of federation and local self-government include such software products as Atlas GIS, ArcView, Mapinfo, WinGis as well as a number of other, both foreign and domestic GIS. All the listed GIS are professional; they allow for providing the classic list of services, are aimed at the work with digital (electronic) maps of territories which are the digital models of map.

The principle of layer-by-layer organization of information when the objects are combined into thematic layers allows for carrying out the multidimensional analysis combining the layers in accordance with tasks and objectives of user. As a rule, the objects included into one layer form some logically (and often physically) separate unit of data, have unified and specific system of identifiers, they can be used as the independent totality and herewith it results in solving the task of complex analysis. Thus, to solve the tasks on the health risk assessment it is possible to combine into one layer all the stationary and movable sources of pollutants emission to the ambient air, to other - the sources of noise. Often in this case also the division of one thematic layer by horizontal is organized - similarly to the separate sheets of maps.

The number of layers during the layer-by-layer data organization can be practically unlimited depending on the certain implementation. This allows for manipulating the large groups of objects represented by layers as the unified whole, for example, including or excluding the layers for visualization, determining the operations based on the interaction of layers (Fig. 3.13).

It should be noted that the models and formats of data in GIS in general are more complicated than in other types of software. This is due to the fact that it is required to maintain the relationship between the attributive and spatial information and with that geographical objects are very different in their nature – individualized objects of different geometrical types with clear borders, the objects with fuzzy boundaries and continuous fields of numerical and nonnumerical features. The complexity of models is also stipulated by the necessity to provide the performance of many, often difficult, functions.

The possibility to use both the integrated and external software allows for solving a wide range of tasks on the spatial analysis of disposition of sources of health risk, exposure and the risks themselves [Lobanov G.V. et al., 2010].

The spatial analysis and mapping of health risks is more actual because at the cross-spectrum analysis of exposure areas and targeted registers of territories there is a possibility to determine correctly the number of affected population taking into account the age-sex structure of this population. Namely this information is the main basis for making the managerial decisions on the population safety provision.

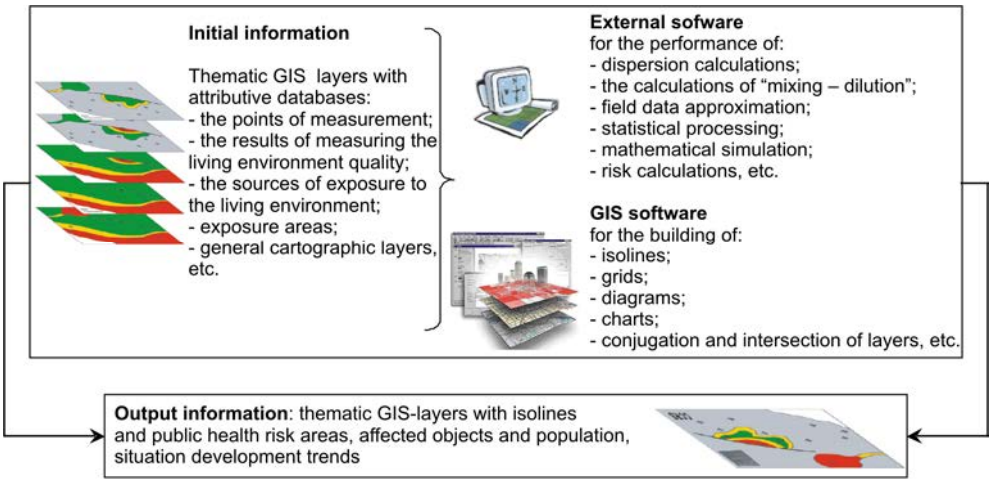

Fig. 3.13. The main components of GIS for the public health risk assessment

To solve the tasks of the spatial risk levels distribution, the zoning of territories and the characterization of affected population, we offer the approaches based on the population exposure assessment in the system of reference points covering the whole investigated territory. When zoning the territory under the risk criteria at the level of country or region (when developing the spatial development schemes) it is necessary to use the large-scale vector maps (1:500000; 1:200000, etc.). The maps provide the coordinate referencing of priority and the largest sources of hazard and the methods of enlarged reconnaissance risks assessment for tasks are used:

– assessing the perspective of territories for further industrial, agricultural and other development;

– determining the spatial vectors for the schemes of settlement;

– selecting the territories for the location of recreative and health-improving, sanatorium-resort and other zones;

– determining the zones of the highest, including the unacceptable, risks in order to introduce the restrictive measures, establishing the special functional areas, etc.

Herewith when solving the tasks of federal or regional level the reference points network can be quite rare and irregular.

When solving the tasks at the level of urban or rural settlement the small-scale maps are used (from 1: 10000 to1: 2000) for the tasks on:

– detecting the zones of the highest, including the unacceptable, health risk;

– determining the objects of residential and social-cultural purpose located in the zones with increased level of risk;

– assessing the number of affected population (with targeted referencing of the places of residence to organize the targeted medical and preventive assistance for the population);

– structuring the health risks;

– the visualization of data on the sources of hazard and risks at the territory of settlement.

Solving the spatial tasks using new methodical approaches and external software significantly extends the possibilities of GIS.

Thus, in relation to the assessment of the territorial health risks distribution and establishment of the cause-and-effect relationships between the hazard factors and the public health parameters we offer the methods of spatial analysis based on the calculation of risk under the system of points covering the whole territory of settlement. The exposure to the certain factor or their combination is assessed at each point. Thus, when assessing the

chemical exposure at each point it is necessary to calculate the short-term and chronic exposure through the accounting of concentrations of each chemically hazardous substance incoming with ambient air, drinking water, soil, etc. For each point it is necessary to perform the calculation of single and/or daily doses of chemically hazardous substances coming to the body by different ways and the calculation of individual carcinogenic risk (*TCR*), cumulative index of hazard of acute noncarcinogenic exposure THI_{ac} (the nosologies or groups of nosologies are considered), cumulative index of hazard of chronic noncarcinogenic exposure THI_{ac} for each nosology *m*.

As a result, each point (*X*; *Y*) has a risk parameters vector:

$$\left\{R\left(x;y\right)\right\}^{T} = \left\{TCR, THI_{ac}^{1} ... THI_{ac}^{n}, THI_{cr}^{1} ... THI_{cr}^{m}\right\}, \quad (3.4.1)$$

where – total carcinogenic risk *TCR* – is an individual risk at the simultaneous exposure of several carcinogenic substances coming by different ways to the human body;

– acute exposure risk THI_{ac} – is a cumulative hazard index of acute exposure at the complex intake of chemical substance to the human body from environment simultaneously by different ways as well as at the multienvironmental and multiroute exposure (for each nosology *n*);

– chronic exposure risk THI_{cr} – is a cumulative hazard index of chronic exposure at the complex intake of chemical substance to the human body from environment simultaneously by different ways as well as at the multienvironmental and multiroute exposure (for each nosology *m*).

The contribution of factor to the total risk is assessed typically as the relation of risk formed by the factor *i* to the common risk. But the interest is focused on assessing the contribution from the separate sources of hazard into the formation of total risk at the territory that can be performed based on the analysis of the system of points in which the contribution of the certain factor from the certain source can vary greatly.

The system of reference points is subjected to the cluster analysis procedure (the clusterization can be performed using the different means, for example, using the package of applied programs SAS or Statistica). The cluster analysis of the system of points results in the groups of points at the territory which are characterized by the similar risk parameters. Each cluster is characterized by the cluster means vector (K_1, K_2, …, K_n) = MEEN, where K_i – is a mean value of each risk parameter in the cluster.

The affected population number criteria are used for prioritizing the problems and justifying the managerial decisions at the territory (Table 3.10).

In order to verify the health risks implementation we offer the approaches based on the assessment of correlations between the levels of exposure and actual existing morbidity of population. Such verification allows for preventing the excessive aggravation of risks or, on the contrary, their underestimation that increases the reliability and adequacy of applied risk management measures.

The proposed approach as the previous one uses the exposure fields established based on the system of reference points at the territory of settlement. The use of regular computational grid which divides the territory of settlement into equal sections (cells) is optimum to solve this task. The fields of exposure or risks (doses, coefficients or indexes of hazard) and fields of health parameters, for example, relative frequency of relative application of population for medical services are the initial data to establish the "exposure – public health condition parameters" dependences.

The following requirements are presented to the initial data:

– the functions of fields reflecting the living environment quality, exposure of population or any other indicators characterizing the probable influence (for example, the concentrations, coefficients or indexes of hazard, etc.) shall be smooth;

– the functions of negotiability fields shall contain no "jumping out" values;

– the functions of fields of living environment and negotiability shall be set by tabulated method under the coordinate grid and shall be agreed under the coordinates.

Table 3.10

The categories of territories taking into account the number of population residing in the different health risk conditions

The number of population in the hazard zone	The level of individual health risk			
	negligible	moderate	high	very high
Up to 100 persons	IV	III	III	II
100 to 1 thous. of persons	III	III	II	II
1 thous. to 10 thous. of persons	III	II	II	I
More than 10 thous, of persons	III	II	I	I

I category	First level priorities. The territories of very high individual health risk with the high number of affected population. Require the measures within the urgent and/or short-term planning
II category	Second level priorities. The territories of high individual health risk with the negligible number of affected population or moderate individual risk with the high number of affected population Require the inclusion into short-term action plans and programs on the public health risks mitigation
III category	No priority. The territories of moderate health risk. Require the planned measures within the medium-term action plans
IV category	No priority. The territories of low health risk. Do not require the risk mitigation measures

When calculating the correlation fields the following shall be taken into account:

– the correlations function shall be smooth;

– the considered area of the correlation function values – [0; 1], i.e. the correlations with positive actions of contamination factors (reverse correlation relationship).

The calculation of correlation coefficients using the "sliding window" method is performed for each cell of coordinate grid using as the observations the cells located in some vicinity. The Fig. 3.14 shows the vicinity of points for the calculation of correlations in the size of 5·5.

The dimensions of vicinity for the qualitative assessment of correlation coefficients are determined taking into account the observed gradients of parameters of independent variable (concentrations of contaminants, doses as the measure of esposure, indexes or coefficients of hazard, etc.).

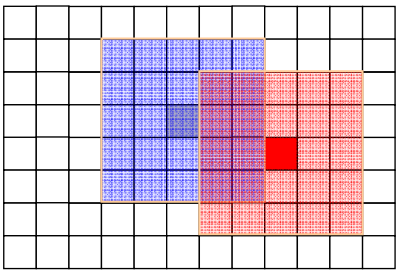

Fig. 3.14. The vicinity of points
for the calculation of correlations

For this the exposure parameter gradient average by territory (R) is calculated:

$$\overline{grad(R)} = \frac{1}{2n_x n_y} \sum_{i=1}^{n_x} \sum_{j=1}^{n_y} \left(abs(R_{i,j} - R_{i,j+1}) + abs(R_{i,j} - R_{i+1,j}) \right), \qquad (3.4.2)$$

where R – is a value of exposure parameters;

n – is a number of points of computational grid.

The number of points in the vicinity is determined as rounding to the nearest integral value of relation 0.1 to the average gradient. It is accepted that 0,1 R – is a significant parameter of the change of exposure:

$$d = \left\lceil \frac{0{,}1}{\overline{grad(R)}} \right\rceil, \qquad (3.4.3)$$

where d – is a size of vicinity around the point.

The calculations performed before demonstrated that at the grid pitch of 100×100 m the size of vicinity shall be applied as 5·5 points. At such parameters 25 points of regular grid participate in calculations.

It is necessary to pay attention to that the negotiability function depends greatly on the conditions of the construction and residence of population at the urban territory. The availability of "bare places" (unsettled areas) adjacent to the residential districts can affect greatly the obtained dependences. That is why it is necessary to exclude the cells with the zero number of population from the calculations. The cells in the vicinity of which less than 5 "settled" cells are locates shall be also excluded from the calculations.

Provided that the design rectangles are not characterized by big drops of values of influencing functions, it is recommended to use the Pirson's linear correlation coefficient to assess the dependences (in general, nonlinear ones).

The correlation fields are obtained carrying out the successive calculations of correlation coefficients for each cell of regular grid. Simultaneously it is necessary to check the significance of correlation coefficients using the Student's t-criterion. For reflection it is necessary to select the correlation coefficients with confidence level of ≤0.05 and the number of observations not more than 5 from each correlated row.

The described methods stipulate the conduction of pair calculations, i.e. the spatial distribution of dependence of each characterization of negotiability from each exposure parameter is built. The calculations result in the system of points at the territories intended for building each of which is characterized by parameter r – the coefficient of correlation between the exposure parameter and response – application of population for medical assistance under the established nosology or class of diseases.

The zoning is performed under criterion r taking into account the ranges under the power of relationship (scale under [Ivanter E.V., Korosov A.V., 2011]): less than 0.3 – weak, 0.3–0.5 – moderate, 0.5–0.7 – average, 0.7–1 strong relationship.

The correlated fields between the parameters of "exposure" and "response" are obtained as a result of the described algorithm implementation. The correlation field between the concentrations of contaminants and indicators of the population diseases prevalence is reflected in GIS that allows for visual presentation of differentiation between the established interrelations at the territory.

The spatial analysis of correlation fields characterizing the spatial distribution of the closeness of relationships between the hazard indexes and public health risk parameter and public health disorders as the application for medical assistance allows for distinguishing the areas of different levels of relationship "risk factors – public health condition parameters" at the territory.

This approach can be used to reflect the interrelations between the living environment parameter and mortality prevalence under reasons, morbidity with nosologies at which the organs/systems sensitive to the influence of the certain media parameters are involved.

The allocation of areas of high correlation coefficients between the living environment exposure parameters and public health disorders under the class of diseases/nosologies as the application for medical assistance is a tool for choosing the most effective managerial decisions and allows during the conduction of additional in-depth epidemiologic studies at these territories:

– to develop the mechanisms and strategy of different regulatory measures on the health risk mitigation measures;

– to distinguish the group of population requiring the preventive and therapeutic and diagnostic measures aimed at the prevention of diseases which are caused by the influence of adverse ecological factors;

– to correct the living environment quality monitoring programs;

– to obtain the qualitative characteristics of damage to health from the influence of harmful human living environment factors;

– to compare and rank the different under the degree of manifestation effects from the influence of living environment factors on the human health;

– to determine the priorities of environmentally friendly policy at the level of enterprise, industrial cluster, territory, region;

– to carry out the priority regulation of those risk sources and factors which impose the largest threat for the health of population;

– to characterize qualitatively and quantitatively the levels of risks preserved after the application of measures on its mitigation;

– to correct the programs of monitoring and industrial control taking into account the priority human living environment contamination sources, priority contaminated environments and chemical substances making the largest contribution to the adverse effects development risk.

The most important such interfacing is during the investigation and forecasting the ecological and sanitary-epidemiological situation at the urbanized territories. The health of citizens at such analysis acts as the integral indicator determining the allowability or non-allowability of technical, planning, organizational and other decisions.

In addition, the described approach can be used also for solving the tasks of parameterization and assessment of multifactorial external environmental influence on the population morbidity prevalence.

The creation of sanitary protective zones is the separate actual issue on the heath risk management using the spatial and planning methods. The sanitary regulations establish the class of hazard for industrial facilities and productions, requirements to the size of sanitary protective zones, basis for the review of these sizes, methods and procedure for their establishment for separate industrial facilities and productions and/or their complexes, limitations to the use of territory of sanitary protective zone, requirements to their organization and improvement, as well as the requirements to the sanitary discontinuities of hazardous communications (automobile, railroad, air, pipelines, etc.) [Vasilyev A.V. et al., 2013].

The main objective of establishing the sanitary protective zones – is a provision of safety for population through decreasing the influence of contamination on the ambient air (chemical, biological and physical) to the values established by the hygienic regulations, and for the enterprises of I and II class of hazard – both to the values established by the hygienic regulations and to the values of acceptable public health risk.

In the conditions of intense development of territories for the housing and public construction and deficit of free areas not having the limitations for construction the land within the boundaries of sanitary protective zones (SPZ) is of urban planning value.

Currently the local self-governing bodies carry out the zoning of the territories of population clusters taking into account the approximate sanitary protective zones based on the sanitary classification; as a result of it the significant part of territories which could be used for construction is limited in use due to the fact that it is located within the sanitary protective zones. The ineffective use of territories within the sanitary protective zones is stipulated by the insufficient legal supporting of the SPZ organization.

The SPZ organization problems include:

– the absence in the Russian Federation of regulatory and legal fixation for the public health risk assessment methodology, including at the influence of different living environment factors;

– the absence of procedure for the recording in the state real estate cadaster of data on the SPZ boundaries and state registration of the limitations of rights to the land plots within the SPZ boundaries in the Unified Public Register of Real Property Titles and Transactions (UPRPTT);

– the absence of procedure for marking the SPZ boundaries on the graphical materials of the current plan of municipal structure;

– the uncertainty of the land status within the SPZ boundaries as the source of payments (as the payment for land contamination or as the payment for land use);

– the absence of procedure for the inactive SPZ liquidation.

As a result, the objects for residence of people and recreational purposes or industrial facilities the location of which is prohibited within the SPZ boundaries are located within the SPZ boundaries; the persons possessing the rights to the land plots within the SPZ boundaries cannot receive the compensation of harm due to the imposed limitations; the local and territorial budgets do not obtain the incomes from the use of specified land plots; the SPZ of liquidated or planned for construction but not constructed enterprises severely constrict the development of municipal structures.

The harmonization of sanitary, land, urban planning and civil legislations shall facilitate the regulation of issues associated with the SPZ boundaries execution and their maintenance as well as the release of territories for their further use for recreational purposes and housing construction.

The execution of the limitations of rights to the land plots within the SPZ boundaries is an important element of the SPZ organization. The requirements to the introduction of data on SPZ to the state real estate cadaster and registration of limitations in UPRPTT are regulated by the Land Code of the Russian Federation No. 136-FZ dd. October 25, 2001, Federal Law No. 78-FZ dd. June 18, 2001 "On the land development", Federal Law No. 221-FZ dd. July 24, 2007 "On the state real estate cadaster", Resolution of the Government of the Russian Federation No. 514 dd. July 11, 2002 "On approval of the Provision on the coordination and approval of "land surveying documentation, creation and maintenance of the state fund of data obtained after the land development conduction", Resolution of the Government of the Russian Federation No. 621 dd. July 30, 2209 "On approval of the form of map (plan) of land development object and requirements to its execution, Order of the Ministry of Economic Development and Trade of the Russian Federation No. 267 dd. June 3, 2011 "On the land development", Letter of the Ministry of Economic Development and Trade of the Russian Federation No. 22066-IM/D23 dd. December 17, 2009 "On the introduction into the state real estate cadaster of data on the zones with special territory use conditions".

However, there is no practice for executing the limitations of rights to the land plots within the SPZ boundaries in the Russian Federation. The absence of data on the boundaries of sanitary protective zones and on the rights to land plots within the SPZ boundaries in the real estate objects cadaster excludes the possibility to take the land tax from these land plots or charge the rental payment causes the availability of falling out incomes of local and consolidated budgets of the subject of the Russian Federation.

The applicable legislation does not provide the liability of enterprise for which the sanitary protective zone is established to conclude the sales and purchase or lease agreement with the owner of land plot completely or partially located within the boundaries of the sanitary protective zone of the enterprise or with person possessing the specified land plot or using the specified land plot under the other real right. Also the applicable legislation does not provide the liability of enterprise for which the sanitary protective zone is established to conclude the sub-lease agreement with the lessee of land plot completely or partially located within the boundaries of the sanitary protective zone of the enterprise. Based on the stated above the enterprise shall not take possession of the land plot completely or partially located within the boundaries of the sanitary protective zone of the enterprise as well as execute the lease agreement for the specified land plot.

In this situation the enterprise does not perform the payment both in the form of land tax and rental payment that significantly decreases the efficacy of management measures, including the public health risk management, because the issues on the sanitary zones organization are directly associated with these risks.

The absence of information about the SPZ boundaries at the bodies of the Federal Service for State Registration, Cadaster and Cartography and the absence at the bodies of Federal Service on the Customers' Rights Protection and Human Well-being Surveillance of

liability on the transfer of the specified data to the local self-governing bodies or the bodies of the Federal Service for State Registration, Cadaster and Cartography does not allow for timely actualization of the current plans of municipal structures and data of the information system for the urban planning activity support that results in the construction of residential and public buildings within the SPZ boundaries of industrial enterprises and creates new risks for the health of citizens.

The significant problem is the urban planning zoning of territories located within the SPZ boundaries. The requirements of SanPiN 2.2.1/2.1.1.1200-03 and SP 42.13330.2011 on the territorial zones establishment conflict with the provisions of the Town Planning Code of the Russian Federation (TPC RF). The TPC RF does not determine the types of territorial areas the composition of which cannot contain the zones with special territory use conditions, including the SPZ. While the item 4.13 and 4.14 of SNiP 42.13330.2011 and item 5.1 of SanPiN 2.2.1/2.1.1.1200-03 underline the necessity to account the limitations to the urban planning activity stipulated by the special regulation zones, including the SPZ, during the territorial zones establishment (item 4.13): it is forbidden to locate in SPZ the objects with rated indicators of the living environment quality.

The non-regulated issue on the territorial zones establishment in relation to the territories within SPZ restrains their use for other purposes, except for production.

The abolition in March 2008 of the requirements of SanPiN 2.2.1/2.1.1.1200-03 to the SPZ landscaping resulted in the loss by the bodies of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance of powers on the bringing to responsibility for the landscaping rules violation. Herewith the landscaping requirements are contained in SP 42.13330.2011 in accordance with which the minimum landscaping area of the sanitary protective zones depends on the SPZ size. At the same time, the Code of the Russian Federation on Administrative Violations (CRFAV) does not provide the responsibility for violating the landscaping requirements.

For the valuable use of the sanitary protective zones organization as the public health risk managements tool the following is feasible:

- to legislate the health risk assessment as the mandatory element for designing the urban planning documentation, including the sanitary zones designing;
- to regulate the procedure for recording in the state real estate cadaster of data on the boundaries of sanitary protective zones (SPZ) and state registration of the limitations of rights to the land plots within the SPZ boundaries in the Unified Public Register of Real Property Titles and Transactions (UPRPTT). To regulate the procedure for recording the data on SPZ in cadaster, it is necessary to harmonize the sanitary and land law in order to include the liabilities of economic entities to carry out the land survey works before or during the SPZ project development and for the bodies of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance – to transfer the data on SPZ to the cadastral accounting bodies for the introduction into register;
- to oblige the organizations possessing the land plots within the SPZ boundaries on the right of ownership, right of permanent (unlimited) use or the right of lifetime ownership with hereditary succession to register in the UPRPTT as well as to establish the responsibility for the avoidance of carrying out the state registration of rights to real estate and transactions with it;
- to regulate the procedure for marking the SPZ boundaries on the current plans of municipal structures and introduction of data into the information systems for the urban planning provision. The bodies of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance are obliged to transfer the copies of sanitary and epidemiological conclusions on the SPZ projects compliance with sanitary standards and regulations as well as the copy of SPZ project to the administration of local self-governing bodies at the territory of which the SPZ is established in order to exercise the authorities of the local self-governing bodies stipulated by the article 56 of the Town Planning Code of the Russian Federation on the marking of SPZ boundaries on the current plan and placing of data on SPZ in the information systems for the urban planning provision.
- to develop and standardize the SPZ liquidation procedure;

♦ to establish the payment for use of lands within the SPZ boundaries (land tax and/or rental payment), to determine the principles of payments for the use of land plots within the SPZ boundaries;

♦ to regulate the issue on the territorial zones establishment in relation to the territories within the SPZ boundaries;

♦ to provide by the legislation the responsibility for violating the rules of landscaping and improvement within the SPZ boundaries;

♦ to determine the procedure for organizing the design of unified SPZ, to provide the local self-governing bodies with authorities on the coordination of work on the unified SPZ designing.

The examples of the use of the health risk assessment methodology in the tasks of regional spatial planning, the development of a scheme for the regional planning and the designing of the unified sanitary protective zones of the large industrial clusters are specified in the chapter 6.

3.5. Methodical approaches to improving the risk-oriented model of control and supervisory activity in the sanitary and epidemiological welfare of population

The principles of risk-oriented approach in the state regulation were formulated in USA already in 1993 [Executive Order, 1993]; however they were developed and implemented in practice little later – at the beginning of XXI century. The imminent and required process of the state management conversion was accelerated by the report of Phillipp Hampton "Reduction of administrative barriers when conducting the inspection and carrying out the control and supervision" [Hampton, 2005] in the Great Britain and renewal of Memorandum of 1995 on the main risk analysis principles [OMB OSTP, 2007].

The orientation of state supervisory systems on the risk assessment methodology was stipulated by the necessity to solve the two main tasks: to increase the efficacy of control and supervisory activity and increase the business conduction comfort. The increase of control efficacy represented the strengthening of reliability and ensuring the safety for society in general at the preservation or reduction of the state costs for the control measures. The increase of business conduction comfort represented the reduction of costs of supervised objects (persons) during the conduction of inspections and the compliance of these costs to the level of hazard (risks) which is imposed by the activity of inspected object.

Under the results of study performed by Hampton it was established that the main burden of the state control (supervision) is put on the small business which spends a lot of time and forces for the preparation of reporting documentation. It was detected that only half of the state authorities in the UK carries out the control (supervision) being guided by the potential hazard of object. Only less than one third of organizations used the system at which the organizations in the activity of which during several years no violations were detected were subjected to the inspections less often. The key recommendation of the Hampton's report was in the implementation of risk-oriented approach into the practice of all state authorities: the main control shall be conducted in relation to the organizations having the highest degree of risk while the subjects which during a number of years did not violate the established requirements shall be subjected to the minimum control measures. The principles and recommendations of report formed the basis for the Regulators Compliance Code of the country [Regulators Compliance Code, 2007] which was and is the regulatory document of Department on the affairs of business, entrepreneurship and management reformation and establishes the standards and principles for the state control implementation mandatory for fulfillment. The same materials were used during the development of Regulatory Enforcement and Sanction Act [Regulatory Enforcement and Sanction Act, 2008]. According

to this document, the control and supervisory bodies shall provide the effective use of available resources through the use of risk assessment based on the significant and qualitative data on the activity of inspected organization. The supervisory bodies shall take into account the previous cases of violations of the safety requirements and degree of risk, the availability of risk management system in the organization, the competence of management and its readiness to the fulfillment of established requirements. Herewith it is declared that the state control bodies shall involve the economic entities (subjects of supervision) into the risk assessment methods development and inform about these methods all the concerned parties. The priority attention shall be focused on the objects having two features:

– the violation of requirements can result in the hazardous consequences;

– there is a risk for the non-fulfillment of requirements at the object of supervision.

For example, the Canadian Food Inspection Agency in 2013 started the significant modernization of the food products control system based on the health risk assessment. The risk to the health of consumer is determined as the main criterion during the determination of frequency for control measures and their content. When assessing the risk, the following is taken into account:

– potential biological, chemical and physical threats (hazards) which are contained in the food product;

– the threats associated with the product manufacturing process (hazards determined by the technological process);

– the volume of manufactured products (the number of potential consumers);

– the specific character of the groups of consumers.

The enterprises (objects) for which the risk is determined as low are inspected every 12–18 months. The average degree of risk determines the frequency of inspections as once every 6–12 months; high degree – every 3–6 months.

The Canadian Public Health Care Agency uses the risk-oriented approach when determining the severity of sanctions if the violations are detected. The severity of violation is determined under the following criteria:

– the level of existing or potential threat of infestation;

– the degree of potential harm which can be inflicted;

– the availability of previous violations;

– the probability of repeated violation;

– the consequences of sanctions.

New (not functioning) objects are subjected to the standard inspection. For example, the public catering objects are subjected to the inspection which is carried out within 6–12 months after the opening.

In the United States of America where the risk analysis at the level of state and municipal management is applied widely each supervisory organization is entitled to determine the additional parameters on which the frequency of control and supervisory measures depends (within the common approaches). Thus, for example, the availability of risk management system at the organization can result in the reduction of the frequency of inspections, and the previously detected violations – to the increase of frequency for such inspections.

The global problems of state control are also typical for the Russian Federation. Thus, the applicable legal system in a majority of cases obliges the control bodies to carry out with certain frequency the complete inspection of all the companies while the volumes of production and corresponding risks are concentrated in the small group of companies (5–10%). Therefore, the expenses for the control and supervisory activity organization are ineffective. Simultaneously, the situation at which the number of controllable entities exceeds even the theoretical abilities of control body on their inspection is created that in turn results in he absence of warranties to ensure the complete safety of society through the state monitoring.

The Decree of the President of the Russian Federation No. 797 dd. May 15, 2008 "On the urgent measures on liquidating the administrative limitations during the

entrepreneurial activity conduction" as well as the Federal laws adopted for its development[1] introduced the significant changes into the execution of control and supervisory authorities by the state bodies, including the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance.

The administrative regulations on the performance of state and municipal functions which allowed for systematization of the authorities of state bodies and local self-governing bodies, adjust their activity and increase the efficacy are developed on the basis of main legislative acts [Babenko A.I., Pushkarev O.V., 2007; The concept for increasing the efficacy of control and supervisory activity; Onishchenko G.G. et al., 2013; Pushkarev O.V., 2008; Selyaninov A.V., Frolova N.V., 2012]. Herewith the risk analysis methodology is recognized as the reliable and effective tool for improving the activity of supervisory structures [Leeves G.D., Herbert R.D., 2002; Ferapontov A.V., 2010; Deming E.,2011; Druker P., 2012; Kvasov I.A., 2013; Kolesov K.I., Antonov A.S., 2013].

In order to decrease the administrative load on the subjects of economic activity at the simultaneous increasing the efficacy of functioning the bodies of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance the risk-oriented model of supervisory activity based on the following principles is developed:

– the use of the health risk assessment methods at all stages of the control and supervisory activity organization;

– the classification of supervised objects depending on the degree of threat and risk of inflicting the harm to the lief and health of citizens;

– the differentiated approach to the control and supervisory measures conduction with the concentration of forces at the objects forming the unacceptable health risk;

– the consistency of information and analytical support for the tasks on assessment and management of health risks, including within the social and hygienic monitoring;

– the accounting of indicators of economic efficacy of control and supervisory measures and the health risk management measures;

– the optimization of control and supervisory activity under the system of risk criteria, harm to health and economic losses.

In general, the model represents the system of interconnected structural and functional elements of service using the health risk assessment methodology (risk assessment and management) at the all stages of collection, processing and analysis of data on the objects of management. The latter include the supervised economic entities and indirectly the living environment of the citizens of country and condition of their health (Fig. 3.15).

The control and supervisory activity as the tool of management is based on:

– the health risk assessment results and their economic equivalents;

– the determination of health risk profiles which are formed by the separate economic entities;

– the selection of supervision mode adequate to the risks (frequency, type, scopes and content of supervision).

The implementation of such model of the control and supervisory activity organization on the sanitary and epidemiological welfare of population requires significant informational and analytical preparation. The identification and documenting the hazards for the typical objects of supervision and accounting of specific character of each of them are required. It is important to determine the severity of probable consequences which can occur due to the violation of those or another mandatory requirements. The determination of scopes for the

[1] The Federal Law No. 294-FKh dd. December 26, 2008 "On protecting the rights of legal entities and individual entrepreneurs when carrying out the state control (supervision) and municipal monitoring".

The Federal Law No. 8-FZ dd. February 9, 2009 "On providing the access to information about the activity of state bodies and local self-governing bodies".

The Federal Law No. 210-FZ dd. July 27, 2010 "On licensing the separate types of activity".

The Federal Law No. 242-FZ dd. July 18, 2011 "On the introduction of changes to the separate legislative acts of the Russian Federation on carrying out the state control (supervision) and municipal monitoring".

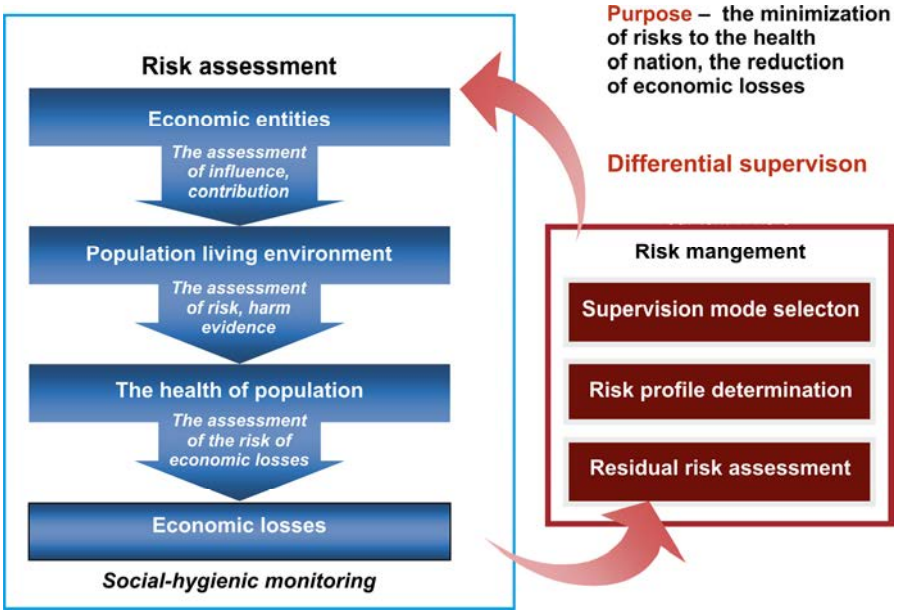

Fig. 3.15. The general diagram of the risk-oriented model of control and supervisory activity in the sanitary and epidemiological welfare of population

probable negative consequences becomes extremely essential. Herewith, in virtue of variety of the sanitary and epidemiological supervision objects (from hairdressing saloons to large industrial enterprises and public service systems) the development of methodical approaches to the assessment of scopes and severity of the probable consequences is a separate task.

It should be noted that in this relation the role of social and hygienic monitoring and scientific epidemiologic studies is increased the results of which can and shall male the basis for the assessment of risks formed by the separate objects of supervision.

The formation of typical risk profiles of the objects of supervision and development of approaches to the accounting of specific character of individual enterprise (organization) become the separate task. The risk profile includes the following elements:

– determining the area of risk (the identification of hazards typical for the object of supervision, the description of manufacturing process; the assessment of scientific data on the characterization of productions; the determination of potential risk for the health of population (employed, consumers); the analysis of existing standards for the hazard assessment; the description of previously established risks among the different layers of population, etc.);

– the risk indicators which depend on the object of supervision and the tasks of study;

– analyzing the main elements of the safety system (the results of monitoring; production control, availability and efficiency of the risk management system at the object of supervision, etc,).

The risk profile shall be detailed to the maximum extent in order to define the relationship between the certain risk factors and their main sources.

The sources of necessary information can be the data of scientific literature, social and hygienic monitoring, international organizations in the field of the public health risk assessment when exposed to the factors of different origin, the expert evaluations, as well as the information about the cases of such diseases.

Currently the risk-oriented model is supported by the actual regulatory and methodical documents of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance developed by the bodies and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance, Russian Academy of

Medical Sciences and the Ministry of Health and Social Development. The documents concern the health risk assessment when exposed to the chemical, biological and physical factors of external environment. As of now the bodies and organizations of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance use more than 50 documents on the different aspects of the risk assessment and management.

It should be noted that already in 2008 the objects supervised by the sanitary and epidemiological service of the Russian Federation were ranked under the level of sanitary and epidemiological significance which was characterized as the criterion determining the potential risk of the adverse influence of the object on the living environment and health of population during the non-observance of sanitary legislation.

Currently the approaches to the categorization of the objects of supervision are based mainly on the systems of expert evaluations, established by the management bodies and does not have clear scientific justification. In the majority of cases the indicators and criteria are intuitive and formed taking into account the long-term control practice. But the classifications of different countries can differ significantly.

For example, in accordance with classification of the Food and Drug Administration the category of public catering enterprises with the low level of risk includes the wast number of shops, hot-dogs sales booths, coffee houses, enterprises which sell the previously packed and non-hazardous food, enterprises which just warm up the food manufactured in industrial volumes. This also includes the enterprises with the average level of risk which under the results of previous inspections demonstrated the good results.

The category of public catering enterprises with the average level of risk includes the supermarkets, schools, fast food points and other objects where the most of products are already packed and/or are cooked and immediately sold. The organizations use the potentially hazardous products (meat, eggs, cut fruit and vegetables) but the quantity of potentially hazardous products is limited.

The group of "very high risk" includes the kindergartens, hospitals, institutions for elderly care and organizations cooking the food in the shops (main criterion for the inclusion of the object of supervision into this group is the availability of vulnerable groups of consumers and the use of specialized food cooking methods – smoking, drying, vacuum packing to extend the terms of storage, etc.).

The specified classification is close to the domestic approaches where during the ranking of the objects of supervision under the degree of hygienic significance the objects of high risk include the children dairy cookeries, public catering enterprises manufacturing and selling the products in the organized collectives, child care centers, orphan asylums, etc.

The categorization (classification, ranking) of the objects of supervision obviously will be gradually improved and become the dynamic system because the residual risks after the implementation of the risk mitigation measures will be changed and the objects of supervision will have the possibility to "transfer" to the categories of lower risk. At the same time appearing of new technologies, materials and substances, increasing the capacity of objects, their transfer to the other territories can result in that the health risks can increase that is associated with change in the category of object to the stiffening of control.

But, regardless of the classification of objects, the criterion for the state supervision efficacy will be the value of prevented losses related to the unit of expenses for the supervisory activity conduction. The same indicator can be used for comparative assessment of supervisory measures of different type and content. How effective in relation to the publicly significant risks mitigation are the administrative enforcement measures? How justified are the laboratory studies of the living environment quality when carrying out the control measures at the industrial enterprises and waste storage facilities?

The methodical approaches to the assessment of actual and prevented as a result of control and supervisory activity economic losses from the mortality, morbidity and disablement of population associated with the negative influence of the living environment factors were developed in order to answer these questions.

The approaches developed "The methodology for calculating the economic losses from the mortality, morbidity and disablement of population" approved by the Order of the Ministry of Economic Development, Ministry of Health and Social Development, Ministry of Finance and Federal State Statistics Service No. 192/323n/45n/113 dd. April 10, 2012 and

determined the rules for performing the calculation of economic losses from the associated with the living environment factors (sanitary and epidemiological, social and economic) mortality, morbidity and disablement of population of different age and social groups before and after the implementation of control and supervisory measures.

When analyzing the effects of measures aimed at the public life and health risk mitigation, including the deposed, the following should be noted: besides that the human produces the public product contributing into its total volume he is also a consumer in the economy (that is very critical for understanding the economic role of the nonworking population). The growth of consumption increases the demand and leads to the growth in the scope of the gross regional product. Herewith the expenses increase the scope of production by the value bigger than the investment themselves. Here the so-called multiplication effect is working (the effect of multiplier) – the possibility of expenses to use the growth of incomes higher than the expenses which caused such growth.

Considering the role of human in the economy (exclusively from the utility point of view) it should be noted that the population today is not only the labor resources; today, looking forward the human is able to reproduce the labor resources that shall be also taken into account in the calculations. In other words, not only the future work in favor of the state but also the "future (potential) children" shall be taken into account during the economic assessment of losses from the children's population mortality.

In this relation the calculation of prevented economic losses from the mortality of population based on the Methodology for calculating the economic losses from the mortality, morbidity and disablement of population (order No. 192/323n./45n./113 dd. April 10, 2012) shall be extended and clarified [Goleva O.I., 2014].

It is accepted that the losses from the mortality, morbidity and disablement of population associated with the negative influence of the living environment factors are the underproduction of the gross domestic product (hereinafter referred to as the GDP) due to the withdrawal of human from the labor activity under the specified reasons (hereinafter referred to as the economic losses) and losses associated with the reduction of tax intakes to the federal budget of the Russian Federation as a result of the gross domestic product underproduction due to the withdrawal of human from the labor activity.

The general algorithm for assessing the efficacy of control and supervisory activity is shown in Fig. 3.16.

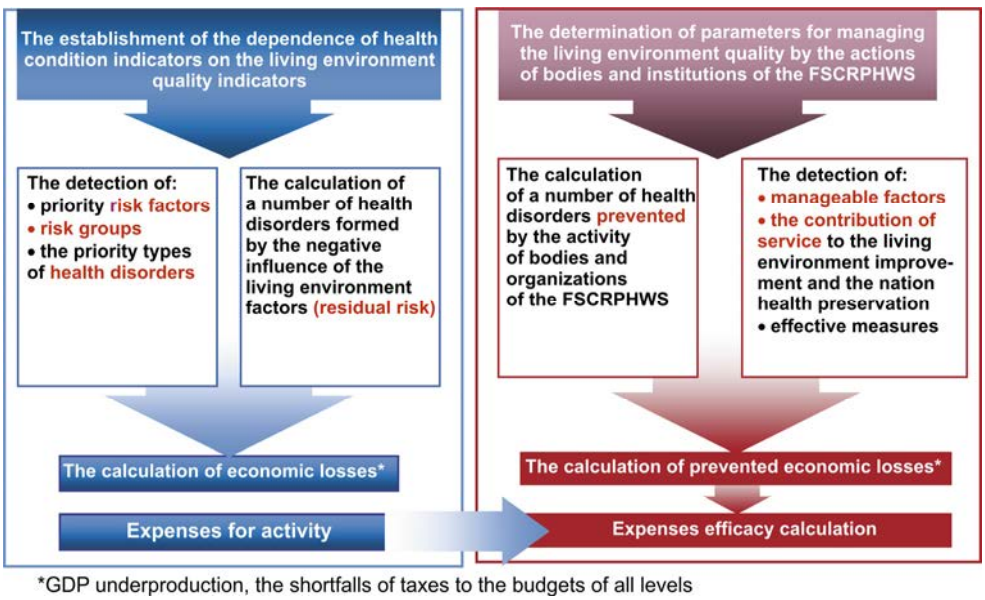

Fig. 3.16. The general algorithm for assessing the efficacy of supervisory actions

The results of the calculation of losses from the mortality, morbidity and disablement of population are as follows:

– the absolute values of the economic losses of reporting year in rubles;

– the values of indexes characterizing the increase (decrease) of the economic losses of reporting year compared to the previous year;

– the structure of losses under the age-sex groups, the causes of mortality and morbidity, disability groups.

The calculation of economic losses from the mortality, morbidity and disablement of population associated with the living environment factors and social and economic factors is performed on the basis of data of official statistical accounting the results of social and hygienic monitoring, including the results of mathematical simulation of dependences between the indicators of the living environment quality and indicators of mortality, morbidity and disablement of population.

The calculation of economic losses from the mortality, morbidity and disablement of population prevented as a result of control and supervisory activity of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance is performed on the basis of official statistical accounting, data of sectoral statistical observation, results of social and hygienic monitoring, including the results of mathematical simulation of dependences between the indicators of the living environment quality and indicators of results of the federal state sanitary and epidemiological supervision.

The list of indicators and sources of information required for calculating the economic efficacy of control and supervisory activity under the results of the mortality, morbidity and disablement of population associated with the negative living environment factors is specified in Table 3.11.

Table 3.11

The list of statistical indicators for calculating the economic losses from the mortality, morbidity and disablement of population associated with the living environment factors

Item No.	The name of indicator	The source of information
1	2	3
1	Gross domestic product (GDP), mln. rubles	Federal State Statistics Service
2	The number of deceased, persons	Federal State Statistics Service, form 1-u "Data on deceased"
3	The number of employed in economy, persons	Federal State Statistics Service. The results of surveying the population under the problems of employment
4	The number of population, persons	The calculation of the Federal State Statistics Service
5	The probability of that the individual in the age of *x* years will live at least for *j* years	Federal State Statistics Service, population mortality table
6	The number of disabled registered in the Federal register of persons having the right to obtain the state social assistance, persons	The ministry of Heath and Social Development of Russia The Pension Fund of the Russian Federation Aggregated data based on the Federal register of persons having the right to obtain the state social assistance
7	The number of working disabled pensioners registered in the system of compulsory pension insurance, persons	The Ministry of Heath and Social Development of Russia. The Pension Fund of the Russian Federation, form 94 (Pension)
8	The number of cases of temporary incapacity, the number of cases	The Ministry of Heath and Social Development of Russia, form 16-VN "Data on the causes of temporary incapacity"

End of Table 3.11

1	2	3
9	The number of days of temporary incapacity, days	The Ministry of Heath and Social Development of Russia, form 16-VN "Data on the causes of temporary incapacity"
10	The number of the cases of contagious diseases, cases; cases per 1000 of population	The Federal Service on Customers' Rights Protection and Human Well-being Surveillance, form No. 2. Data on the contagious and parasitic diseases
11	The number of the cases of noncontagious diseases, cases; cases per 1000 of population	The results of social and hygienic monitoring (the data of federal information fund)
12	Data on the quality of living environment of population, % of non-standard samples	The Federal Service on Customers' Rights Protection and Human Well-being Surveillance, form No. 18 "Data on the sanitary condition of subject of the Russian Federation"
13	Data on the social and economic condition of territory, depending on the indicator	The results of social and hygienic monitoring (the data of federal information fund)

The economic losses in the GDP production from the mortality of population are calculated as the lost benefit (the scopes of underproduced GDP) due to the permanent withdrawal (death) of human from the field of production in the reporting year under the reason associated with the negative influence of the living environment factors. The losses from the mortality of population for reporting year under each differential factor are calculated as the factum of the number of persons died in the age of 15 years and more by the GDP volume per one employed corrected by the level of employment of the relevant age-sex group of population. Herewith the averaging of time of death during year is taken into account (adjustment factor 0.5). In addition, the reduced duration of work hours and increase duration of leave for the persons of 15–18 years are also taken into account:

$$УВГС_{x,s,d} = ЧУ_{x,s,d} \frac{ЧЗ_{x,s}}{ЧН_{x,s}} \frac{ВВП}{ЧЗ} 0,5K_x, \quad (3.5.1)$$

where $УВГС_{x,s,d}$ – is the lost benefit in the GDP production (scope of underproduced GDP) as a result of associated with the living environment factors mortality of persons in the age (x) of sex (s) due to the death (d) in the Russian Federation in the reporting year, mln. rubles;

$ЧУ_{x,s,d}$ – the number of deceased in the age (x) of sex (s) due to the death (d) associated with the living environment factors in the Russian Federation, persons;

ЧЗ – the total number of employed in the Russian Federation in the reporting year, persons;

$ЧЗ_{x,s}$ – the number of employed in the age (x) of sex (s) in the Russian Federation, persons;

$ЧН_{x,s}$ – the total number of employed in the age (x) of sex (s) in the Russian Federation, persons;

GDP – is a gross domestic product of the Russian Federation, mln. rubles;

K_x – adjustment factor to account the reduced working hours and increased duration of leave for persons in the age (x) younger than 18 years (for x = 15 K_x = 0.5922 for x = 16 K_x = 0.8636, for x = 17 K_x = 0.8636, for x > 17 K_x = 1);

0.5 – is a coefficient accounting the distribution of the time of deaths during one year.

Calculating the number of deceased ($ЧУ_{x,s,d}$), as well as further – the other cases of the public health disorders associated with the negative influence of the living environment factors is performed based on the data of social and hygienic monitoring and official medical

statistics. The method of simulation is the step-by-step regression analysis modified by the sorting of line, square and exponential functions for the independent variables. More detailed the method is described in the section 7.1.1 (equations 7.1.1–7.1.5).

The simplified calculation of mortality associated with the living environment factors can be carried out using the population mortality change coefficients, depending on the change in the level of the living environment factor.

$$\text{ЧУ}_{x,s,d} = \frac{\text{ФСО} \cdot S^{\text{ФСО}}_{x,s,d} \cdot \text{ЧН}_{x,s}}{100000}, \qquad (3.5.2)$$

where $S^{\text{ФСО}}_{x,s,d}$ – are the population mortality change coefficients (cases/100000) per one unit of measurement of the living environment factor value (living environment factor – LEF);

$\text{ЧН}_{x,s}$ – the total number of population in the age (*x*) of sex (*s*) in the Russian Federation, persons;

LEF – is a value of living environment factor (chemical, microbiological, physical, social) summarized in general for the Russian Federation within the social and hygienic monitoring and/or state statistics. When calculating the social and economic factors the difference between the actual and target value of factor is used. The values of indicators determined by the strategic documents of the state authorities of the Russian Federation are accepted for a number of social and economic factors as the target level.

The values of magnitude $S^{\text{ФСО}}$ are determined as a result of linearization of models obtained under the algorithm specified in the section 7.1.1. The linearization method provides the replacement of non-linear model by its linear equivalent. The linearization is performed at the expense of differentiation of the nonlinear function at the point corresponding to the average Russian level of factor.

The economic losses from the mortality of population associated with the living environment factors for the period of possible reaching by the deceased in the reporting year the end of the economic activity age (72 years) are calculated also for deceased in the age of up to 15 years. Herewith to calculate the losses for the period of possible living the parameters of future years are not predicted but are taken as equal to the relevant values of year in the parameters of which the calculation of losses is performed (reporting, previous, etc.).

The calculation is feasible when forecasting the porbable losses in the conditions of "zero" option, i.e. in the absence of positive changes in the sanitary and epidemiological situation and preservation of the living environment quality at the level of reporting year.

The economic losses from the mortality of population associated with the living environment factors for the period of possible living are calculated under the following formulas:

for deceased in the age under 15 years:

$$\text{УВС}_{x,s,d} = \text{ЧУ}_{x,s,d} \frac{\text{ВВП}}{\text{ЧЗ}} \left(\sum_{j=15}^{72} \frac{\text{ЧЗ}_{j,s}}{\text{ЧН}_{j,s}} P_{j-x} K_j \right); \qquad (3.5.3)$$

for deceased in the age of 15 years and more:

$$\text{УВС}_{x,s,d} = \text{УВСГ}_{x,s,d} + \text{ЧУ}_{x,s,d} \frac{\text{ВВП}}{\text{ЧЗ}} \left(\sum_{j=x+1}^{72} \frac{\text{ЧЗ}_{j,s}}{\text{ЧН}_{j,s}} P_{j-x} K_j \right), \qquad (3.5.4)$$

where $\text{УВС}_{x.s.d}$ – is the lost benefit in the GDP production (scope of underproduced GDP) as a result of associated with the living environment factors mortality of persons in the age (*x*) of sex (*s*) due to the death (*d*) in the Russian Federation in the reporting year taking into account the probability of living and level of employment, mln. rubles;

$\text{ЧУ}_{x,s,d}$ – the number of deceased in the age (*x*) of sex (*s*) due to the death (*d*) associated with the living environment factors in the Russian Federation, persons;

GDP – is a gross domestic product of the Russian Federation, mln. rubles;

NE – the number of employed in the Russian Federation, persons;

$ЧЗ_{j,s}$ – the number of employed in the age (*j*) of sex (*s*) in the Russian Federation, persons;

$ЧН_{j,s}$ – the number of population in the age (*j*) of sex (*s*) in the Russian Federation, persons;

P_{j-x} – the probability of living from the age (*x*) to the age (*j*) based on the mortality tables;

K_j – adjustment factor for accounting the reduced working hours and the increased duration of leave for persons in the age (*j*) younger than 18 years (for $j = 15$ $K_j = 0.5922$, for $j = 16$ $K_j = 0.8636$, for $j = 17$ $K_j = 0.8636$, for $j > 17$ $K_j = 1$);

$УВГС_{x,s,d}$ – is the lost benefit in the GDP production (the scope of underproduced GDP) as a result of mortality of persons in the reporting year in the age (*x*) of sex (*s*) due to the death (*d*) in the Russian Federation in the reporting year, mln. rubles.

The summation of economic losses under each differential factor is performed to calculate the aggregate economic losses.

The result of the calculation of economic losses from the mortality of population associated with the living environment factors is the index determined as the relation of economic losses from the mortality of population in the reporting year calculated in the conditions of the previous year to the value of economic losses from the mortality of population in the previous year calculated in the conditions of the previous year.

The data characterizing the mortality of population (mortality coefficients, expected lifespan), including under the differential factors, are taken for the year for which the calculation of economic losses from mortality is performed.

The economic losses from the disablement of population associated with the living environment factors are calculated as the sum of the lost benefit in the GDP production due to the withdrawal of person from the field of production because of disablement. Herewith the total number of disabled in the reporting year is taken into account, regardless of the disablement establishment year.

The economic losses from the disablement of population are calculated as the difference between the GDP scope which could be created by the persons became disabled (the factum of the number of disabled by the GDP value per one employed taking into account the employment level of the relevant age-sex group of population) and the GDP scope created by the working disabled (the factum of the number of disabled by GDP per one employed taking into account the employment level of disabled of the relevant group as well as from the reduced duration of working hours and increased duration of leave of the disabled).

The calculation of economic losses from the disablement of population is performed under the following formula:

$$УВИ_{x,s,g} = \frac{ВВП}{ЧЗ}\left(ЧИ_{x,s,g}\frac{ЧЗ_{j,s}}{ЧН_{j,s}} - \frac{ЧЗИ_g}{ЧИ_g}ЧИ_{x,s,g}K_g\right), \quad (3.5.5)$$

where $УВИ_{x,s,g}$ – is the lost benefit in the GDP production (the scope of underproduced GDP) as a result of associated with the living environment factors disablement of persons in the age (*x*) of sex (*s*) and disability group (*g*) in the Russian Federation, mln. rubles;

$ЧИ_{x,s,g}$ – the number of disabled in the age (*x*) of sex (*s*) and disability group (*g*) in the Russian Federation, persons;

$ЧИ_g$ – the number of disabled of disability group (*g*) in the Russian Federation, persons;

GDP – is a gross domestic product of the Russian Federation, mln. rubles;

NE – the number of employed in the Russian Federation, persons;

$ЧИ_{x,s}$ – the number of employed in the age (*x*) of sex (*s*) in the Russian Federation, persons;

$ЧН_{x,s}$ – the number of population in the age (*x*) of sex (*s*) in the Russian Federation, persons;

$ЧЗИ_g$ – the number of disabled of engaged in economy of disability group (*g*) in the Russian Federation, persons;

K_g – adjustment coefficient for accounting the reduced working hours and increased duration of leave for disabled (for $g < 3$ $K_g = 0.8674$, for $g = 3$ $K_g = 0.991$).

The simplified calculation of disablement associated with the living environment factors can be carried out using the population disablement change coefficients, depending on the change in the level of the living environment factor.

$$ЧИ_{x,s,g} = \frac{ФСО \cdot I^{ФСО}_{x,s,g} \cdot ЧН_{x,s}}{100000}, \quad (3.5.6)$$

where $I^{ФСО}_{x,s,g}$ – are the population disablement change coefficients (cases/100000) per one unit of measurement of the living environment factor value (living environment factor – LEF).

LEF – is a living environment factor (for the social and economic factors the difference between the actual and target value of factor is used). The values of indicators determined by the strategic documents of the state authorities can be accepted for a number of social factors as the target level.

The economic losses from the morbidity of population associated with the living environment factors are calculated as the sum of the lost benefit in the GDP production (scope of underproduced GDP) due to the temporary withdrawal of person from the field of production because of temporary incapacity. When calculating the actual and prevented economic losses from the morbidity of employed population it is feasible to include into the lists of considered indicators the classes of diseases and nosologies the stabilization of the levels of which is included into the strategic perspective plans of the Government of the Russian Federation and the Federal Service on Customers' Rights Protection and Human Well-being Surveillance (roseola, wild type virus of poliomyelitis, hepatitis B, diphtheria, morbilli, diseases of digestive organs in the children of educational institutions, etc.).

The economic losses from the morbidity of population associated with the living environment factors are calculated under the age (single-year age groups of population), sex and cause of incapacity using the following formula:

$$УВЗ_{x,s,m} = Заб_{x,s,m} \frac{Дл_{x,s,m}}{СВН_{x,s,m}} \frac{ЧЗ_{x,s}}{ЧН_{x,s}} \frac{ВВП}{365 \cdot ЧЗ}, \quad (3.5.7)$$

where $УВЗ_{x,s,m}$ – is the lost benefit in the GDP production (scope of underproduced GDP) as a result of associated with the living environment factors morbidity of persons in the age (*x*) of sex (*s*) due to the incapacity (*m*) in the Russian Federation, mln. rubles;

$Заб_{x,s,m}$ – the number of the diseases of persons involved into production in the age (*x*) of sex (*s*) due to the causes (*m*) associated with the living environment factors, cases;

$Дл_{x,s,m}$ – the number of the days of the temporary incapacity of person in the age (*x*) of sex (*s*) due to the disease (*m*), days;

$СВН_{x,s,m}$ – the number of days for the cases of temporary incapacity for persons in the age (*x*) of sex (*s*) due to the incapacity (*m*) in the Russian Federation in the reporting year;

GDP – is a gross domestic product of the Russian Federation, mln. rubles;

NE – the number of employed in the Russian Federation.

The simplified calculation of temporary incapacity associated with the living environment factors can be carried out using the population morbidity change coefficients, depending on the change in the level of the living environment factor ($Z^{ФСО}_{x,s,m}$):

$$\text{Заб}_{x,s,m} = \frac{\text{ФСО} \cdot Z^{\text{ФСО}}_{x,s,m} \cdot \text{ЧН}_{x,s}}{100000}, \quad (3.5.8)$$

where $Z^{\text{ФСО}}_{x,s,m}$ – is the population morbidity change coefficient (cases/100000) depending on changing the living environment factor level;

LEF – is a living environment factor (for the social and economic factors the difference between the actual and target value of factor is used).

When assessing the economic losses under the tax intakes from the mortality, disablement and morbidity of population associated with the living environment factors for the reporting year it it necessary to use the statistical indicators specified in Table 3.12.

Table 3.12

The list of statistical indicators for calculating the economic losses from the reduction of tax intakes to the budget due to the mortality, morbidity and disablement of population associated with the negative influence of the living environment factors

Item No.	The name of indicator	The unit of measurement	The source of information
1	Birth rate	Unit	Federal State Statistics Service, demographical indicators
2	Expenses for the end consumption of households	Rubles/month	Federal State Statistics Service, statistical bulletin "Incomes, expenses and consumption of households"
3	Expenses for the end consumption of households the heads of which have the age of up to 60 years and more	Rubles/month	Federal State Statistics Service, statistical bulletin "Incomes, expenses and consumption of households"
4	The profitability of the organizations activity	%	Federal State Statistics Service, finances of organizations
5	Average monthly salary	Rubles/month	Federal State Statistics Service, labor market, employment and salary
6	Basic profit tax rate	%	"Tax Code of the Russian Federation (part II)" No. 117-FZ dd. August 5, 2000
7	Basic profit tax rate paid to the federal budget	%	"Tax Code of the Russian Federation (part II)" No. 117-FZ dd. August 5, 2000
8	Basic individual income tax rate	%	"Tax Code of the Russian Federation (part II)" No. 117-FZ dd. August 5, 2000
9	The share of average salary paid as the benefits in case of temporary incapacity to work according to the insurance experience of worker	%	Federal Law No. 255-FZ dd. December 26, 2006 г. (version dd. November 25, 2013) "On the compulsory medical insurance in case of temporary incapacity to work and in association with maternity"

The calculations are performed under the equations (3.5.9–3.5.13):

$$\text{УВГСН}_{x,s,d} = \text{УВГС}_{x,s,d} \cdot t_{\text{НДС}} + \text{УВГС}_{x,s,d} \cdot R \cdot t_{\text{НП}} + \\ + \text{ЧУ}_{x,s,e} \frac{\text{ЧЗ}_{x,s}}{\text{ЧН}_{x,s}} (\text{СМЗП}_{x,s} \cdot 12 \cdot 0,5 t_{\text{НДФЛ}} / 1000), \quad (3.5.9)$$

where $УВГСН_{x,s,d}$ – are the losses under the tax intakes to all the levels of budgetary system as a result of associated with negative influence of living environment factors mortality of persons in the reporting year in the age (*x*) of sex (*s*) due to the death (*d*) in the Russian Federation, mln. rubles;

$УВГС_{x,s,d}$ – are the losses of GDP as a result of associated with living environment factors mortality of persons in the reporting year in the age (*x*) of sex (*s*) due to the death (*d*) in the Russian Federation, mln. rubles;

$t_{НДС}$ – is a design value added tax rate, share. Taking into account the different VAT rates in the Russian Federation, availability of special tax regimes and peculiarities of the tax base calculation $t_{НДС}$ = 3.5 % (0.035);

R – the profitability of the activity of organizations in the Russian Federation, share;

$t_{НП}$ – basic tax rate under the income tax, share;

$СМЗП_{x,s}$ – the average monthly salary of persons in the age (*x*) of sex (*s*) in the reporting year in the Russian Federation, thous. rubles;

$t_{НДФЛ}$ – basic tax rate under the individual income tax, share;

12 – the number of months in a year;

0.5 – is a coefficient accounting the distribution of deaths during one year;

1000 – coefficient for the conversion of thous. of rubles to the mln. of rubles.

$$УВГСН(ФБ)_{x,s,d} = УВГС_{x,s,d} \cdot t_{НДС} + УВГС_{x,s,d} \cdot R \cdot t_{НП(ФБ)}, \quad (3.5.10)$$

where $УВГСН\ (ФБ)_{x,s,d}$ – are the losses under the tax intakes to the federal budget as a result of mortality of persons in the reporting year in the age (*x*) of sex (*s*) due to the death (*d*) in the Russian Federation, mln. rubles;

$t_{НП\ (ФБ)}$ – basic tax rate under the income tax paid to the federal budget, share;

$$УВИН_{x,s,g} = УВИ_{x,s,g} \cdot t_{НДС} + УВИ_{x,s,g} \cdot R \cdot t_{НП} + \\ + ЧИ_{x,s,g} \frac{ЧЗ_{x,s}}{ЧН_{x,s}} \left(\left(СМЗП_{x,s} - СМЗП_{x,s,g} \right) 12 \cdot 0{,}5 \cdot t_{НДФЛ} / 1000 \right), \quad (3.5.11)$$

where $УВИН_{x,s,g}$ – are the losses under the tax intakes to all the levels of the budgetary system due to the disablement of persons in the age (*x*) of sex (*s*) under the disability group (*g*) in the Russian Federation, mln. rubles;

$УВИ_{x,s,g}$ – are the losses in the GDP production due to the disablement of persons in the age (x) of sex (*s*) under the disability group (*g*) in the Russian Federation, mln. rubles;

$t_{НДС}$ – is a design value added tax rate, share. Taking into account the different VAT rates in the Russian Federation, availability of special tax regimes and peculiarities of the tax base calculation $t_{НДС}$ = 3.5 % (0.035);

R – the profitability of the activity of organizations in the Russian Federation, share;

$t_{НП}$ – basic tax rate under the income tax, share;

$СМЗП_{x,s}$ – the average monthly salary of persons in the age (*x*) of sex (*s*) in the reporting year in the Russian Federation, thous. rubles;

$СМЗП_{x,s,g}$ – the average monthly salary of persons in the age (*x*) of sex (*s*) and disability group (*g*) in the reporting year in the Russian Federation, at *g* =1 $СМЗП_{x,s,g}$ = 0.0 thous. rubles;

$t_{НДФЛ}$ – basic tax rate under the individual income tax, share;

12 – the number of months in a year;

1000 – coefficient for the conversion of thous. of rubles to the mln. of rubles.

The losses under the tax inakes to all the levels of the budgetary system of the Russian Federation from the morbidity of population are calculated under the following formula:

$$УВЗН_{x,s,m} = УВЗ_{x,s,m} \cdot t_{НДС} + УВЗ_{x,s,m} \cdot R \cdot t_{НП} + \\ + \left(СМЗП_{x,s} 12(1 - d_x) \frac{ДВН_{x,s,m}}{365} t_{НДФЛ} \right) / 1000, \quad (3.5.12)$$

where $УВЗН_{x,s,m}$ – are the prevented losses under the tax intakes to all the levels of the budgetary system due to the morbidity of persons in the age (*x*) of sex (*s*) due to the incapacity (*m*) in the Russian Federation, mln. rubles;

$УВЗ_{x,s,m}$ – are the prevented losses in the GDP production due to the morbidity of persons in the age (x) of sex (*s*) due to the incapacity (m) in the Russian Federation, mln. rubles;

$t_{НДС}$ – is a design value added tax rate, share. Taking into account the different VAT rates in the Russian Federation, availability of special tax regimes and peculiarities of the tax base calculation $t_{НДС}$ = 3.5 % (0.035);

R – the profitability of the activity of organizations in the Russian Federation, share;

$t_{НП}$ – basic tax rate under the income tax, share;

$СМЗП_{x,s}$ – the average monthly salary of persons in the age (*x*) of sex (*s*) in the reporting year in the Russian Federation, thous. rubles;

d_x – coefficient corresponding to the share of average salary paid as the benefits in case of temporary incapacity to work according to the experience of worker;

$t_{НДФЛ}$ – basic tax rate under the individual income tax, share;

12 – the number of months in a year;

365 – the number of days in a year.

The economic losses prevented by the supervisory actions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance are calculated under the results of the simulation of the dependence of the living environment quality indicators on the parameters of control and supervisory activity of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance and determination of a number of cases for every type of health disorders,

The procedure of simulation is the direct continuation of simulation performed within the social and hygienic monitoring is carried out based on the statistical information on the living environment quality used during the assessment of dependences "environment – health" and parameters of activity of the bodies and organizations of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance collected within the departmental statistical observation: form 1–11 (in 2011), form 1–12 (since 2012.) "Data on the results of federal state supervision conduction by the territorial bodies of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance". The set of indicators is formed by regions.

The following algorithm is used:

1) the assessment of change in the living environment quality indicator at the expense of control and supervisory actions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance for each observation as the difference of assessments by model at the actual levels of independent variables and minimum possible (zero) at all the points (at the level of Russia – regions) participating in the calculations:

$$\Delta ФСО_k = b_1 f_1 (Дв_{1k}) + b_2 f_2 (Дв_{2k}) + \ldots, \quad (3.5.13)$$

where $Дв_{1k}$, $Дв_{2k}$,….– are the values of independent variables for observation *k* (region).

The average change in the living environment quality indicators is determined by simple averaging under all the observations (regions):

$$\Delta ФСО = \Sigma (\Delta ФСО_k) / n, \quad (3.5.14)$$

where *n* – is a number of observations (regions) participating in the calculation;

2) the calculation of the number of the cases of health disorders prevented as a result of the activity of the bodies and organizations of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance as the difference of values calculated under the model at the actual levels of the living environment quality indicators and the values of indicators, taking into account the change in the living environment quality indicators due to the control and supervisory activity of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance:

$$\Delta y_k = a_1(f_1\,(\Phi CO_{1k} + \Delta\,\Phi CO_1) - f_1(\Phi CO_{1k})) +$$

$$+\, a_2\,(f_2(\Phi CO_{2k} + \Delta\,\Phi CO_2) - f_2(\Phi CO_{2k})) + \ldots\,. \qquad (3.5.15)$$

The absolute number of the prevented cases of health disorders (deceased, disabled, diseases) is determined under the relations:

$$\Delta Y_k = \Delta y_k ЧН_k/100\,000, \qquad (3.5.16)$$

where ΔY_k – is an absolute number of the prevented cases of health disorders (death, disability, diseases) prevented by the actions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance in the observation (region) k;

$ЧН_k$ – is a number of population in the region k.

The share of the prevented cases of health disorders due to the activity of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance for the Russian Federation is determined under:

$$\Delta y = \Sigma(\Delta Y_k)\,/\Sigma(Y_k). \qquad (3.5.17)$$

The calculation of the absolute number of cases for the Russian Federation is performed as the factum of cumulative number of cases in the Russian Federation by the calculated average share of additional cases associated with the living environment factors:

$$\Delta Y = Y_{РФ}\delta y, \qquad (3.5.18)$$

where ΔY – is an absolute number of the cases of health disorders for population (deceased – ЧУ; disablement – ЧИ; diseases – СВН) prevented at the expense of the activity of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance.

The economic losses from the prevented as a result of actions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance mortality, disablement and morbidity of population associated with the living environment factors by the substitution of obtained values $ЧУ^{Д}_{x,s}$ in the equations (3.5.1), (3.5.9), (3.5.10), $ЧИ^{Д}_{x,s}$ – in the equations (3.5.5), (3.5.12), (3.5.13), $Заб^{Д}_{x,s}$ – in the equations (3.5.7), (3.5.14), (3.5.15).

The assessment of the economic efficacy of conrol and supervisory activity is calculated as the relation of the sum of all the types of losses prevented by the actions of service to the expenses for the control measures implementation:

$$Э_к = \frac{ПУВ^{ФСО}_{x,s}}{Zatrat_k}, \qquad (3.5.19)$$

where $ПУВ^{ФСО}$ – are the GDP losses prevented by the actions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance which could occur due to the mortality, disablement and morbidity of persons in the age (x) of sex (s) in the reporting year, mln. rubles;

$Zatrat_k$ – are the expenses for the control and supervisory activity conduction in the reporting year, mln. rubles.

The obtained models of interrelations between the living environment factors and the public health condition indicators as well as between the factors and parameters of activity of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance for the certain time interval in the Russian Federation can be considered as universal and used both for obtaining the assessments of the efficacy of control and supervisory activity in the field of the sanitary and epidemiological welfare provision in general throughout the country and in the separate regions.

The assessment of the separate types of supervisory measures is more difficult but at the accumulation of certain data the methodology has the prospects of development and application in the service activity practice.

In general the risk-oriented model for organizing the supervisory activity in the field of the sanitary and epidemiological welfare provision for population with the economic assessment tool allows:

– to optimize the control and supervisory activity ensuring the safety of population with the parallel minimization of pressure on the business;

– to assess and present to the decision makers the economic equivalents of the public health risks;

– to detect the priority risk factors, risk groups and the priority types of health disorders determining the economic losses;

– to determine the parameters for managing the living environment quality by the actions of bodies and institutions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance;

– to calculate the contribution of service into the living environment improvement and the public health preservation;

– to assess the economic losses prevented by the control and supervisory measures and associated with the GDP underproduction and the non-coming of taxes to the budgets of all levels, including the federal budget;

– to distinguish the most and, on the contrary, the least effective control and supervisory measures and determine which population living environment factors are affected (not affected) by the actions of supervisory organizations;

– to form the information and analytical base for the further improvement of supervisory activity in the field of provision the sanitary and epidemiological welfare of population.

3.6. Medical-preventive technologies for managing the risk of health disorders associated with the influence of living environment factors

The priority direction of the preventive medicine activity is the search of methods for solving the problem of negative influence of the living environment on the health of population and prevention of development of diseases associated with the negative influence of factors among which the leading are the sanitary and hygienic. About 73% of population of the Russian Federation are affected by them [On the condition of the sanitary and epidemiological welfare in the Russian Federation in 2012, 2013].

The results of multiple studies confirm that the public health condition in the regions to a greater extent is determined by the level of sanitary and epidemiological welfare of the living environment [Baranov A.A., Shcheplyagina L.A., 2005; Bukharin O.V. et al., 2010; Parakhonsky A.P., 2010; Zaytseva N.V., 2011*d*; Total morbidity of children's population…, 2013]. The data of epidemiologic and clinical surveillance evidence that the population residing the conditions of the sanitary and epidemiological ill-being of living environment has increased by 1.2–2.6 times indicators of morbidity with chronic diseases of respiratory, nervous, cardio-vascular and digestive systems, by 1.6–1.8 times more often is registered the pathology of locomotor system, by 1.2–1.5 – the endocrine system diseases, by 1.2–1.4 – the prevalence of morphological and functional deviations of the internal organs and systems [Parakhonsky A.P., 2010; Onishchenko G.G. et al., 2011; Setko A.G. et al., 2005; Zaitseva N. Et al., 2012; Goncharenko A.V., Goncharenko M.S., 2012; Total morbidity of children's population…, 2013].

In the Russian Federation at the territories of the sanitary and epidemiological risk the respiratory diseases associated with the inhalation influence of nitrogen oxide, sulfur dioxide, suspended substances, ammonia, phenol, etc. make up about 6% (6656.7 of case per 100 thous. of population, including the acute laryngitis and tracheitis – up to 1077.8 of case, allergic rhinitis – up to 12.7 of case, bronchitis and asthma – up to 42.3–58.3 of case) and at the territories with ambient air contamination with aromatic hydrocarbons and

formaldehyde the level of their prevalence is by 2.1–2.6 times higher than the same indicator of the territories of relative sanitary and hygienic welfare [Zaytseva N.V. et al., 2008*a*; Bukharin O.V., 2010; Change of morbidity…, 2012]. In the regions with the violation of sanitary and hygienic standards for the content of metal aerosols in the ambient air the prevalence of allergic dermatitis, polyvalent sensibilization, systemic forms of atopic illnesses is by 1.2–1.9 times higher than the average All-Russian indicator [Koroteeva E.N., 2005]. The presence in the drinking water of the residual products of hyperchlorination and heavy metals stipulates the occurrence of additional cases of gastro-duodenal diseases at the level of 18 ‰ per year and contributed to the increase of the frequency of the prevalence of atypical, severe and complicated forms with recurrent course and resistance to the basic therapy [Fayzullina R.A., 2002; Rudaeva E.G. et al, 2008]. Under the official statistics data the morbidity of population in the industrial regions of the Russian Federation by the chronic glomerular and tubulointerstitial renal diseases exceeds the All-Russian level by 1.4–1.5 times; herewith the maximum indicators are registered at the territories with unacceptable risk of the renal diseases development stipulated by the ambient air contamination with cadmium, lead, chromium and phenol [Aplikhin O.I. et al., 2010; Vyalkova A.A., 2008; Zaytseva N.V. et al., 2011*c*; Total morbidity of children's population in Russia, 2013]. In the conditions of the chronic exposure of population to the chemical substances with the neurotropic effect of actions (manganese, lead, chloroform) the indicator for the prevalence of diseases of the vegetative nervous system by more than 2.5 times exceeds the same in the non-exposed population [Zemlaynova M.A. et al., 2012; Maklakova O.A. et al., 2013; Baydina A.S. et al., 2013]. During the last five years the morbidity rate for the population of the Russian Federation with diseases of locomotor system increased by more than 20%; herewith at the territory with anthropogenic contamination the frequency of registration and growth rates of this pathology by 1.3–1.5 times exceed the All-Russian level [Onishchenko G.G., 2011; Total morbidity of children's population in Russia, 2013].

The results of multiple studies demonstrate that the unsatisfactory condition of the living environment is one of the leading factor for reducing the duration and quality of human life [Baranov A.A., Shcheplyagina L.A., 2005; Koroteeva E.N., 2005; Baranov A.A., Albitsky V.Yu., 2007; Zaytseva N.V., 2011*c*; Onishchenko G.G., 2011]. The existing level of prevalence in the Russian Federation of diseases associated with the negative influence of the living environment factors requires not only the targeted complex scientifically justified measures aimed at the mitigation of risks but also the development of new approaches to the provision of specialized medical and preventive assistance to the population of territories of the sanitary and hygienic ill-being.

At the same time regardless of demographical and the social and economic significance of problem the system of practical healthcare of the Russian Federation does not provide the provision of specialized therapeutic and diagnostical assistance to the population residing in the areas of sanitary and hygienic ill-being; the existing specialized standards and protocols have the character of recommendations; there is no regulatory and legislative base for their implementation; the specialists of practical healthcare are insufficiently informed on the medical technologies of diagnostics and prevention of diseases associated with the negative influence of the living environment factors.

The purpose of the creation of a system for the provision of specialized preventive and therapeutic and diagnostic assistance to the population of the territories of sanitary and epidemiological ill-being is the minimization of the potential risk of health disorders. First of all, it concerns the diseases associated with the negative influence of the living environment factors. The implementation of targeted medical and preventive technologies aimed at the prevention of occurrence of risk-associated somatic pathology ensures their early detection, prevention of progress and chronization, facilitates the improvement of quality and lifespan of population, decreases the disablement and mortality.

The creation and development of the system of specialized preventive and therapeutic and diagnostic assistance based on the medical-preventive technologies on the management of risks for population of the territories of sanitary and epidemiological ill-being will allow for not

only to decrease significantly the level of total and chronic morbidity associated with the influence of the living environment factors but also will have the significant positive effect on the social and demographical indicators of regions and the Russian Federation in general.

Being the independent direction, the effective prevention of diseases associated with the influence of the living environment factors cannot be performed without solving the whole complex of sanitary, hygienic and clinical tasks: the problems of standardization, the establishment of the "threshold" of the adaptation possibilities of the different groups of population to the influence of the living environment factors, including at their complex and combined action, the study of the peculiarities of the clinical manifestation of pathologic conditions at the different level of external environmental influence, the detection of the relationship of pathologic process with the active factor, study the genetic, metabolic, pathochemical, pathophysiological and functional markers of the risk-associated pathology development, etc. [Zaytseva N.V. et al., 2011*d*; Luzhetsky K.P. et al., 2012; Zaytseva N.V. et al., 2013*a*; Patent of the Russian Federation No. 2491549 dd. August 27, 2013; Patent of the Russian Federation No. 2012157896 dd. February 27, 2014].

The long-term experience of own studies demonstrates that at the same conditions of living environment the response reaction of each individual is determined by the aggregate of the whole number of factors: its genetic status, condition and the volume of the reserve possibilities of adaptation system, the presence/absence of acute/chronic pathology, social and economic conditions, etc. In this relation the approach proposed at the early stage of the development of the prevention of risk-associated pathology based on the large-scale use of preventive programs emphasizing the set of elimination measures not only exaggerates the complexity of pathochemical, pathophysiological and morphological basis of the risk-associated process but also due to the absence of the correction of pathogenic significants shifts in the homeostasis supporting systems, enzyme disorders at the level of cellular and sub-cellular structures of target organs, the restoration of main types of exchange does not allow to achieve the target results. The problem solution strategy shall be based on the results of the deep scientific analysis of the degree of risk associated with the influence of the living environment factors, epidemiological data, the establishment of early markers of the risk-associated process formation, the study of its clinical manifestation. The developed medical-preventive technologies cannot have the universal character, their content is determined first of all by the peculiarities of the action of the living environment factors on the human body, the leading links of the pathogenesis of pathologic process both at the level of homeostasis supporting systems and target organs, certain nosology, the stage of the pathologic process course, etc.

In general for the successive development of system for the provision of specialized preventive assistance to the population residing at the territory of sanitary and epidemiological ill-being the following tasks shall be solved:

– the further development of methodological approaches to the diagnostics and the demonstration of the pathogenetic relationship of somatic pathology with exposure based on the modern high informative hygienic, epidemiologic, clinical and laboratory, chemical and analytical and mathematical methods of study (the justification of criteria and the safe levels of exposure markers, the biomarkers of negative effects, the development of standards and the protocols of clinical and laboratory diagnostics, specific diagnostic test systems, etc.);

– the development of standardized targeted medical-preventive technologies adequate to the level of diseases development risk, the degree of the validity of pathogenetic relationship with exposure and intensity of clinical and laboratory manifestation, etc.;

– the development of organizational basis for the use and assessment of the efficacy of medical-preventive technologies providing the different directions, level and scope of specialized preventive assistance [May I.V. et al., 2008; Ryzhakov S.A. et al., 2009; Zayseva N.V. et al., 2008*b*, 2009*b*; Ustinova O.Yu., 2010; Zayseva N.V. et al., 2011*d*, 2013*a*, 2014*a*; 2014*b*].

Based on the long-term experience and results of own scientific studies the specialists of FBSI "Federal scientific center for medical and preventive health risk management technologies" (Perm) developed and improve the methodological basis for diagnostics of somatic pathology associated with the influence of the living environment factors within which

the possibility of occurrence, progress and chronization of pathologic process is assessed in relation to the degree of hazard of the active risk factors, confirmed exposure, identification of the biological markers of effect with use of cellular-molecular, proteomic and nanotechnologies, analysis of systemic relationships of exposure markers with the negative response markers [May I.V. et al., 2008; Zayseva N.V. et al., 2008*b*, 2011*d*, 2013*a*; Patent of the Russian Federation No. 2491548 dd. August 27, 2013; Patent of the Russian Federation No. 2012157896 dd. February 27, 2014; Zayseva N.V. et al., 2014*a*, 2014*b*].

The complex application of modern sanitary and hygienic, epidemiological, chemical and analytical, clinical, functional, clinical and laboratory and mathematical methods of study allowed to establish the pathogenetic regulations for the development of the most actual and socially meaningful diseases associated with external environmental risk factors, develop the targeted technologies for their prevention, unify the diagnostic approaches, develop the standards and protocols for the provision of specialized assistance [Zayseva N.V. et al., 2008*a*; Ustinova O.Yu., 2010; Zvezdin V.N. et al., 2010; Zemlaynova M.A., 2011].

3.6.1. Requirements to the development of medical-preventive technologies for managing the risk of health disorders associated with the influence of living environment factors

When developing the medical-preventive technologies the following is mandatory:

– the fulfillment of the stages of development in accordance with SIGN criteria (2011) [Federal clinical recommendations on the diagnostics and treatment of pneumoconiosis, 2013];

– the determination of the purpose of the design of the medical-preventive technologies and target medical auditorium;

– the use of the recommended sources of information;

– the assessment of the level and power of conclusiveness of proposed diagnostic criteria and therapeutic and preventive recommendations in accordance with SIGN criteria (2011);

– the observance of the independent developer principles;

– the validation of medical-preventive technologies;

– the compliance of developed medical-preventive technologies with legislative base and main regulatory documents of the Russian Federation [Federal clinical recommendations…, 2013].

The stages of the development of medical-preventive technologies shall comply with SIGN criteria (2011) and shall include the following: the definitions of the purposes of the execution of medical-preventive technology; the determination of key issues which shall be solved; the creation of the group of developers; the consecutive search of literature (the search of relevant systemic reviews, randomized controlled studies, other publications), the formulation of recommendations as the responses to the key issues; their ranking under the level of conclusiveness and the degree of power; distribution, implementation and further improvement.

The purpose of development of medical-preventive technologies is to offer based on the demonstrative data the step-by-step protocols for making the decision on assessing the relationship of health disorders of patient/population with the action of living environment factors, determine the direction, scope, content and form of implementation of therapeutic and preventive measures at the risk-associated pathology

The target medical auditorium is the physicians, pediatricians, general practitioners, occupational pathologists, doctors of particular specialities participating in the health survey programs implementation, specialists on the organization of health care and public health, the hygiene of children and teenagers and other hygienic specialities.

The sources of information, the depth of search and the levels of confidence – when developing the medical-preventive technologies the authors shall carry out the systemic search of information in the following sources:

– the search of published studies;

– the search in the electronic databases;

– the search in the published recommendations of professional medical associations: the Russian Federation, European Union, USA, Scottish intersocietal group on the development of clinical recommendations (SIGN), etc.;

– the search in the databases of systematic reviews: Cochrane Database of Systematic Reviews.

The period which shall be covered by search can be limited by 5 previous years; if the number of the found publications is insufficient the period of search is increased to 10 years.

When selecting the publications as the potential sources of evidence the developers shall use the methodology for assessing the applicability of the results of every study. The result of this assessment is expressed in the levels of conclusiveness that determines the power of each recommendation. In this relation it can be useful to use the criteria for assigning the levels of conclusiveness and ranking proposed by SIGN (2011) (Table 3.13, 3.14).

Table 3.13

The levels of conclusiveness for recommendations in accordance with SIGN criteria (2011)

Level	Criteria
1++	High-quality meta-analysis, systematic review or randomized controlled study (RCS), or RCS with very low level of bias
1+	Well conducted meta-analysis, systematic review or RCS, or RCS with low level of bias
1–	Meta-analysis, systematic review or RCS, or RCS with the high level of bias
2++	High-quality systematic review, "case – control" study or cohort study ("case – control" study or cohort study with very low risk of error or bias and high probability of the cause-and-effect relationship)
2+	Well conducted "case – control" study or cohort study with the low risk of error or bias and moderate probability of the cause-and-effect relationship
2–	"Case-control" study or cohort study with the high risk of error or bias and the significant probability of the absence of the cause-and-effect relationship
3	Non-analytical studies, for example, the description of case or the series of cases
4	Opinion of experts

Table 3.14

Rating scheme for assessing the power of recommendations in accordance with SIGN criteria (2011)

Parameter	Characteristics
A (the high degree of the power of recommendations)	At least, one meta-analysis, systemic review or RCS assessed as 1++ and directly applicable to the target group of population, or the group of evidence consisting mainly of the studies assessed as 1+ directly applicable to the target group of patients and demonstrating the common homogeneity of results
B (the moderate degree of the power of recommendations)	The aggregate of studies assessed as 2++ directly applicable to the target group of population and demonstrating the homogeneity of results; or extrapolation of the data of studies assessed as 1++ or 1+
C (the low degree of the power of recommendations)	The aggregate of studies assessed as 2+ directly applicable to the target group of population and demonstrating the homogeneity of results; or extrapolation of the data of studies assessed as 2++
D (the insufficient degree of the power of recommendations)	Studies with the level of conclusiveness 3 or 4, or the extrapolation of the data of studies assessed as 2+
Acceptable clinical practice	Best recommended practice based on the clinical experience of developers of clinical recommendations

Note: the degrees of recommendations depend on the power of evidence on which the recommendations are based. They do not reflect the clinical importance of recommendations.

Methods used for the evidence analysis:

– The reviews of published meta-analysis;

– Systematic reviews with the tables of evidence;

– The independence of opinions.

Good Practice Points (GPPs)

The recommended good practice is based on the clinical experience of members of work group on the development of medical-preventive technologies.

The method of the medical-preventive technologies validation:

- external expert evaluation;
- internal expert evaluation

Normative references

The developed medical-preventive technologies shall comply with the legislative base and main regulatory documents of the Russian Federation:

- The Constitution of the Russian Federation, article 42. On the right of citizens to the favorable environment, reliable information about its condition and the compensation of damage inflicted to their health or property by the ecological offense.
- The Federal Law of the Russian Federation No. 52-FZ dd. March 30, 1999, "On the sanitary and epidemiological welfare of population".
- The Federal Law of the Russian Federation dd. November 1, 2011 "On the fundamentals of health protection for citizens in the Russian Federation".
- The Resolution of the Government of the Russian Federation No. 569 dd. September 15, 2005 "Provision on conducting the state sanitary and epidemiological surveillance in the Russian Federation".
- The Resolution of the Government of the Russian Federation No. 322 dd. June 30, 2004 "On the approval of Provision on the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance".
- The Regulation of the Government of the Russian Federation No. 2511-r dd. December 24, 2012 "On the approval of the state program of the Russian Federation "Healthcare development" (subprogram "The prevention of diseases and healthy lifestyle formation")".
- The Resolution of the Chief State Sanitary Doctor of the Russian Federation No. 25 dd. November 10, 1997 and chief state inspector of the Russian Federation on the nature protection No. 03-19/24-3483 dd. November 10, 1997 "On the use of risk assessment methodology for the environment quality management and public health in the Russian Federation".
- The Federal Law of the Russian Federation No. 184-FZ dd. December 27, 2002 "On the technical regulation".
- The Letter of the President of the Russian Federation No. Pr-2573 dd. November 1, 2013 "The fundamentals of the state policy on the provision of chemical and biological safety of the Russian Federation for the period to 2025 and further perspective".
- The national standard of the Russian Federation GOST-R 52379–2005 "Good clinical practice" (ICH E6 GCP) (approved by the order of the Federal Agency on Technical Regulation and Metrology No. 232-st dd. September 27, 2005).
- The Order of the Ministry of Health of the Russian Federation No. 455 dd. September 23, 2003 "On the improvement of activity of healthcare bodies and institutions on the prevention of diseases in the Russian Federation".
- Applicable sanitary standards and regulations establishing the hygienic standards of the living environment quality.
- Guidelines on the conduction of chemical and analytical studies in the biological media and objects of environmental medium.

The developed medical-preventive technologies shall be harmonized with international and domestic documents:

- The Declaration of Helsinki on the ethical principles of the World Medical Association (1964, 1975, 1983, 1989).

♦ Manual 2.1.10.1920-04. "Manual on the assessment of risk to human health from the exposure to chemical substances that pollute the environment" / M.: Federal center of the State sanitary and epidemiological supervision of the Ministry of Health of Russia, 2004. 143 p.

♦ International consensuses on the problems of the diagnostics and treatment of diseases.

♦ The National programs of strategy for the treatment and prevention of diseases.

♦ Baranov A.A. Russian national pediatric official list / M.: GEOTAR-Media. 2009. 912 p.

♦ Industry-specific standards for the scopes of rendering the medical assistance for children. M.: Dzhangar, 2001. 608 p.

♦ The Orders of the Ministry of Health of RF, regulating the standards and procedure for the provision of medical assistance at the certain diseases.

♦ The Order of the Ministry of Health and Social Development of the Russian Federation No. 60n dd. February 4, 2010 (annex).

When preparing the medical-preventive technologies it is feasible to use the following domestic and foreign documents:

♦ Andreeva N.S., Rebrova O.Yu., Zorin N.A. et al. Systems for assessment of reliability of scientific evidence and credibility of recommendations: comparative characterization and the prospects of unification. Medical technologies. Assessment and selection. 2012. No. 4. P. 10–24. URL: http: //medpro.ru/groups/sistemy otsenki dostovernosti nauchnykh dokazatelstv i ubeditelnosti rekomendatsii sravniteln.

♦ Andrews J.C., Guyatt G.H., Oxman A.D. et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations // J. Clin. Epidemiol. 2013*a*. Vol. 66, No. 7. P. 719–725.

♦ Andrews J.C., Schünemann H.J., Oxman A.D. et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength // J. Clin. Epidemiol. 2013*b*. Vol. 6, No. 7. P. 726–735.

♦ Balshem H., Helfand M., Schünemann H.J. et al. GRADE guidelines: 3. Rating the quality of evidence // J. Clin. Epidemiol. 2011. Vol. 64, No. 4. P. 401–406. URL: http: //www.jclinepi.com/article/S0895-4356 (10) 00332-X/fulltext.

♦ Guyatt G.H., Oxman A.D., Kunz R. et al. GRADE Working Group (Going from evidence to recommendations // BMJ. 2008*a*. Vol. 336, No. 7652. P. 1049–1051. URL: http: //www.ncbi.nlm.nih.gov/pmc/articles/PMC2376019.

♦ Guyatt G.H., Oxman A.D., Kunz R. et al. GRADE Working Group. Incorporating considerations of resources use into grading recommendations // BMJ. 2008*b*. Vol. 336, No. 7654. P. 1170–1173. URL: http: //www.ncbi.nlm.nih.gov/pmc/articles/PMC 2394579.

♦ Guyatt G.H., Oxman A.D., Kunz R. et al. GRADE Working Group. What is «quality of evidence» and why is it important to clinicians? // BMJ. 2008*c*. Vol. 336, No. 7651. P. 995–998. URL: http: //www.ncbi.nlm.nih.gov/pmc/articles/PMC2364804.

♦ Guyatt G.H., Oxman A.D., Kunz R. et al.; GRADE Working Group // GRADE guidelines: 7. Rating the quality of evidence – inconsistency // J. Clin. Epidemiol. 2011*d*. Vol. 64, No. 12. P. 1294–1302. URL: http: //www.jclinepi.com/article/S0895-4356 (11) 00182-X/fulltext.

♦ Schünemann H.J., Oxman A.D., Brozek J. et al. GRADE: assessing the quality of evidence for diagnostic recommendations // Evid. Based Med. 2008*a*. Vol. 13, No. 6. P. 162–163.

♦ Schünemann H.J., Oxman A.D., Brozek J. GRADE Working Group. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies // BMJ. 2008*b*. Vol. 336, No. 7653. P. 1106–1110. URL: http: //www.ncbi.nlm.nih.gov/pmc/ articles/PMC2386626.

♦ Tatsioni A., Zarin D.A., Aronson N. et al. Challenges in systematic reviews of diagnostic technologies // Ann. Intern. Med. 2005. Vol. 142, No. 12 (Pt 2). P. 1048–1055.

♦ West S., King V., Carey T.S. et al. Systems to Rate the Strength of Scientific Evidence. Evidence Report/Technology Assessment. 2002. № 47 (Prepared by the Research

Triangle Institute–University of North Carolina Evidence-based Practice Center under Contract No. 290-97-0011).

♦ Scientific-methodical justification and standardization of methods for the prevention of diseases and recreation of children when exposed to the living environment factors and lifestyle: report on the scientific and research work / registered at the Federal State Scientific Institution "Center of Information Technologies and Systems", state registration No. 01201154017 M., 2011. 177 p.

3.6.2. The content of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors

The content of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors has the following key sections:

1) the list of the components of medical-preventive technologies and the description of procedure for their implementation;

2) the characterization of the structural-functional model of the medical-preventive technology implementation;

3) the place of medical-preventive technology in the operative and strategic public health risk management.

The components of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors

The main components of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors include:

– the classification of medical-preventive technology;

– the purpose of medical-preventive technology with criteria for the target groups allocation;

– the list of criteria for the diagnostics of risk-associated pathologic conditions, the description of procedure for their identification;

– the list of primary and additional diagnostic measures;

– diagnostic measures implementation algorithm;

– the list of recommended therapeutic and preventive measure with the indication of pathogenetic directions;

– therapeutic and preventive measures implementation procedure;

– the program of pharmacological support for the medical-preventive technology;

– the list of individual contraindications to the implementation of therapeutic and preventive measure of the medical-preventive technology;

– individual criteria and terms for the assessment of clinical efficacy of technology;

– prognostic social and economic effect from the implementation of medical-preventive technology.

The classification of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors

Main principles forming the base of the classification of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors [Zaytseva N.V. et al., 2014*a*] are as follows:

– the typology of medical-preventive technologies under the level and characterization of the risk of harm to the health associated with the influence of living environment factors;

– the systematization of technologies under the pathogenetic directions and the intensity of the clinical manifestation of the risk-associated pathologic process;

– the grouping of medical-preventive technologies under the objective, solved tasks and content of therapeutic and preventive measures;

– the separation of technologies under the field of application and the material base of practical implementation (Fig. 3.17).

Under the level and characterization of the risk of harm to the public health the medical-preventive risk management technologies are characterized as follows and implemented only:

– with the moderate risk of health disorders, mainly of low and average severity;

– with the high risk of health disorders, mainly of average severity;

– with very high risk, mainly of severe health disorders;

– with implemented risk and harm inflicted to health.

Under the pathogenetic directions and intensity of clinical manifestation of risk-associated pathologic process the medical-preventive technologies are divided as follows:

– aimed at the correction of the transitory disorders of the functional condition of system for adaptation and supporting of homeostasis in patients with deconditioning syndrome;

– aimed at the treatment and prevention of the recurrent diseases of critical organs and systems in the patients with transitory sub/decompensation of the functional condition of system for adaptation and supporting of homeostasis;

– aimed at the treatment and prevention of recurrent diseases of critical organs and systems in the patients with somatic diseases of the critical organs and systems in the patients with persisting sub/decompensation of the functional condition of system for adaptation and supporting of homeostasis;

– aimed at the treatment and prevention of risk-associated diseases in the patients with persisting sub/decompensation of the functional condition of system for adaptation and supporting of homeostasis;

Under the objective, solved tasks and content of therapeutic and preventive measures the following is distinguished:

– technologies for the prevention of the development of risk-associated pathologies aimed at the increase of the functional activity of system for adaptation and supporting of homeostasis taking into account the potential health risk;

– technologies for the prevention of development of risk-associated pathologies aimed at the prevention of the backset of recurrent diseases, the restoration of the functional activity of system for the adaptation and supporting of homeostasis, the increase of functional resistance of critical organs and systems taking into account the average level of potential health risk;

– technologies for the prevention of the development of risk-associated pathologies aimed at the treatment and prevention of chronic somatic diseases, the pathogenetic correction of the functional activity of system for adaptation and the supporting of homeostasis, the restoration of the morphofunctional resistance of critical organs and systems taking into account the high level of potential health risk;

– technologies for the treatment and prevention of the development of risk-associated diseases, the prevention of the development of complications and disablement aimed at the correction of the pathogenetic mechanisms of the development of risk-associated pathologies, enzyme disorders at the level of cellular and sub-cellular structures of target organs, the restoration of the main types of exchange and the support of the functional activity of system for adaptation and supporting of homeostasis.

Under the field of application the following types of medical-preventive technologies for managing the risk of health disorders associated with the influence of living environment factors are distinguished:

– health-improving programs;

– target preventive programs;

– target rehabilitation programs;

– group treatment and prevention programs;

– individual treatment and prevention programs;

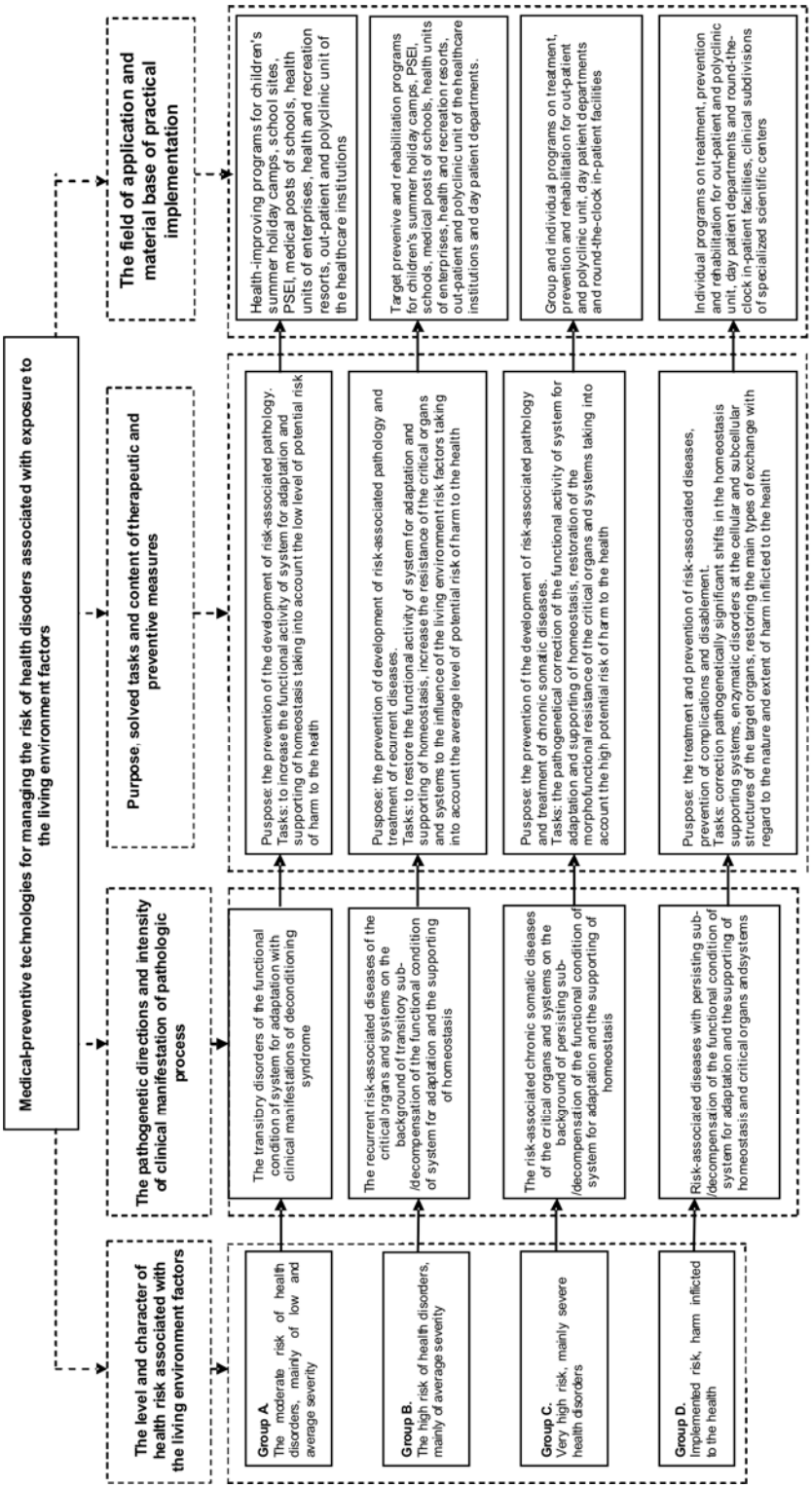

Fig. 3.17. The scheme of the classification of medical-preventive technologies for managing the risk of health disoders associated with exposure to the living environment factors [Zaytseva N.V. et al., 2014a]

Under the material base of practical implementation the technologies can be designed for:
– children's summer holiday camps, summer school sites;
– pre-school educational institutions;
– the health units of enterprises;
– health and recreation resorts;
– the out-patient and polyclinic units of the healthcare institutions;
– day patient departments;
– round-the-clock in-patient facility;
– the clinical subdivisions of specialized scientific centers.

The classification of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors [Zaytseva N.V. et al., 2014*a*]

I. Group A.

The technologies for the prevention of the risk-associated transitory disorders of the functional condition of system for adaptation and the supporting of homeostasis:

1) pathogenetic directions – the increase of the functional activity of system for adaptation and the supporting of homeostasis taking into account the low potential risk of harm to the health;

2) clinical directions – maladjustment syndrome manifesting by acute infectious diseases and disorders of the functional state of organs and systems transient in nature;

3) the field of application – health-improving programs;

4) the form of implementation – organized collectives;

5) the frequency of application – 1–2 times per year;

6) implementation base – children's summer holiday camps, summer school sites, pre-school educational institutions, the medical posts of schools, the health units of enterprises, health and recreation resorts, the out-patient and polyclinic unit of the healthcare institutions.

II. Group B.

Technologies for the prevention of risk-associated recurrent diseases:

1) pathogenetic directions – the increase of functional resistance of the critical organs and systems to the influence of the living environment factors, restoration of the functional activity of system for adaptation and the supporting of homeostasis taking into account the average level of potential risk of harm to the health;

2) clinical directions – the recurrent diseases of the critical organs and systems (repeated acute inflammatory diseases, the functional pathology of organs and systems) on the background of transitory sub- or decompensation of the functional condition of system for adaptation and supporting of homeostasis;

3) the field of application – target preventive programs, target rehabilitation programs;

4) the form of implementation – organized collectives, individual prevention;

5) the frequency of application – 2 times per year;

6) implementation base – children's summer holiday camps, summer school sites, pre-school educational institutions, the medical posts of schools, the health units of enterprises, health and recreation resorts, out-patient and polyclinic unit of the healthcare institutions,day patient departments.

III. Group C.

Technologies for the treatment and prevention of risk-associated chronic somatic diseases with the persisting sub- or decompensation of the functional condition of system for adaptation and the supporting of homeostasis:

1) pathogenetic directions – the restoration of the morphofunctional resistance of the critical organs and systems to the influence of the living environment factors, the increase of the functional activity of system for adaptation and the supporting of homeostasis taking into account the high level of potential risk of harm to the health;

2) clinical directions – chronic diseases of the critical organs and systems on the background of persisting sub- or decompensation of the functional condition of system for adaptation and supporting of homeostasis;

3) the field of application – target treatment programs, prevention and rehabilitation;

4) the form of implementation – individual, group;

5) the frequency of application – 2–3 times per year;

6) implementation base – day patient departments,round-the-clock in-patient facility or the out-patient and polyclinic unit of the healthcare institutions.

IV. Group D.

Technologies for the treatment and prevention of risk-associated diseases with persisting sub- or decompensation of the functional condition of system for adaptation and the supporting of homeostasis:

1) pathogenetic directions – the correction of specific disorders at the level of cellular and sub-cellular structures of target organs, the restoration of morphofunctional resistance of the critical organs and systems, the pathogenetic correction of the main types of exchange, neuroendocrine regulation, immune reactivity, etc. taking into account the nature and degree of harm inflicted to the health;

2) clinical directions – the risk-associated diseases of the critical organs and systems with gradual course and resistance to the basic therapy on the background of persisting sub- or decompensation of the functional condition of system for adaptation and supporting of homeostasis;

3) the field of application – target treatment programs, prevention and rehabilitation;

4) the form of implementation – individual;

5) the frequency of application – individually;

6) implementation base – day patient departments, round-the-clock in-patient facility, the out-patient and polyclinic unit of the healthcare institutions, the clinical subdivisions of specialized scientific centers.

The results of the long-term experience of the specialists of FBSI "Federal scientific center for medical and preventive health risk management technologies" demonstrate that at the territories of sanitary and epidemiological ill-being among the population requiring the specialized medical assistance the demand for different types of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors is:

– for technologies on the prevention of the risk-associated transitory disorders of the functional condition of system for adaptation – 35 %;

– for technologies on the prevention of the risk-associated recurrent diseases – 30 %;

– for technologies on thetreatment and prevention of the risk-associated chronic diseases – 20 %;

– for technologies on the treatment and prevention of risk-associated diseases – 15 % [Zaytseva N.V. et al., 2011*d*; Luzhetsky K.P. et al., 2012; Patent of the Russian Federation No. 2491549 dd. August 27, 2013; Patent of the Russian Federation No. 2012157896 dd. February 27, 2014] (Fig. 3.18).

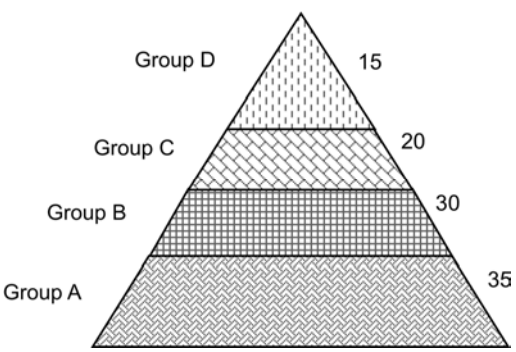

Fig. 3.18. Demand for the different types of the specialized medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors (%)

The content of medical-preventive technologies, in particular, the field of application of technology, the list of the biomarkers of exposure and biomarkers of adverse effects, the orientation of therapeutic and preventive measures, pharmacological and physical therapy software, the base of practical implementation, etc., in addition to the sanitary and hygienic criteria is determined by a number of etiological, epidemiological and clinical features of the risk-associated processes the leading ones are as follows:

1. The nature of the living environment risk factor:

a) chemical factors;
b) physical factors;
c) biological factors;
d) psychophysiological factors;
e) social factors;
f) production factors;
g) a combination of the factors of different nature.

2. The mechanisms and routes of the risk factor exposure:

a) inhalation;
b) exposure to *per os* risk factors (water, alimentary);
c) transcutaneous;
d) combined, complex, cumulative exposure.

3. The pathogenetic mechanisms of the risk factor exposure:

a) toxic;
b) inflammatory;
c) sensitizing;
d) carcinogenic;
e) teratogenic, etc.

4. Target group characterization:

a) children's population;
b) teenagers;
c) working-age population;
d) pregnant women;
e) the population of pension age;
f) disabled;
g) the women of reproductive age;
h) the men of reproductive age;
i) the workers of enterprises with harmful and hazardous labor conditions;
j) persons with the low level of social and economic support.

5. The class and nosologic form of risk-associated pathologic process (according to MKB-10):

a) respiratory diseases (J00-J99);
b) the diseases of nervous system (G00-G99);
c) the diseases of circulatory system (I00-I99);
d) the diseases of digestive organs (K00-K93);
e) the diseases of endocrine system, the disorders of nutrition and metabolism disorders (E00-E90);
f) the diseases of the genitourinary system (N00-N99);
g) the diseases of the musculoskeletal system and connective tissue (M00-M99);
h) the diseases of blood, blood-making organs and separate disorders involving the immune mechanism (D50-D89);
i) the diseases of skin and subcutaneous tissue (L00-L99);
j) the diseases of eyes and their adnexa (H00-H59);
k) the diseases of ears and their mastoid (H60-H95);
l) mental and behavioral disorders (F00-F99).

6. The severity of the course of the risk-associated process:

a) low severity;
b) average severity;

c) high severity.

7. The stage of manifestation and the course of risk-associated process:

a) acute sage;

b) chronic course stage;

c) aggravation stage;

d) remission stage.

8. The presence of the complications of the risk-associated process:

a) risk-associated disease with the presence of complications;

b) risk-associated disease without complications.

9. The directions of technology:

a) for organized collectives (groups, samplings, etc.);

b) for individual treatment and the prevention of risk-associated health disorders.

The objective of medical-preventive technologies for managing the risk of public health disorders associated with the influence of living environment factors, criteria for the target groups determination

1. *The purpose of the medical-preventive technologies of group A* is to prevent the development of risk-associated diseases.

Target groups determination criteria:

– the residence / performance of labor activity under the conditions of exposure to risk factors (exceeding of hygienic standards);

– the presence of the moderate risk of health disorders predominantly of mild to moderate severity, associated with exposure to risk factors;

– the clinical manifestations of risk-associated maladjustment syndrome as repeated frequent acute respiratory diseases, asthenoneurotic reactions, psychological and emotional lability in children – the delays of physical and neuropsychological development;

– resistance to basic prevention;

– the relationship of the clinical manifestations of risk-associated pathological process with the deterioration of the sanitary and hygienic situation;

– the biomarkers of exposure for chemical factors – content in biological media at the level of 1,1–1,5 RL;

– the biomarkers of negative risk-associated effects: at the system level – the persisting elevation of stress hormones, the activation of oxidative-antioxidative processes and apoptosis, the reduction of non-specific resistance, the indicators of humoral immune response, the disturbance of autonomic reactivity, etc. [Zaytseva N.V. et al., 2008*b*, 2011*b*; Ustinova O.Yu., 2011; Patent of the Russian Federation No. 2494401 dd. September 27, 2013; Patent of the Russian Federation No. 2491548 dd. August 27, 2013].

2. *The purpose of the medical-preventive technologies of group B* is to prevent the development of risk-associated diseases and treatment of recurrent diseases.

Target groups determination criteria:

– the residence / performance of labor activity under the conditions of exposure to risk factors;

– the presence of the high risk of health disorders predominantly of moderate severity, associated with exposure to risk factors;

– the clinical manifestation of the risk-associated recurrent diseases of critical organs and systems (recurrent acute inflammatory and proliferative processes, the functional disorders of organs and systems, the transitory violations of neurovegetative and endocrine regulation, etc.);

– the low efficiency of basic therapy;

– the relationship of the clinical manifestations of risk-associated pathological process with the deterioration of the sanitary and hygienic situation;

– the biomarkers of exposure for chemical factors – content in biological media at the level of 1,6–2,0 RL;

– the biomarkers of negative risk-associated effects: organ tissue level – the stable presence of markers of cytolysis, organ specific enzymes; at the system level - a transient inhibition of apoptosis, specific sensitization, the activation of oxidative processes, the persistent decompensation of antioxidant processes, the transient violations of the hormonal profile, persistent immunodeficiency, the functional disorders of the critical organs and systems, metabolic disorders in the myocardium, and psihoastenichesky neurotic syndrome, signs of hepatocellular disorders etc. [Patent of the Russian Federation No. 2459622 dd. August 27, 2012; Patent of the Russian Federation No. 2449276 dd, April 27, .2012; Zemlyanova M.A. et al., 2012; Ustinova O.Yu., 2013; Patent OF THE RUSSIAN FEDERATION NO. 2012157896 dd. February 27, 2014].

3. The purpose of the medical-preventive technologies of group C is to prevent the development of risk-associated and treatment of chronic somatic diseases.

Target groups determination criteria:

– the residence / performance of labor activity under the conditions of exposure to risk factors;

– the presence of very high risk of serious health problems mainly associated with exposure to risk factors;

– the clinical manifestation of the risk-associated chronic somatic diseases of critical organs and systems, polyorganic affections on the background of persistent violations of neurovegetative and endocrine regulation, immune deficit under the mixed type, in some cases - the development of autoimmune or allergic processes, etc.;

– resistance to basic therapy;

– a progressive nature of the course of pathological process with frequent relapses;

– the biomarkers of exposure for chemical factors – content in biological media at the level of more than 2.0 RL;

– the biomarkers of negative risk-associated effects: at the molecular-cellular level – the persistent changes of metabolic profile, the inhibition of apoptosis, general sensitization, the activation of oxidative processes, the decompensation of antioxidant protection; at the organ tissue level – a transient presence of the markers of damage to cellular-subcellular structures, pathological changes in organs and tissues; at the system level – acid-base imbalance, persistent immunodeficiency, dishormonosis, transient hepatocellular and renal failure, the process of bone marrow hematopoiesis, metabolic processes, the long-term violation of the functional state of organs and systems [Akatova A.A. et al., 2004; Verikhov B.V., Ustinova O.Yu., 2007; Zaytseva N.V. et al., 2008*a*; May I.V. et al., 2008; Aminova A.I. et al., 2009; Patent of the Russian Federation No. 2471190 dd. December 27, 2012].

4. *The purpose of the medical-preventive technologies of group D* is to prevent and treat the development of risk-associated diseases.

Target groups determination criteria:

– the residence / performance of labor activity under the conditions of exposure to risk factors exceeding the hygienic standards;

– the presence of the risk of health problems associated with exposure to risk factors;

– The clinical manifestation of the risk-associated diseases of critical organs and systems, polyorganic affections on the background of the persistent violations of neuro-vegetative, immune and endocrine regulation, the development of autoimmune or allergic processes, etc.;

– resistance to traditional therapy;

– a progressive nature of the course of pathologic process with frequent relapses on the background of traditional therapy, the development of complications;

– the biomarkers of exposure for chemical factors – content in biological media at the level of more than 2.5 RL;

– the biomarkers of negative risk-associated effects: at the genetic level – allelic disorders and gene polymorphism; at the molecular-cellular – the persistent changes of metabolic and proteomic profiles, apoptosis inhibition, general / specific hypersensitization, hyperactivation of oxidation processes, resistant decompensation of antioxidant protection; organ tissue – the stable presence of the specific markers of the specific damage of cellular-

subcellular structures, pathological changes in organs and tissues; at the system level – deep acid-base imbalance, secondary immunodeficiency, dishormonosis, hepatocellular and renal failure, persistent morphofunctional violations of the critical organs and systems [Verikhov B.V., Ustinova O.Yu., 2007; Zaytseva N.V. et al., 2008b; Patent of the Russian Federation No. 2459622 dd. August 27, 2012; Patent of the Russian Federation No. 2491548 dd. August 27, 2013].

The list of criteria for the diagnostics of risk-associated pathologic conditions-diseases, the description of procedure for their identification

The diagnostics of risk-associated pathological processes / diseases is conducted on the basis of:

– hygienic criteria (the identification of risk factors for the living environment and the assessment of the level of hazard to health);

– epidemiological criteria (identifying the epidemiological patterns of development of risk-associated pathological processes / diseases in the population of the territories of sanitary and epidemiological ill-being, the employees of enterprises with harmful and dangerous working conditions, etc.);

– sociological criteria (identifying the sociological risk factors);

– clinical criteria (identifying the diagnostically significant clinical symptoms of the manifestation of risk-associated pathological process / disease);

– functional criteria (diagnostics of morphological and functional risk-associated disorders of systems and target organs);

– for chemical risk factors – the identification of the biomarkers of exposure (the content of chemical substances in biological media);

– laboratory criteria (the biomarkers of the negative effects of the multi-level exposure of risk factors at the systemic, organ-tissue, cellular and subcellular levels).

The cumulative use of sanitary and hygienic, epidemiological, sociological and medical-biological researches allows to conduct the system analysis of risk factors, provide the objective assessment of the degree of their hazard, detect the epidemiological regularities of the consequences of their negative influence on the health of population, establish the pathogenetic, clinical-functional, chemical-analitical and laboratory peculiarities of forming the risk-associated pathologic processes / diseases.

The mathematical processing of the results of studies allows establishing the list of biological exposure markers and the biological markers of the negative effects of the multi-level action of the risk factors of living environment on the human body (macrolevel – body, mesolevel – the system of organs/target organ, microlevel – cell/subcellular structures).

The conclusiveness level assessment and ranking the biological markers of exposure and biological markers of negative effects carried out in accordance with the recommendations of SIGN (2011) allow to establish the list of diagnostically significant biological markers of risk-associated pathologic processes / diseases with the specification of each conclusiveness level.

Performance procedure:

1. Hygienic diagnostics criteria are established:

– under the results of field observations or data monitoring researches carried out by the territorial services of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance, Federal Service for Hydrometeorology and Environmental Monitoring, etc, in accordance with the existing normative documents (for example, Resolution of government of the Russian Federation No. 60 dd. February 2, 2006 "Provision on the conducting of the social and hygienic monitoring» with the changes dd. September 4, 2012);

– on the basis of the calculation of the risk of health problems associated with the negative impact of environmental factors, identifying the contribution of each of the relevant factors. The evaluation of the health risk is carried out on a standardized methodology in accordance with the P 2.1.10.1920-04 "Guidelines for estimating health risk when exposed to chemicals that pollute the environment" and other documents.

As a result of research the list of risk factors for the environment, their exposure, compliance / noncompliance with applicable hygienic standards, the level of health risk are established.

2. Epidemiological diagnostic criteria are established based on the results of large-scale randomized multicenter targeted epidemiological studies or official data of state and departmental statistics. The studies analyze:

– the morbidity of the population of the studied area / the employees of enterprises with hazardous or dangerous working conditions / the specific group of population with risk-associated pathological processes / diseases in relation to the incidence rate of population at the territories of sanitary and hygienic welfare / enterprises with no harmful or dangerous factors of production / comparison groups, or regional average, average territorial, average rates;

– the growth and / or increase of the population morbidity of the studied area / the employees of enterprises with hazardous or dangerous working conditions / specific population risk-associated pathological processes / diseases in relation to the indicators of areas the territories of sanitary and hygienic welfare / enterprises with no harmful or dangerous factors of production / comparison groups or regional average, average territorial, the average Russian data.

The conducted studies establish the epidemiological patterns and trends in the development of risk-associated pathological processes / diseases in specific population groups.

3. The sociological criteria of diagnostics are established based on the results of rendomized sociological studies.

4. The identification of the clinical and functional criteria of risk-associated pathological processes / diseases is performed based on the results of targeted large-scale randomized multicenter comparative medical-biological studies. It is necessary to analyze the results of medical-biological studies carried out on the basis of the licensed under the established order medical facilities, in compliance with the ethical principles of biomedical research outlined in the Declaration of Helsinki 1975 with additions of 1983 and meeting the national standard of the Russian Federation GOST-R 52379-2005 "Good Clinical Practice" (ICH E6 GCP), approved by the order of the Federal agency for Technical regulation and Metrology No. 232-st dd. September 27, 2005.

The study establishes the clinical and functional diagnostic criteria for risk-associated pathological process / disease, taking into account whether the risk is potential or realized.

5. The identification of the biomarkers of exposure (for chemical risk factors) is conducted by the chemical analytical methods for studying the biological media (blood, urine, umbilical cord blood, breast milk, etc.) in accordance with approved methods in the accredited and licensed laboratories on the calibrated equipment.

The result of the study is a list of biomarkers of exposure to the risk-associated pathological process / diseases.

6. The identification of the laboratory biomarkers of the negative effects of the multi-level risk factors of living environment based on the results of targeted randomized comparative laboratory studies performed under the approved methods in the accredited and licensed laboratories on the calibrated equipment. It is necessary to analyze the results of laboratory studies carried out in compliance with ethical principles of biomedical research outlined in the Declaration of Helsinki 1975 with additions of 1983 and meeting the national standard of the Russian Federation GOST-R 52379-2005 "Good Clinical Practice" (ICH E6 GCP), approved by the order of the Federal agency for Technical regulation and Metrology No. 232-st dd. September 27, 2005.

The study established a list of laboratory criteria (biomarkers of negative effects of multi-level exposure to risk factors) for the risk-associated pathological process / disease.

7. The methods of mathematical statistics are used (Statistica 6.0, etc.) to establish a diagnostically significant biomarkers of exposure, as well as clinical and functional and laboratory biomarkers of risk-associated pathological processes. The comparison of high-quality binary attributes in the two groups is carried out by the methods of nonparametric statistics with the construction and analysis of two-dimensional contingency tables, using the chi-square criterion (χ^2). The Student's criterion is used to compare the groups under the

quantitative features. Assessment of relationships between the features is carried by one-factorial dispersion analysis method (for qualitative characteristics) and the method of correlation-regression analysis (for quantitative variables). The assessment of the level of evidence and ranking of diagnostic criteria is performed in accordance with the recommendations of SIGN (2011) (Table 3.13, 3.14) [Federal clinical guidelines ..., 2013].

The list of primary and additional diagnostic measures

The primary diagnostic measures include the studies, which resulted in the identification of biomarkers of risk-associated pathological process / disease with high and moderate level of evidence (level *A* and *B*, in exceptional cases – I) (see. Table 3.14).

The additional diagnostic measures include the studies, which resulted in the identification of biomarkers of risk-associated pathological process / disease with moderate and low level of evidence (level *B* and *C*) (see. Table 3.14).

The list of diagnostic measures does not include the study, biomarkers of which have a level of evidence D (insufficient level of evidence).

The algorithm of diagnostic measures

In patients with suspected risk-associated pathological process / disease living / engaged in labor activities under the impact of environmental risk factors, exceeding hygienic standards and defining an unacceptable risk of risk-associated pathological process / disease during clinical examination diagnose the presence / the absence of clinical markers with level of evidence a and B (in exceptional cases – C).

In the presence of 80% of clinical markers of risk-associated pathological processes / diseases conduct complex functional, laboratory (if necessary – chemical-analytical, sociological) research.

When the results obtained according to 80% or more diagnostic criteria of risk associated pathological process / disease by specialized therapeutic and prophylactic measures envisaged technology.

Upon the receipt of the results of primary diagnostic measures corresponding to only 50–79% diagnostic criteria for risk-associated pathological process / disease, carried out additional diagnostic measures.

Upon the receipt of the results of primary diagnostic measures corresponding to less than 49% of the diagnostic criteria for risk-associated pathological process is carried out differential diagnosis of somatic pathology.

The socket results of additional diagnostic measures by 80% or more diagnostic criteria for risk-associated pathological process by specialized therapeutic and prophylactic measures envisaged technology.

The list of recommended therapeutic and preventive measures

The general characteristics of the treatment and the prevention of the health-care technology risk management of health problems associated with exposure to environmental factors

Treatment and prevention technologies are based on data on pathogenetic patterns of risk-associated pathological process / illness in general should provide:

- the correction of risk-associated pathophysiological and pathological disorders in the target organs;
- the restoration of the main types of exchange, the balance of oxidative and antioxidant processes, acid-base balance at the systemic, cellular and subcellular levels;
- the stimulation of the factors of immunological protection and non-specific reactivity;
- the restoration of the adaptive reserves of organs and systems, autonomic regulation, hormonal homeostasis;
- when exposed to chemical hazards – the restoration of membrane-cell, the organ mechanisms of biotransformation and the elimination of chemicals and their metabolites.

Therapeutic and preventive measures include a complex pharmacological agents, physiotherapy and spa techniques, diet therapy, physiotherapy, etc. The pharmacological component of therapeutic and preventive measures should be based on the preparations made in the clinical practice, having compatibility and the minimum number of possible side effects.

Programs therapeutic and preventive measures include two main blocks:

- basic, aimed at correcting the risk associated pathophysiological and pathological disturbances in the systems and target organs;

- pathogenetic aimed at correcting the secondary risk-associated changes in the system to adapt and maintain homeostasis.

The base unit technology risk management of health problems associated with exposure to chemical factors, further includes measures aimed at reducing the levels of chemicals and their metabolites in the body (efferent therapy). Efferent therapy involves the stimulation of the natural mechanisms of the elimination (enhanced mode drinking, breathing exercises, speleotherapy, thermotherapy, hydrotherapy, etc.) of chemical substances and their metabolites and the normalization / increased activity of biotransformation processes (diet, pharmacopoeial preparations). When the content of chemical substances in the blood exceeding 2 RL, requires additional elimination event (appointment enterosorbents, choleretic, holesektetikov, methods of detoxification therapy in some cases – complexing).

The treatment and prevention of health-care technology group A are aimed at improving the functional activity of systems to adapt and maintain homeostasis, given the low level of potential risk of injury. The basis of therapeutic and preventive measures is the integrated use of diet, climatic factors, physical therapy and spa treatments, pharmacological agents (metabolics, adaptogens). The compulsory part of these programs is the inclusion of pathogenetically directed balanced complex micro- and macronutrients, special complexes of physical therapy, enhanced drinking regime, etc. [Zaitseva N.V. et al., 2012, 2013b; Patent of the Russian Federation No. 2163483 dd. 27.02.2001; Patent of the Russian Federation No. 2206327 dd. 20.06.2003; Patent of the Russian Federation No. 2478395 dd. 04/10/2013].

The treatment and prevention of health-care technology group B are aimed at increasing the resistance of critical organs and systems to the effects of environmental risk factors, taking into account the average level of the potential risk of harm to the health and the recovery of the functional activity of systems to adapt and maintain homeostasis. The content of therapeutic and preventive measures provides the pathogenetic correction of the basic mechanisms of pathological processes (inflammatory and allergic reactions, impaired immune reactivity and the balance of trace elements microcirculation processes, etc.) and is provided by the desensitizing and anti-inflammatory drugs, membrane protectors, antioxidants, immunomodulators, improving agents microcirculation, etc. In the case of risk-associated recurrent diseases associated with exposure to chemical risk factors, further comprising measures aimed at the reduction of chemical substances and their metabolites in biological media to the level of the reference values (using pharmacological means and methods of physical therapy to ensure absorption and evacuation of chemicals through the gastrointestinal tract, the activation mechanism of renal elimination and microcirculatory processes, acceleration of the biliary transport, etc.) [Zaitseva NV Ustinov O., 2002; Ryzhakov SA et al., 2009; Zaitseva NV et al., 2014a; Aminova AI et al., 2010; Patent of the Russian Federation No. 2436574 dd. 20.12.2011; Patent of the Russian Federation No. 2421233 dd. 20.06.2011].

The treatment and prevention of health-care technology group C are aimed at restoring the morphological and functional resistance critical organs and systems with a view of the high potential risk of harm to the health and functional activity of pathogenetic correction systems to adapt and maintain homeostasis.

The content of therapeutic and preventive measures determined by a complex pharmacological agents pathogenic focus and symptomatic therapy (anti-inflammatory and desensitizing agents, correctors enzymatic biotransformation processes, and antihypoxants cytoprotectors, immunotropic drugs, enzymes, nootropics, sedatives, vitamins and minerals, etc.) [Aminova A.I. et al., 2010; Rumyantsev A.N. et al., 2011*a*, 2011*b*; Zaytseva N.V. et al., 2014*a*].

The treatment and prevention of health-care technology group D are aimed at treating the underlying risk-associated disease with an obligatory correction pathogenetically significant shifts in systems maintain homeostasis, enzymatic disorders at the cellular and subcellular structures of the target organs, restoring the main types of exchange with regard to the nature and extent of inflicted injury

The content of therapeutic and preventive measures determined by a complex pharmacological agents pathogenic focus and symptomatic therapy (infusion-detoxifying agents, anti-inflammatory and desensitizing agents, hormones, proofreaders enzymatic biotransformation processes, cholagogue, immune preparations antihypoxants, cytoprotectors, enzymes, bronchodilators, nootropics, Decongestant, antihypertensive drugs, antiplatelet agents, stimulants hematopoiesis, lipid-lowering drugs, drugs replacement therapy, vitamins and minerals, adaptogens, sedatives, analgesics, etc.) [Zaitseva N.V. et al., 2009*a*, 2009*b*; Rumyantsev A.N., 2011*a*, 2011*b*; Zaitseva N.V., 2011*a*].

Therapeutic and preventive measures implementation procedure

Originally implemented measures aimed at correcting the pathological changes in the systems and target organs, if necessary, they are supplemented by an elimination-detoxication activities replacement therapy (base unit). Pathogenetic block therapeutic and preventive measures aimed at correcting the secondary pathogenesis of risk-associated pathological process / illness, appointed after the disappearance / sigficant reduction in the severity of symptoms of the critical organs and systems. The program of therapeutic and preventive measures specified sequence and timing of the appointment of pharmacological drugs and physiotherapy.

The program of pharmacological support for the medical-preventive technology

The program provides the pharmacological treatment and prevention of medical and preventive technology specified group recommended pharmacological agents with mandatory bringing ATC classification code (Anatomical Therapeutic Chemical Classification System), 2–3 indicates the most appropriate drug selection, as well as the duration of a course of treatment for each of them.

The list of individual contraindications to implement treatment and prevention of medical and preventive technology

Individual contraindications are:
– mismatch complex hygienic, epidemiological and medical-biological criteria;
– idiosyncrasy drugs and physical therapy;
– up to 4 years;
– acute infectious diseases;
– acute mental disorders;
– hepatic and renal failure;
– chronic somatic diseases in the stage of decompensation.

Individual criteria and terms for the assessment of clinical efficacy of technology

Evaluating the effectiveness of preventive medical technology at the individual level is carried out by the specialists of outpatient care territorial public health institutions in 6–12 months after its completion. At the population level assessment of the effectiveness of medical and preventive technologies carried out by experts of the territorial service of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance12 months after its completion.

The individual criteria of the effectiveness of medical-preventive technology group A are:
– a decline of 50–70% incidence of acute diseases;
– the absence of symptoms and asthenovegetative and astenoneurotic character;

– the absence of clinical and laboratory signs of risk-associated disease;

– the normalization of the state of the main systems maintain homeostasis (antioxidant activity, nonspecific reactivity and specific immune protection, etc.);

– the content of chemicals in biological media ≤1,1 RL.

The individual criteria of effectiveness of medical-preventive technology group B are:

– the positive dynamics of clinical and laboratory markers of functional and risk-associated recurrent disease;

– a decline of 30 % incidence of acute diseases;

– the reduction of 2–3 times the number of relapses of recurrent risk-associated diseases;

– The increase of 2–3 times the number of relapses of recurrent risk-associated diseases;

– 50% reduction in the duration of the current cases of recurrence risk of recurrence-related illness;

– the absence of clinical and laboratory markers of progression of recurrent risk-related illness;

– the normalization of the functional activity of critical organs and systems;

– recovery indicators antioxidant protection;

– the increase of nonspecific immunological resistance by 30–50%;

– the normalization of the main types of exchange;

– the content of chemicals in biological media ≤1,5 RL.

The individual criteria of the effectiveness of medical-preventive technology group C are:

– the positive dynamics of the clinical and laboratory markers of functional and risk-associated chronic physical illness;

– the reduction of 1.5–2.0 times the number of relapses;

– a decline of 25 % incidence of acute diseases;

– Increase by 2 times the length of remission of chronic risk-associated somatic disease;

– a decrease of 30% long-term course of one case of recurrence risk associated chronic physical illness;

– the absence of the clinical and laboratory markers of progress of risk-associated chronic somatic disease;

– the absence of complications;

– an increase of 30–50% of the functional activity of critical organs and systems;

– an increase of 30% of the indicators of antioxidant defense, and non-specific immunological resistance;

– the content of chemicals in biological media ≤1,9 RL.

The individual criteria of effectiveness of medical-preventive technology group D are:

– the positive dynamics of clinical and laboratory markers of functional and risk-associated disease;

– the reduction of 1.5–2.0 times the number of relapses;

– A decline of 20 % incidence of acute diseases;

– the absence of signs of intoxication;

– 1.5-fold increase in the duration of remission of the disease-associated risk;

– a reduction of 25% of the current one case of recurrence risk-associated diseases;

– the absence of the clinical and laboratory markers of disease progression;

– the absence of complications;

– the increase of the functional activity of critical organs and systems;

– an increase of 25–30% of the indicators of antioxidant defense, and non-specific immunological resistance;

– the content of chemicals in biological media ≤2,5 RL.

Prognostic socio-economic impact from the implementation of preventive medical technology

The population-based performance criteria of medical and preventive technologies are clinical and economic performance:

– reduction in the territories of the implementation of health-care technology risk management of health problems associated with exposure to environmental factors, the number of reported cases of appeals of the population for medical assistance regarding the risk-associated pathological processes / diseases;

– reduction in the territories of the implementation of health-care technology risk management indicator "for the first time reported cases of" health problems associated with exposure to environmental factors;

– reducing the economic losses associated preventing morbidity.

The evaluation of the clinical efficacy of the preventive health management of the health risk associated with exposure to environmental factors at the population level

The clinical effect of preventive health at the population level is calculated by the number of averted *($N_{пр}$)* and a decrease in the duration of the current cases of recurrence ($Д_{пр}$) for the group, for which the technology has been implemented, according to (3.6.1), (3.6.2):

$$N^{i}_{пр\,j} = \sum N^{i}_{до_j} - \sum N^{i}_{после_j}\ , \qquad (3.6.1)$$

where $N_{пр}{}^{i}_{j}$ – the number of prevented cases of recurrence *j*-th view of the underlying disease;

$N_{до}$ – the number of relapses of the *j*-th type of underlying disease within 1 year prior to treatment;

$N_{после}$ – the number of relapses of the *j*-th type of underlying disease within 1 year after treatment;

i – the age group of the population;

j – the nosological form or class of diseases.

$$Д^{i}_{пр_j} = \frac{\sum Д^{i}_{до\,j}}{\sum N^{i}_{до_j}} - \frac{\sum Д^{i}_{после\,j}}{\sum N^{i}_{после_j}}\ , \qquad (3.6.2)$$

where $Д_{пр}{}^{i}_{j}$ – The number of days prevented the flow of recurrences j-th view of the underlying disease;

$Д_{до}$ – the duration of the current recurrence *j*-th type of underlying disease within 1 year prior to treatment;

$Д_{после}$ – the duration of the current recurrence *j*-th type of underlying disease within 1 year after treatment;

$N_{до}$ – the number of relapses of the *j*-th type of underlying disease within 1 year prior to treatment;

$N_{после}$ – the number of relapses of the *j*-th type of underlying disease within 1 year after treatment;

i – the age group of the population;

j – the nosological form or class of diseases.

The economic evaluation of the health-care technology risk management of health problems associated with exposure to environmental factors at the population level

Economic effect (the prevention of damage) associated with the prevention of te morbidity of the population in respect of which was implemented preventive medical technology consists of avoided health care costs as a result of illness averted costs of social benefits to employees of the Social Security Fund for the period of temporary or permanent disability occurred as a result of illness or child care due to illness averted costs of foregone production due to the loss of days of labor activity.

For the age group 0–18 years (period before work), the value of avoided costs associated with preventing morbidity i-th species (C_d^i), is defined by the formula.

$$C_d^i = (C_m + \alpha C_c + \alpha C_t)h^i , \quad (3.6.3)$$

where C_m – the average cost of health care, rub. / day;

C_c – The average cost of social benefits to the employee (payment of disability days, occurred as a result of child care), rub. / Day;

C_t – The mean value of foregone production due to the loss of days of labor activity, rub. / Day;

h^i – the average number of days illness prevented as a result of treatment per 1 person days;

α – The proportion of children who are being treated under the supervision of their parents;

d – the children's category of the population.

The cost of medical care as a result of a single case of the disease (Cm) is calculated by the formula

$$C_m = \gamma_1 \frac{C_{\text{ст}}}{h_{\text{ст}}} + \gamma_2 \frac{C_{\text{амб}}}{h_{\text{амб}}} , \quad (3.6.4)$$

where $C_{\text{ст}}$ – the average cost of medical care in a hospital, rub. / case;

$C_{\text{амб}}$ – The average cost of medical care in the outpatient clinic, rub. / Case;

γ_1 – The share of health care in the hospital;

γ_2 – The share of health care in the outpatient clinic;

$h_{\text{ст}}$ – The average duration of 1 case of inpatient days;

$h_{\text{амб}}$ – The average duration of 1 case in outpatient clinics, day.

The share of health care in a hospital is determined by the formula

$$\gamma_1 = N_{\text{ст}}/N , \quad (3.6.5)$$

where $N_{\text{ст}}$ – the number of cases in which were treated in the hospital;

N – The number of cases of diseases.

The share of health care in the ambulatory determined by the formula

$$\gamma_2 = N_{\text{амб}}/N , \quad (3.6.6)$$

where $N_{\text{амб}}$ – the number of cases in which an outpatient medical care;

N – The number of cases of diseases.

In this case, the relation is performed: $\gamma_2 + \gamma_1 = 1$

The cost of social benefits to workers for the period of temporary or permanent disability, was the result of disease (SS), is determined by the indicator of payment of temporary disability per day according to the formula

$$C_c = C/n , \quad (3.6.7)$$

where C_c – the average cost of the payment of temporary disability benefits, rub. / day

C – The average cost of the payment of temporary disability benefits, rub. / month;

n – the number of working days in a month.

The cost of social payments to employees for the period of temporary or permanent disability, was the result of child care due to illness, defined as 0.8 Cc, as the proportion of children who are treated under the supervision of parents, an average of 80%.

Information on the amount of the payment of temporary disability per 1 employee per month is represented in the territorial body of the Federal State Statistics Service.

The cost in lost production due to lost days of work activity due to illness of the employee or child care due to illness is defined by the formula

$$C_t = \sum Tt, \tag{3.6.8}$$

where T – cost of underproduced production per day for 1 person, rub.

$$T = G/N_a, \tag{3.6.9}$$

where G – the value of output per day, rub.;

N_a – The number of economically active population, people.

t – labor activity days (t = 248).

Information on the value of production per year is presented in the territorial body of the Federal State Statistics Service.

The cost-effectiveness of health-care technology (E) is defined as the ratio of the economic impact resulting from the implementation of technology, to the costs, to ensure its receipt.

Economic efficiency is calculated for each age group of the population according to the formula

$$Э = C_z^i / З, \tag{3.6.10}$$

where Э – economic efficiency of prevention technologies for 1 person, rub. / rub.;

C_z^i – preventing losses (economic benefit) attributable to one person who provided specialized medical care, rub.;

З – the costs of implementing measures for 1 person for a course of prevention, rub.

The implementation costs of medical and preventive technologies are based on investments made

$$З = (З_1 + З_2 + ...З_n) Д, \tag{3.6.11}$$

where З – the costs of implementing measures for 1 person for a course of prevention, rub.

$З_1 … З_n$ – the cost of activities of the various sources of funding 1 person rub. / day;

Д – the length of the course prophylaxis for 1 person days

Medical and preventive technologies are effective in case of exceeding the value of economic benefits resulting from the implementation of technologies, the amount of expenses that ensured his receipt, ie condition must be satisfied: the resulting economic efficiency > 1 ruble per 1 ruble costs.

A comparative evaluation of different health-care technology that is the most effective technology that achieves the greatest amount of economic efficiency.

The characteristic structural-functional model of the implementation of preventive health technology risk management of health problems associated with exposure to environmental factors

Structural and functional model for the implementation of preventive health management of the health risk associated with exposure to environmental factors, based on the practice of interaction of bodies and organizations and institutions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance practical public health division of functions and powers (Fig. 3.19).

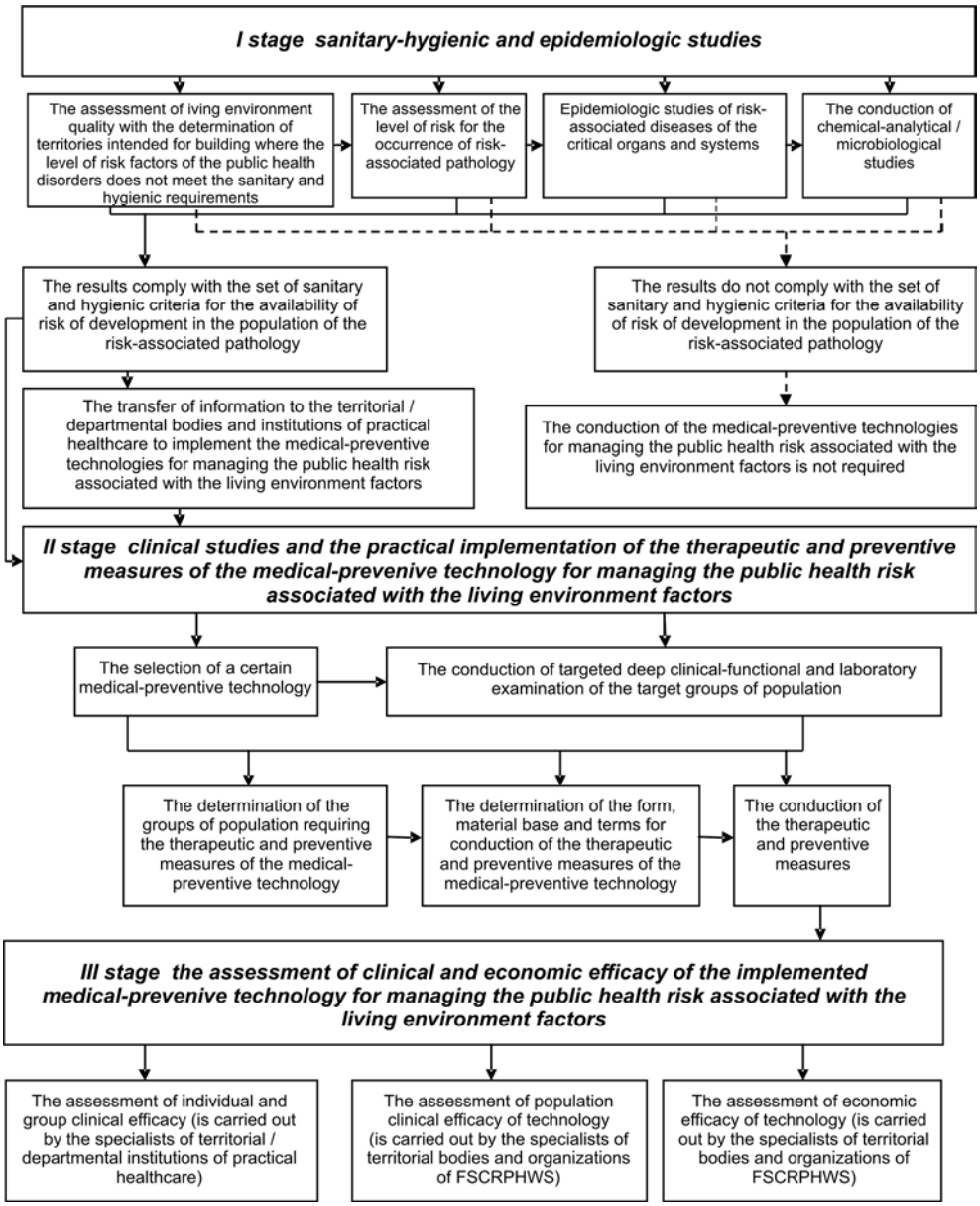

Fig. 3.19. The algorithm of the implementation of health-care technologies
risk management of health problems associated with exposure to environmental factors

The implementation of technologies implemented in phases in the next algorithm of actions:

Stage I – sanitary and epidemiological studies.

1. The assessment of quality of habitat with the release of residential areas, where the level of risk of health problems of the population does not meet sanitary requirements (this is done on the basis of public health monitoring and / or the results of field studies);

2. Assessing the level of risk of the risk associated pathology (performed on a standardized methodology in accordance with the P 2.1.10.1920-04 "Guidelines for estimating health risk when exposed to chemicals that pollute the environment" or other documents, duly approved);

3. The analysis of uptake of the population for medical advice about risk-associated diseases of critical organs and systems (carried out according to official figures state and departmental statistics).

4. In case of violation of habitat quality in chemical or biological factors – carrying out chemical analysis or microbiological studies in representative populations (research carried out with the involvement of regional / departmental institutions of practical public health);

5. The transmission of information territorial / departmental bodies and institutions of practical public health).

Stage II – the clinical research and practical implementation of therapeutic and preventive measures and preventive medical technology risk management of health problems associated with exposure to risk factors.

1. Choose a specific preventive health technology risk management of health problems associated with exposure to risk factors, in accordance with the results of phase sanitary research.

2. A focused in-depth clinical and functional and laboratory examination of the target population (selection of target groups, determination of diagnostic tests and the order of their execution is carried out according to the recommendations given preventive medical technologies, with the need for chemical analysis to perform diagnostic procedures involved in territorial organization of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance).

3. The isolation segment of the population, are in need of treatment and prevention measures of medical and preventive technologies.

4. The determination of the shape, material resources and the timing of the treatment and preventive measures of medical and preventive technologies.

5. Carrying out preventive and curative action.

Stage III – to evaluate the clinical and cost effectiveness of implemented preventive medical technology risk management of health problems associated with exposure to risk factors.

1. The assessment of individual and group clinical efficacy carried out by experts of the territorial / departmental institutions of practical healthcare criteria for medical and preventive technologies.

2. The evaluation of the clinical efficacy population technologies carried out by experts of territorial bodies and organizations of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance (item 2.10.11);

3. Economic evaluation techniques carried out by the experts of territorial bodies and organizations of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance (item 2.10.11).

The place of medical-preventive technology in the operative and strategic public health risk management.

The strategic management of risks to human health associated with exposure to environmental factors, large-scale introduction of specialized medical and preventive technologies in the provision of specialized preventive care areas for sanitary trouble habitat is a self-pronged strategy of making management (regulatory) decisions. The strategic decision to the need to implement a system to provide specialized preventive care through health-care technologies of risk management adopted by territorial bodies of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance. Strategic decision-making requires the formulation of goals and objectives of the activities of specialized preventive care, specifying outcomes, scheduling of the practical implementation of measures to identify the mechanisms of interaction of territorial organizations and institutions of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance practical health care, energy, and resources for the functioning of the whole system, etc.

Operational risk management is carried out jointly by the Federal Service on Customers' Rights Protection and Human Well-being Surveillance territorial organizations and institutions of practical public health and is a dynamic establishment of the list of the most significant in terms of risk factors and characteristics of habitat, vulnerable or labor groups, qualitative and quantitative characteristics of epidemiological patterns of risk-associated pathology (territorial organization of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance), the choice of a particular technology, target groups, the material basis of the implementation of the technology, the establishment of the multiplicity of its implementation, the implementation of therapeutic and preventive measures, etc. (institutions of practical public health) (Fig. 3.32).

Thus, a well-defined area of application (health programs, prevention programs focus group, individual treatment programs or prevention), the purpose (prevention of the formation of risk-associated diseases, treatment and prevention of the progression of risk-associated disease), characteristic of the target group, the list of diagnostic and therapeutic – preventive events allow us to determine the specific location of medical and preventive technologies in strategic and operational management of risks to public health. Technologies aimed at preventing the development of a risk-associated diseases (group A, B, C) provide a practical solution to reduce the overall strategic objectives of morbidity and prevent the growth of certain classes of diseases, while technologies aimed at treatment and prevention of the progression of risk-associated (group D) disease – reducing morbidity and mortality. The whole system of rendering specialized medical and preventive care to manage the risk of health problems associated with exposure to environmental factors, provides strategic issues to improve the quality and length of life of the population, reduction of mortality and disability.

In order to improve strategic approaches FBSI "Federal scientific center for medical and preventive health risk management technologies" justified and put into practice hygienic assessment of 90 criteria for molecular genetic (genes cytochrome-450 genes metabolism of organic and inorganic substances, proliferative and metabolic genes processes, etc.), immunogenetic (genes transcription and immuno reception), cytogenetic (markers of destructive and proliferative processes), proteomics (haptoglobin, transferritin, apolipoprotein A1, etc.), biochemical (markers of bone metabolism disorders, the state of the glutathione system, bone marrow blood, liver detoxification function, neuroendocrine-humoral regulation, intra- and extracellular markers of oxidative stress and the state of energy processes), reflecting pathomorphosis risk-associated diseases. Recommended safe levels of exposure in the blood markers (manganese, nickel, chromium, benzene, formaldehyde, phenol, vanadium, methanol). Developed and implemented diagnostic test systems for monitoring 15 indicators of the respiratory system with screening and in-depth studies (identification of specific immunoglobulins to formaldehyde, chromium, nickel, manganese, vanadium, lead, strontium, benzene, phenol, formaldehyde, and others.). Offered more than 35 medical and preventive technologies, 5 standards and protocols preventing disease associated with exposure to chemical factors, including: "Medico-prevention technologies prevent the development of uncontrolled forms of asthma caused by exposure to airborne aerosols metals (manganese, vanadium)", "Technology preventing the risk-associated respiratory diseases (manganese and its compounds)", "Technology preventing the risk-associated respiratory diseases (formaldehyde) ", "Preventive medical technologies for prevention of chronic bronchitis in the population living under the impact of fine dust", "Technology-related risk prevention of respiratory diseases in children living in the zone of influence of the industrial enterprises of metallurgical profile (manganese)", "Preventive medical technology prevent the development of risk-associated asthma in patients with recurrent obstructive bronchitis (manganese, chromium, formaldehyde)", "Medical preventive technology dispensary observation of the population with the risk associated with bronchial asthma (social factors, manganese, chromium)", "Technology prevention of risk associated rhinosinusitis (formaldehyde, manganese)", "Standard of prevention of secondary immunodeficiency diseases in populations living in areas with poor quality of drinking water for chemical indicators", "Technology prevention risk-associated diseases of the immune system and respiratory (aromatic hydrocarbons) for healthcare institutions offering wellness

and preventive care", "Clinical supervision for children from the group of chronically ill living in the inhalation exposure of chemicals", "Preventive medical technology improvement of children living in conditions of air pollution aromatic hydrocarbon-based camps summer holiday", "Technology prevention in children risk-associated autonomic dysfunction (lead, manganese)", "Technology prevention in children risk-associated cognitive impairment (lead, manganese)", "Technology prevention of chronic gastroduodenitic population living in areas with poor quality of drinking water for chemical indicators", "Preventive medical assistance to populations consuming drinking water with residual amounts of products hyperchlorination", "Technology secondary prevention of risk-associated chronic gastroduodenitis (manganese, nickel)", " Technology secondary prevention of risk-associated hepatobiliary dysfunction (phenol, formaldehyde, methanol)", "Prevention of risk associated chronic glomerular and tubulointerstitial kidney disease in children with minimal urinary syndrome (cadmium, lead, chromium and phenol)", "Standard of specialized health -prventive aid to the population risk associated with endemic goiter (manganese, chromium, nickel, vanadium)", "Technology prevention of risk associated hypothyroidism in patients with a minimum size of the thyroid gland (natural iodine-deficiency, manganese, chromium, nickel)", "Technology risk of treatment-associated atopic dermatitis (chromium, manganese)", "Technology of treatment-associated risk of atopic dermatitis (benzene, toluene)" and others.

In the territories of the Russian Federation (Perm, Orenburg region, Kirov region, the Republic of Tatarstan, Moscow, St. Petersburg, Vladivostok, Yuzhno-Sakhalinsk, and others.) the clinical efficacy of the developed health-care technologies was confirmed. The cost-effectiveness of preventive activities was about 1,6–6,5 rubles. / Rub. cost per patient.

As an example, preventive medical technology to prevent the occurrence and progression of allergic respiratory diseases associated with the inhalation of chemical exposure of environmental factors with the sensitizing mechanism of action.

3.6.3. The medical-preventive technologies of prevention of the incidence and progression of allergic respiratory diseases associated with the aerogenic exposure of chemical factors with the sensitizing mechanism of action

The pathogenetic mechanisms of allergic respiratory diseases associated with metal allergens and/or aldehydes exposure

The chronic aerogenic exposure of metal allergens (*manganese, chromium, nickel)* and/or aldehydes *(formaldehyde),* in concentrations exceeding the hygienic standards of ambient air quality,causes the progression of cytotoxic effect at the level of the epithelium of the mucous membranes of the respiratory system associated with activation of peroxidation processes of cell membranes bilipid layer. The oxidative degradation of the membranes is accompanied by changes in their membrane potential, transport properties, permeability, imbalance of intracellular element that initiates the destabilization of intracellular oxidative phosphorylation processes, inhibition of ATP synthesis, blockade of ATPase and NADP-oxidoreductase, inhibition of respiratory enzymes of epithelial cells mitochondrial apparatus. Damage to the receptor apparatus of the cell contributes to a disorder of its biocommunication and functional activity, reduces the possibility of regulatory self-regeneration of the respiratory tract epithelium.

The development of immunopathological reactions cascade – the basis of allergic respiratory diseases, which increases their expressed systemic immunotoxic action is a consequence of the cytotoxic action of manganese, chromium, nickel and formaldehyde. Reduce T-dependent humoral immune response, more than twofold inhibit production by alveolar macrophage factors, which inhibits leukocyte migration, increase the activity of B-lymphocytes, interleukins and natural killers, reduce the absolute content and functional activity of phagocytes, thereby maintain high activity of phlogistic and allergic reactions of immediate and delayed types. At the same time metals reduce immunological resistance to viral and bacterial respiratory infections.

Metal ions are haptens and in conjunction with proteins alter their conformation and achieve adequate molecular weight for the progression of adaptive immune responses. Antibodies are produced to the antigenic determinants of the whole complex "hapten-carrier", that promotes the progression of delayed allergic reactions. Furthermore, as a low molecular weight antigens, metals potentiate the progression of autoimmune processes in the bronchial mucosa.

The general resorptive effect of metal allergens and formaldehyde is accompanied by changes in the functional state of the autonomic nervous system with a predominance of vagotonic variant of baseline autonomic tone and asympathetic tonic variant of reactivity on the background of cholinergic reactions domination. In addition, high level of activity of cholinergic reactions caused by metal allergens and formaldehyde, is supported by impaired synthesis of acetylcholinesterase, which enhances the severity of local immunopathological reactions, hypersecretion and bronchospasm processes.

There are established cause-and-effect relationships between the frequency of allergic respiratory diseases, dysfunction of external respiration and ventilatory lung capacity (PEF and FEV1 reduction) process of sensitization (increase of eosinophils in nasal secretions, reduction of secretory IgA, increase of total and specific IgE to chromium, manganese, nickel, formaldehyde), disorders of the immune response (reduction of phagocytic activity of leukocytes, CD4+i pools, level of *γ*-interferon against increase in $CD8^+$, $CD19^+$-lymphocytes, IL-4, IL-6, IL-10, leukotrienes), disbalance of oxidative and anti-oxidative process (increase/reduction of antioxidant activity, increase of the level of malondialdehyde, lipid hydroperoxides, superoxide dismutase), disorders of the enzymatic activity of hepatocytes (reduction of the activity of glutathione peroxidase, increase of the activity of aspartate aminotransferase and alanine aminotransferase), markers of imbalance of intracellular energy supply (increase of cyclic adenosine monophosphate, reduction of cyclic guanosine monophosphate), content of neurotransmitters (glutamate increase, γ-aminobutyric acid reduction) with increased content of metal allergens (manganese, chromium, nickel) and aldehydes (formaldehyde) in the blood.

In the conditions of stable ambient air contamination by metal allergens and aldehydes, the level of their content in the blood of the population greatly exceeds the reference limits. The presence of a genetic predisposition to metals and formaldehyde metabolic imbalance (pathological alleles of CPOX, CYP1A1, SULTIA1 gene polymorphism) is an additional risk factor for increased content of chemical compounds in vivo. Set of immune, pathochemical and pathophysiological reactions induced by long aerogenic impact of metal allergens and aldehydes is an additional link of initialization of immunopathological reactions that form the basis of the progression of allergic respiratory diseases, potentiates the processes of genetic atopy implementation, reduces the efficacy of natural resistance factors (Table 3.15).

The general resorptive effect of chemical compounds is accompanied by the development of autonomic dysfunctions, endocrine dysregulation, transient immunosuppression and hepato-cellular disorders that form the basis of pathomorphism of allergic respiratory diseases.

Table 3.15

Factors, which have an effect on the incidence and progression of allergic respiratory diseases associated with the aerogenic exposure of chemical factors with the sensitizing mechanism of action

Factors	Description
1. Internal	1. Genetic predisposition to atopy and bronchial hyperresponsiveness (presence of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)
	2. Genetic predisposition to metals, formaldehyde metabolism disorders (pathological alleles CPOX, CYP1A1, polymorphism of SULTIA1 gene)
	3. Gender (in childhood boys suffer from a disease more often)
	4. Adiposity
2. Living environment	Chemicals with sensibilizing actions in ambient air: formaldehyde, chromium, nickel, manganese, zinc, beryllium, cobalt, titanium; In housing air – formaldehyde

The clinical manifestation of allergic respiratory diseases associated with exposure to metal allergens and aldehydes, is characterized not only by the earlier formation of the pathological process and the severity of clinical manifestations from the respiratory organs and the development of atopic dermatitis, biliary dysfunction, syndrome of autonomic disturbances and psycho-emotional and psychomotor status disorders of the patient, which requires the development of new approaches to prevention and therapy.

The *purposes* of medical-preventive technologies:

1. The prevention of bronchial asthma progression in patients with acute and chronic respiratory diseases (chronic bronchitis with obstructive syndrome (J44.8), allergic rhinitis (J30.3), recurrent simple bronchitis (J20.9), and combinations thereof).

2. The prevention of the progression of bronchial asthma associated with impact of metal allergens (manganese, chromium, and nickel) and/or aldehydes (formaldehyde) (J45.9), prevention of formation of uncontrolled forms of disease, complications (lung tissue atelectasis – J98.1, pneumofibrosis – J84.9).

The target groups of patients:

1) patients with bronchial asthma, associated with the impact of metal allergens (manganese, chromium, and nickel) and/or aldehydes (formaldehyde) (J45.9);

2) patients with chronic bronchitis with obstructive syndrome (J44.8) and allergic rhinitis (J30.3), associated with impact of metal allergens (manganese, chromium, nickel) and/or aldehydes (formaldehyde).

3) patients with allergic rhinitis (J30.3), associated with impact of metal allergens (manganese, chromium, and nickel) and/or aldehydes (formaldehyde);

4) patients with recurrent simple bronchitis (J20.9), living in the conditions of ambient air contamination by metal allergens (manganese, chromium, nickel) and/or aldehydes (formaldehyde).

Nosologic form

1. Bronchial asthma associated with theimpact of metal allergens (manganese, chromium, nickel) and/or aldehydes (formaldehyde) (ICD-10 code – J45.9 Unspecified asthma).

Definition

Bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel) and/or aldehydes (formaldehyde) – is a chronic, progressive allergic bronchitis with the progression of their hyperreactivity and persistent bronchoconstriction, clinically manifested by recurring attacks of expiratory dyspnea.

The classification of bronchial asthma

1) by severity: mild intermittent, mild persistent, moderate persistent and severe persistent;

2) by the periods of the disease: exacerbation and remission.

The complications of bronchial asthma

the atelectasis of the lungs, mediastinal and subcutaneous emphysema, spontaneous pneumothorax.

The medical-preventive technologies of the prevention of the development and progression of risk-associated bronchial asthma in patients living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

The medical-preventive technology of prevention of the development of risk-associated bronchial asthma in patients with recurrent acute bronchitis (J20.9), living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

The technology of group A:

1) pathogenetic orientation is an increase of the functional activity of homeostasis adaptation and balance systems, given the low potential risk of harm to the health;

2) clinical orientation is deconditioning syndrome, manifesting by recurrent acute bronchitis and impaired functional state of organs and systems of transient nature;

3) scope – health-improving programs;
4) the form of realization – organized groups;
5) the frequency of application – annually, biannually;
6) implementation base – the children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities.

Table 3.16

Diagnostic criteria for the moderate risk of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel), in patients with repeated acute bronchitis (J20.9)

Criteria	Criteria characteristic
Hygienic	1. Poor ambient air quality in content of manganese and/or chromium, nickel in the territory of residence of the patient. 2. The presence of a moderate risk of respiratory diseases caused by inhalation effects of chromium and/or manganese, nickel. 3. Fixed higher level of acute bronchitis morbidity in the territory of residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recurrent nature of the course, lack of disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence of the patient. 2. The occurrence of the disease after acute respiratory viral infections, hypothermia. 3. Cough with little expectoration, subfebrile temperature; duration of episodes of disease recrudescence – about 2 weeks. 4. The absence of episodes of bronchial obstruction. 5. During the recrudescence – an abundance of dry rale, harsh breathing, in remission – harsh breathing, singular dry rale. 6. The absence of atopic dermatitis. 7. The absence of lymphadenopathy, hypertrophy of palatine tonsils and adenoids of II–III degree. 8. Development of moderate intoxication syndrome during disease recurrence. 9. The efficacy of basic therapy
Functional	1. Minor restrictive respiratory disorders in the period of the disease; absence of respiratory disorders during remission (at spirography). 2. The normal speed of the airflow and transnasal resistance during disease recrudescence (at rhinomanometry). 3. The eitonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography)
Laboratory	1. The levels of chromium and/or manganese, nickel in the blood up to 1.5 RL. 2. Clinical blood analysis: leukocytosis with neutrophilic shift, accelerated ESR, physiological level of hemoglobin. 3. Biochemical blood analysis: physiological level of serum ferrum, total and unsaturated Fe-binding potency of the blood; increase of the level of malondialdehyde, increase/reduction of antioxidant activity. 4. Immune blood analysis: physiological level of specific IgE to manganese, chromium, nickel; increase of the absolute content and functional activity of phagocytes; a slight reduction of $CD4^+$-lymphocytes, secretory IgA; moderate increase of $CD8^+$, $CD19^+$-lymphocytes; moderate increase of interleukins IL-4, IL-10 lipid hydroperoxides. 5. EIA physiological level of cortisol, glutamate, serotonin, γ-aminobutyric acid. 6. The absence of pathological alleles CPOX, CYP1A1

Table 3.17

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of simple acute bronchitis. 2. The association of the disease incidence with acute respiratory viral infections, hypothermia. 3. The diagnostics of atopic dermatitis, allergic rhinitis, astenoneurotic or neurosis syndrome, signs of variable immunodeficiency. 4. The assessment of the level of cognitive functions activity. 5. The assessment of the efficacy of basic therapy
2	Spirography	The assessment of the state of external respiration in terms of FEV1 and PEF in the period of disease recrudescence and remission
3	Rhinomanometry	The assessment of the state of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence
4	Cardio-intervalography	The assessment of initial autonomic tone and autonomic reactivity during stress tests
5	Chemico-analytical blood test	The analysis of chromium and/or manganese, nickel content
6	General blood analysis	The analysis of the number of leukocytes, leukogram state, ESR, hemoglobin content
7	Biochemical blood analysis	The analysis of serum ferrum, total and unsaturated Fe-binding potency of the blood, malondialdehyde, state of antioxidant activity, lipid hydroperoxide
8	Immunological blood analysis	The analysis of the content of specific IgE to manganese, chromium, nickel; $CD4^+$, $CD8^+$, $CD19^+$- lymphocytes, secretory IgA, absolute content and functional activity of phagocytes
9	Genetic typing	The identification of pathological alleles CPOX, CYP1A1

The level of criteria evidence

Clinic criteria

The clinical signs of recurrent acute simple bronchitis, the development of the disease on the background of acute respiratory diseases, hypothermia; lack of the disease association with the deterioration of ambient air quality in content of metal allergens; absence of atopic dermatitis, astenoneurotic or neurosis syndrome with a predominance of symptoms of parasympathetic nature, physiological level of cognitive functions activity, the efficacy of basic therapy – *Level of evidence A.*

Frequent acute respiratory diseases, moderate intoxication during disease recurrence, the absence of lymphadenopathy, the hypertrophy of palatine tonsils and adenoids of II-III degree – *Level of evidence B*.

Functional criteria

Minor restrictive respiratory disorders during recrudescence and lack thereof in remission; eitonic type of initial autonomic tone with hypersimphatical-tonic autonomic reactivity – *Level of evidence A*.

Laboratory criteria

The content of manganese, chromium, nickel in blood at the level up to 1,5 RL; leukocytosis with neutrophilic shift, accelerated ESR, physiological level of hemoglobin, serum ferrum, total and unsaturated Fe-binding potency of the blood; physiological level of specific IgE to manganese, chromium, nickel; a slight reduction of $CD4^+$-lymphocytes; a moderate increase of $CD8^+$, $CD19^+$-lymphocytes, absolute content and functional activity of phagocytes; elevated levels of interleukins IL-4, IL-10, lipid hydroperoxides; absence of pathological alleles CPOX, CYP1A1 – *Level of evidence A*.

The increase of secretory IgA, the increase of malondialdehyde, the increase/reduction of antioxidant activity – *Level of evidence B*.

Table 3.18

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	The enzyme immunoassay of the blood	The analysis of cortisol, glutamate, serotonin, γ-aminobutyric acid.
2	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Laboratory criteria

Th physiological level of cortisol, glutamate, serotonin, γ-aminobutyric acid – *Level of evidence A.*

The absence of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes with a predominance of symptoms of parasympathetic nature, reduction of the activity of cognitive functions, features of variable immunodeficiency, frequent acute respiratory diseases, sensitivity/resistance to basic therapy are diagnosed in patients with clinical signs of recurrent simple bronchitis, living in conditions of ambient air contamination by metal allergens (*manganese and/or chromium, nickel*) during *clinical research*.

The chemicoanalytical analysis of the blood is performed in patients with recurrent simple bronchitis, symptoms of intoxication during disease recurrence, asthenic syndrome and efficacy of basic therapy for the determination of manganese, chromium, nickel content.

Functional analysis (spirography, rhinomanometry, cardiointervalography) and a *complex of laboratory diagnostics* (general, biochemical, immunological blood analysis, genetic typing) are conducted at determination of manganese and/or chromium, nickel in the blood at the level of up to 1.5 RL.

Medical and preventive measures shall be performed when the results obtained correspond to 80% and more criteria of recurrent simple bronchitis (J20.9).

An additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to at least *80%* of the criteria of recurrent simple bronchitis (J20.9) diagnosis.

Medical and preventive measures shall be performed when the results of additional diagnostic measures correspond to *80%* or more criteria of recurrent simple bronchitis (J20.9).

Medical and preventive measures in patients with recurrent simple bronchitis (J20.9) and content of metals, allergens (manganese, chromium, nickel) in blood at the level of up to 1.5 RL are based on standard approaches for the prevention of broncho-pulmonary diseases in children. Combined use of pharmacopoeial drugs, physiotherapy, climatic factors, diets aimed at prevention of asthma (J45.9), associated with impact of metal allergens in these patients (J20.9), allows us to stop the processes of non-specific bronchitis, improve the immunoresistance of the patient's body, prevent the progression of the process (Table 3.19).

The form and timing of technology

The technology of prevention of risk-associated bronchial asthma in patients with recurrent simple bronchitis (J20.9) and content of metal allergens (manganese, chromium, nickel) in the blood at the level of up to 1.5 RL is designed for implementation on the basis of children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities.

Table 3.19

The pathogenetic orientation of the medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in patients with recurrent simple bronchitis (J20.9) and elevated levels of metal allergens (manganese, chromium, nickel) in the blood

Ser. No.	Pathogenetic link	The orientation of exposure	The type of exposure
1	The elevated levels of manganese and/or chromium, nickel in the blood (up to 1.5 RL)	Reduced to 1 RL	The activation of natural elimination mechanisms
2	The disorder of nasal muco-ciliary clearance transport	An increase of functional activity of ciliated epithelium, restoration of muco-ciliary clearance transport	The stimulants of motor function of the respiratory tract. Physiotherapy measures
3	Inflammatory process	Inflammatory reactions depression	Antibiotics. Antiphlogistic
4	The reduction of the activity of natural resistance mechanisms	The increased activity of nonspecific and specific resistance factors	Physiotherapeutic procedures. General tonic preparations, adaptogens
5	The development of asthenoneurotic or neurosis-like syndromes with a predominance of parasympathetic symptoms character, the reduction of cognitive functions activity	The improvement of the blood circulation and oxygenation of brain tissues, delay of lipid peroxidation, protection of neuronal and mitochondria membrane from damage	Physiotherapeutic procedures. Nnootropics

The treatment and preventive measures of medical-preventive technology are implemented annually or biannually.

The total duration of the course – 21 days (Table 3.20).

Table 3.20

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	Drugs of choice	Duration of use
Drugs with mucolytic, expectorative action ATX: R05CB10	Ascoril expectorant	from the 1-st to the 14-th day
Stimulants of motor function of the respiratory tract, ATX: R05CB06	Bronchobos	from the 11-st to the 11-th day
Immunostimulants ATX: L03AX	Bronchomunal	from the 10-st to the 18-th day
Multivitamin Complex, ATC: A11BA.	Jungle	from the 1-st to the 21-th day
Antimicrobials ATX: J01FA10; ATX: J01GB06; J01BA02	Thiamphenicol glycinate atsetiltsisteinat	In the period of the disease (for the main indications)
Nootropics, general tonic preparations. N06BX13, A13A	Noben Stimol	During 3 weeks (adults); from the 1-st to the 14-th day
Physiotherapy methods		
Electrophoresis with potassium iodide to the root zone of the lung		7–8 times
Electroaerosol therapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day
Massage		from the 1-st to the 21-th day

Individual contraindications for treatment and prevention: inconformity to clinical criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the treatment and prevention; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

The medical-preventive technology of the prevention of the development of risk-associated bronchial asthma in patients with allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

The technology of group B:

1) pathogenetic orientation is an increase of functional upper airway resistance to the effects of living environment risk factors, restoration of functional activity of homeostasis adaptation and sustention systems with regard to the average level of the potential risk of health harm;

2) clinical orientation is chronic allergic rhinitis with transient sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target prevention programs;

4) the form of realization – organized groups, individual preventive measures;

5) the frequency of application – biannually;

6) implementation base – children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities, day hospitals.

Table 3.21

The diagnostic criteria of high risk of the development of bronchial asthma associated with impact of metal allergens (magnesium, chrome, nickel) in patients with allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

Criteria	Criteria characteristic
1	2
Hygienic	1. Poor ambient air quality in content of manganese and/or chromium, nickel in the territory of residence. 2. The presence of a high risk of respiratory diseases caused by inhalation effects of chromium and/or manganese, nickel. 3. Higher level of allergic rhinitis morbidity in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recrudescent nature of the course, disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence. 2. Rheum and nasal congestion, sneezing attacks. 3. The duration of episodes of disease recrudescence – from several days to several months. 4. Allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media. 5. Atopic dermatitis 6. Lymphadenopathy, hypertrophy of palatine tonsils and adenoids of II-III degree. 7. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 8. Chronic intoxication. 9. Asthenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 10. The cognitive functions activity reduction. 11. Resistance to basic therapy
Functional	1. The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, retention of reduced indicators of airflow and transnasal resistance (at rhinomanometry) during remission. 2. Negative functional tests with decongestants (at rhinomanometry). 3. Vagotonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography)

End of table 3.21

1	2
Laboratory	1. The levels of chromium and/or manganese, nickel in the blood up to 1.5–2.0 RL. 2. General blood analysis: leukopenia with limphomonocytic shift, reduction of hemoglobin; increase in eosinophil-lymphocytic index. 3. Rhinocytogram Increase of the content of eosinophils, neutrophils in nasal secretions, eosinophils index. 4. Biochemical blood analysis: increased level of malondialdehyde, lipid hydroperoxides, superoxide dismutase, decreased serum ferrum, increase/reduction of antioxidant activity. 5. Immune blood analysis: increase of specific IgE to manganese, chromium, nickel; reduction of the functional activity of phagocytes, gamma-interferon, total and serum IgA, $CD4^+$; increased $CD8^+$, $CD19^+$-lymphocytes. 6. EIA increase of the levels of cortisol, interleukin IL-4, IL-10, glutamates, cyclic adenosine monophosphate; reduction of cyclic guanosine monophosphate. 7. Genetic typing: presence of pathological alleles CPOX, CYP1A1

Table 3.22

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of allergic rhinitis. 2. Disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence. 3. Determination of the recurrence duration. 4. The diagnostics of chronic intoxication symptoms. 5. The diagnostics of clinical signs of secondary transient immunodeficiency. 6. The diagnostics of allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media. 7. The diagnostics of atopic dermatitis. 8. The diagnostics of astenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 9. The assessment of the level of cognitive functions activity. 10. The assessment of the efficacy of basic therapy
2	Rhinomanometry	1. The investigation of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional tests with decongestants
3	Cardio-intervalography	The investigation of initial autonomic tone, assessment of autonomic reactivity during stress tests
4	Chemico-analytical analysis of the blood	The investigation of chromium and/or manganese, nickel content in the blood
5	Rhinocytogram	The investigation of the content of eosinophils, neutrophils in nasal secretions, eosinophils index assessment
6	General blood analysis	The investigation of the number of leukocytes, leukocyte status, hemoglobin level, eosinophilic lymphocyte index assessment
7	Biochemical blood analysis	The investigation of malondialdehyde level, antioxidant activity state, lipid hydroperoxides, serum ferrum, superoxide dismutase
8	Immune blood analysis	The analysis of the content of specific IgE to manganese, chromium, nickel; cortisol, $CD4^+$, $CD8^+$, $CD19^+$- lymphocytes, secretory IgA, IL-4, IL-10 interleukins, functional activity of phagocytes
9	Genetic typing	The identification of pathological alleles CPOX, CYP1A1

The level of criteria evidence

Clinic criteria

The clinical signs of allergic rhinitis; disease recrudescence associated with the worsening of ambient air quality in content of metal allergens in the territory of residence; long-term (up to several months) recurrence duration; allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media, atopic dermatitis; asthenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms, reduction of the activity of cognitive functions, resistance to basic therapy – *Level of evidence B*.

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication, clinical signs of variable immunodeficiency – *Level of evidence C.*

Functional criteria

The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, negative functional tests with decongestants, vagotonic type of initial vegetative tone with hypersimphatic-tonic autonomic reactivity variant – *Level of evidence B*.

Laboratory criteria

The elevated levels of manganese, chromium, nickel in the blood; leukopenia with limphomonocytic shift, reduction of hemoglobin; increase in eosinophil-lymphocytic index, content of specific IgE to manganese, chromium, nickel, cortisol; reduction of the functional activity of phagocytes, $CD4^+$-lymphocytes, serum ferrum; increase of lipid hydroperoxides, superoxide dismutase, content of $CD8^+$, $CD19^+$-lymphocytes, interleukins IL-4, IL-10; pathological alleles CPOX, CYP1A1 – *Level of evidence A*.

The reduction of secretory IgA, increase of malondialdehyde, increase/reduction of antioxidant activity – *Level of evidence B*.

Table 3.23

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Rhinomanometry	The investigation of the functional state of nasal breathing in terms of airflow and transnasal resistance during remission
2	Rhinocytogram	The investigation of the level of eosinophils, neutrophils in nasal secretions, eosinophilia index assessment
3	Enzyme immunoassay of the blood	The investigation of the content of glutamates, cyclic adenosine monophosphate, cyclic guanosine monophosphate.
4	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Functional criteria

The saving of moderate reduced indicators of airflow and high transnasal resistance during remission – *Level of evidence B*.

Laboratory criteria

The increase of glutamates, cyclic adenosine monophosphate; reduction of cyclic guanosine monophosphate – *Level of evidence A*.

The increase of the content of eosinophils in the nasal secretions, increase of eosinophilic and lymphocytic index, identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media, atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes with a predominance of symptoms of parasympathetic nature, reduction of the activity of cognitive functions, features of variable immunodeficiency, resistance/sensitivity to basic therapy are diagnosed in patients with clinical signs of allergic

rhinitis, living in conditions of ambient air contamination by metal allergens (*manganese and/or chromium, nickel*) during *clinical research*.

The chemicoanalytical analysis of the blood is performed in patients with allergic rhinitis in combination with allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media, atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes of parasympathetic nature, reduction of the activity of cognitive functions, features of variable immunodeficiency and resistance to basic therapy for the determination of manganese, chromium, nickel content.

Functional analysis (rhinomanometry, functional test with decongestants, cardiointervalography) and a *complex of laboratory diagnostics* (general, biochemical, immunological blood analysis, genetic typing) are conducted at determination of high concentration of manganese and/or chromium, nickel in the blood (1.5–2.0 RL).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria for the diagnostics of allergic rhinitis associated with impact of metal allergens (manganese and/or chromium, nickel).

Additional differential diagnostics with allergic rhinitis (J30.2 Other seasonal allergic rhinitis) shall be performed upon receipt of the results of primary diagnostic measures corresponding to *no less than 50 %* of criteria for the diagnostics of allergic rhinitis associated with impact of metal allergens (manganese and/or chromium, nickel).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel).

The medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in children with allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel) was developed based on the existing approaches to the prevention of upper respiratory airways allergic diseases, standards and protocols with regard to the features of disease processes associated with impact of manganese, chromium and nickel. Medical and preventive measures of technology serve to prevention of disease progression and development of bronchial asthma associated with impact of metal allergens.

The joint action of used pharmacopoeial preparations and physiotherapeutic methods is directed to the main pathogenetic links of the pathologic processes induced by the impact of manganese, chromium, and nickel (immunopathological and cytotoxic responses) that prevents/interrupts the progression of the pathological process.

The form and timing of technology

The technology of risk-associated bronchial asthma in patients with rallergic rhinitis and high concentration of metal allergens (manganese, chromium, nickel) in the blood (≥1,5 RL) is designed for implementation on the basis of children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities, day hospitals.

At chemicals concentration in the blood at the level of 1.5–2.0 RL – medical and preventive measures shall be carried out annually, at a higher level – biannually. The total duration of the course – 14 days.

Individual contraindications for technology: inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

The combined use of pharmacopoeial drugs with systemic and local action and physiotherapy is accompanied by an elimination effect, suppresses immunoallergic inflammatory, restores motor and secretory function of the nasal epithelium, enhances the natural immune resistance and normalizes the patient's autonomic homeostasis.

Table 3.24

The pathogenetic orientation of medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in patients with allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel)

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	The elevated levels of manganese and/or chromium, nickel in the blood (1.5–2.0 RL)	Reduced to 1 RL	The activation of natural elimination mechanisms
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The depression of immunopathological reactions, immune inflammation, reduction of vessel wall permeability, inhibition of mucosa hyperresponsiveness, restoration of damaged epithelium	Local action glucocorticosteroids. Immunomodifiers. Mucolytics Physiotherapeutic procedures
3	The activation of free radical oxidation, depletion of antioxidant protection	The restoration of oxidative-anti-oxidative process homeostasis	Antihipoxants and antioxidants
4	Parasympathetic functional disorders of the central and autonomic nervous system	The restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens

Table 3.25

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
GC for intranasal use ATX: R01AD08	Flixonase	from the 1-st to the 5-th day
Drugs with mucolytic, secretomotor and anti-inflammatory action. ATX: R07AX	Sinupret	from the 7-st to the 14-th day
Antihistamines for systemic administration. ATX: R06AX	Aerius	from the 1-st to the 14-th day
Immunostimulants ATX: L03AX	Polyoxidonium	from the 7-st to the 14-th day
Drugs that improve metabolism and energy supply of tissues. ATX: A16AA01, N07XX	Elcar (children) Cytoflavin (adults)	from the 7-st to the 14-th day from the 7-st to the 14-th day
Multivitamin Complex, ATC: A11BA	Jungle	from the 1-st to the 21-th day
Physiotherapy methods		
Variable magnetic field on paranasal sinus		7–8 times
Electroaerosol therapy		7–8 times
Speleotherapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 14-th day
Electrical sleep		from the 1-st to the 14-th day

The medical-preventive technology of the prevention of the development of risk-associated bronchial asthma in patients with chronic obstructive bronchitis (J44.8) and allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

The technology of group C:

1) pathogenetic orientation is a restoration of respiratory organs morphofunctional resistance to the effects of living environment risk factors, increase of functional activity of homeostasis adaptation and sustention systems with regard to the high level of the potential risk of health harm;

2) clinical orientation is chronic obstructive bronchitis (J44.8) and allergic rhinitis against the background of persistent sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target treatment and prevention programmes;

4) the form of realization – individual, group;

5) the frequency of application – biannually, triannually;

6) implementation base – day hospital, hour stay hospitals or outpatient care health facilities.

Table 3.26

The diagnostic criteria of very high risk of the development of bronchial asthma associated with impact of metal allergens (magnesium, chrome, nickel) in patients with chronic obstructive bronchitis (J44.8) and allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

Criteria	Criteria characteristic
1	2
Hygienic	1. Poor ambient air quality in content of manganese and/or chromium, nickel in the territory of residence. 2. The presence of a very high risk of respiratory diseases caused by inhalation intake of chromium and/or manganese, nickel. 3. The higher level of chronic bronchitis and allergic rhinitis morbidity in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recrudescent nature of the course, disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence. 2. Inefficient cough, worsening in the evening and at night, after physical and psycho-emotional stress; the duration of the episodes of disease recrudescence – more than 2 weeks. 3. Wheezing episodes. 4. The abundance of different dry and moist rales, elongated breath in the period of recrudescence; individual dry scattered rales in the period of remission. 5. Profuse rheum and nasal congestion, sneezing attacks with a duration of 2–3 weeks to several months. 6. The allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media. 7. Atopic dermatitis 8. Lymphadenopathy, hypertrophy of palatine tonsils and adenoids of II-III degree. 9. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 10. Chronic intoxication symptoms. 11. Asthenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 12. The cognitive functions activity reduction. 13. Resistance to basic therapy

Continuation of Table 3.26

1	2
Functional	1. The presence of restrictive, occasionally obstructive breathing disorders during disease recrudescence; retention of restrictive disorders in remission period (at spirography). 2. The reduction of air flow rate and significant increase of transnasal resistance during the disease recrudescence, retention of reduced indicators of airflow and transnasal resistance (at rhinomanometry) during remission. 3. Positive tests with bronchodilators during the recrudescence (at spirography). 4. Negative functional tests with decongestants during the recrudescence (at rhinomanometry). 5. The vagotonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography)
Laboratory	1. The levels of chromium and/or manganese, nickel in the blood ≥ 2RL. 2. General blood analysis: moderate leukopenia with limphomonocytic shift, decreased hemoglobin. 3. Biochemical blood analysis: Reduction of serum ferrum, increase of total and unsaturated Fe-binding potency of the blood; increase of the level of malondialdehyde, lipid hydroperoxides, glutathione peroxidase, superoxide dismutase, increase/reduction of antioxidant activity. 4. Immune blood analysis: increase of specific IgE to manganese, chromium, nickel; reduction of the functional activity of phagocytes, moderate reduction of $CD4^+$-liphocytes, serum IgA,; increase of $CD8^+$, $CD19^+$-lymphocytes. 5. EIA moderate increase of cortisol, glutamate, content of interleukins IL-4, IL-6, IL1-0, cyclic adenosine monophosphate; reduction of γ-interferon, γ-aminobutyric acid, cyclic guanosine monophosphate. 6. Genetic typing: presence of pathological alleles CPOX, CYP1A1

The level of criteria evidence

Clinic criteria

The combination of chronic bronchitis with obstructive syndrome and allergic rhinitis; recurrence of disease against the deterioration of ambient air quality in content of metal allergens; long (more than 2 weeks), inefficient cough, worsening in the evening and at night, after physical and psycho-emotional stress; nasal congestion, constant rheum, sneezing attacks (from 2–3 weeks to several months, atopic dermatitis, allergic diseases of the pharynx, larynx, nasal polyposis, maxilloethmoidal sinusitis, otitis media; asthenoneurotic or neurotic syndrome with a predominance of parasympathetic nature of symptoms, depression of cognitive functions, resistance to basic therapy – *Level of evidence B*.

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication, clinical signs of variable immunodeficiency – *Level of evidence C.*

Functional criteria

Restrictive respiratory impairment in the period of disease remission; reduction of air flow rate, negative functional tests with decongestants and increase of transnasal resistance during the recrudescence; vagotonic type of initial autonomic tone with hypersymphatic-tonic autonomic reactivity variant – *Level of evidence A*.

The reduction of spirography by restrictive and obstructive type, positive tests with bronchodilators during the disease recrudescence – *Level of evidence B*.

Laboratory criteria

The elevated content of manganese, chromium, nickel in the blood; leukopenia with limphomonocytic shift, decreased hemoglobin, serum ferrum, increase of total and unsaturated Fe-binding capacity of the blood; increase of specific IgE to manganese, chromium, nickel; reduction of $CD4^+$-lymphocytes, functional activity of phagocytes; elevated levels of $CD8^+$, $CD19^+$-lymphocytes, glutathione peroxidase, superoxide dismutase; pathological alleles CPOX, CYP1A1 – *Level of evidence A*.

The reduction of secretory IgA, increase of malondialdehyde, lipid hydroperoxides, increase/reduction of antioxidant activity – *Level of evidence B*.

Table 3.27

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of chronic bronchitis with obstructive syndrome in combination with allergic rhinitis. 2. Disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence. 3. The diagnostics of chronic intoxication, clinical implications of secondary transient immunodeficiency. 4. The diagnostics of atopic dermatitis. 5. The diagnostics of allergic diseases of pharynx, larynx, nasal polyposis, gaymoroetmoidit, otitis media. 6. The diagnostics of astenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 7. The assessment of cognitive functions condition. 4. The assessment of the efficacy of basic therapy
2	Spirography	1. The functional study of external respiration in terms of FEV1 and PEF in the period of disease recrudescence and remission. 2. Functional test with bronchodilators during the recrudescence
3	Rhinomanometry	1. The investigation of nasal patency in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional test with decongestants during the recrudescence
4	Cardiointervalography	The investigation of initial autonomic tone, and autonomic reactivity during stress tests
5	Chemicoanalytical analysis of the blood	The analysis of chromium and/or manganese, nickel content
6	General blod analysis	The analysis of the number of leukocytes, leukogram, hemoglobin level
7	Biochemical blood analysis	The analysis of serum ferrum, total and unsaturated Fe-binding potency of the blood; the level of malondialdehyde, lipid hydroperoxides, glutathione peroxidase, antioxidant activity state, superoxide dismutase
8	Immune blood analysis	The analysis of the content of specific IgE to manganese, chromium, nickel; $CD4^+$, $CD8^+$, $CD19^+$- lymphocytes, secretory IgA, assessment of functional activity of phagocytes
9	Genetic typing	The identification of pathological alleles CPOX, CYP1A1

Table 3.28

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Rhinomanometry	The investigation of nasal breathing in terms of airflow and transnasal resistance during disease remission
2	Immune blood analysis	The investigation of the content of γ-interferon, γ-aminobutyric acid, interleukins IL-4, IL-6, IL-10
3	Enzyme immunoassay of the blood	The investigation of the content of cortisol, glutamate
4	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

Th e level of criteria evidence

Functional criteria

The saving of the moderate reduced indicators of airflow and increase of transnasal resistance during remission – *Level of evidence B*.

Laboratory criteria

The increase of cortisol, glutamate, content of interleukins IL-4, IL-6, IL1-0, γ-aminobutyric acid; reduction of content of interleukins IL-4, IL-6, IL1-0 – *Level of evidence A.*

The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of epipharynx allergic diseases, atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes with a predominance of symptoms of parasympathetic nature, reduction of the activity of cognitive functions, features of variable immunodeficiency, sensitivity/resistance to basic therapy are diagnosed in patients with clinical signs of chronic obstructive bronchitis and allergic rhinitis, living in conditions of ambient air contamination by metal allergens (*manganese and/or chromium, nickel*) during *clinical research*.

The chemicoanalytical analysis of the blood is performed in patients with chronic obstructive bronchitis and epipharynx allergic diseases, atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes of parasympathetic nature, reduction of the activity of cognitive functions, features of variable immunodeficiency and resistance to basic therapy for the determination of manganese, chromium, nickel content.

Functional analysis (spirography, rhinomanometry, functional test with bronchodilators and decongestants, cardiointervalography) and a *complex of laboratory diagnostics* (general, biochemical, immunological blood analyses, genetic typing) are conducted at determination of high concentration of manganese and/or chromium, nickel in the blood (2.0 RL and more).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of chronic obstructive bronchitis and allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria of chronic obstructive bronchitis and allergic rhinitis associated with impact of metal allergens (manganese and/or chromium, nickel).

Differential diagnostics shall be performed to confirm the diagnosis of chronic bronchitis (J42 chronic bronchitis, unspecified) and allergic rhinitis (J30.2 Other seasonal allergic rhinitis) upon receipt of the results of primary diagnostic measures corresponding to less than 50% of the criteria of chronic bronchitis with obstructive component and allergic rhinitis associated with exposure to metal allergens (manganese and/or chromium, nickel).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of chronic obstructive bronchitis and allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel).

The medical and preventive measures of the technology of the prevention of bronchial asthma in patients with chronic obstructive bronchitis and allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel), are developed based on the existing standard approaches to the prevention of bronchopulmonary pathology of allergic genesis with regard to the disease pathogenesis features associated with impact of manganese, chromium and nickel.

The form and timing of technology

The medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in patients with chronic obstructive bronchitis and allergic rhinitis associated with impact of metal allergens (manganese, chromium, nickel) is designed for implementation on the basis of outpatient care health facilities, convalescent centers, as well as day hospitals and day and night clinics.

Table 3.29

The pathogenetic orientation of the medical and preventive measures of the technology of prevention of risk-associated bronchial asthma in patients with chronic obstructive bronchitis and allergic rhinitis

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	Elevated levels of manganese and/or chromium, nickel in the blood (2.0 RL and more)	Reduced to 1 RL	Th activation of natural elimination mechanisms. Sorption therapy
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The depression of immunopathological reactions, immune inflammation, reduction of vessel wall permeability, inhibition of bronchus mucosa hyperresponsiveness, subepithelial fibrosis, restoration of damaged epithelium	Local action glucocorticosteroids. Antihistamines for systemic administration. Immunomodifiers. Physiotherapeutic procedures
3	Bronchial spasm	Bronchial apparatus recovery	Beta-adrenergic agonists Physiotherapeutic procedures
4	Expectoration hyperviscosity, disorder of nasal muco-ciliary clearance transport	An increase of functional activity of ciliated epithelium, expectoration viscosity reduction, restoration of muco-ciliary clearance transport	Secretolytics, mucolytics and stimulants of respiratory airways motor function
5	Activation of free radical oxidation, depletion of antioxidant protection	Restoration of oxidative-antioxidative process homeostasis	Antihipoxants and antioxidants
6	Functional disorders of the central and autonomic nervous system in parasympathetic form	Restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens

At chemicals concentration in the blood at the level of 2.0 RL measures shall be carried out annually, at the level higher than 2.0 RL – triannually.

The total duration of the course – 21 days.

Individual contraindications for medical and preventive measures of technology of prevention: inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

Table 3.30

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
1	2	3
Beta-adrenergic agonists ATX: 03AK03	Berodual	In the period of recrudescence
GC for intranasal use ATX: R01AD08	Flixonase	from the 1-st to the 10-th day
Antihistamines for systemic administration. ATX: R06AX	Aerius	from the 1-st to the 21-th day
Drugs with antiinflammatory and antibronchoconstrictive activity. ATX: R03DX03	Erespal	from the 1-st to the 10-th day

Continuation of Table 3.30

1	2	3
Drugs with mucolytic, expectorant and broncholytic action. ATX: R05CB10	Ascoril expectorant	from the 1-st to the 14-th day
Immunoamplifiers ATX: L03AX05	Imunorix	from the 10-st to the 21-th day
Drugs that improve metabolism and energy supply of tissues. ATX: A16AA01, N07XX	Elcar (children) Cytoflavin (adults, intravenous infusion)	from the 10-st to the 21-th day from the 10-st to the 17-th day
Multivitamin Complex. ATC: A11BA	Jungle	from the 1-st to the 21-th day
Physiotherapy methods		
Electrophoresis with potassium iodide to the root zone of the lung		7–8 times
Electric tranquilization		10 times
Variable magnetic field on paranasal sinus		10 times
Electroaerosol therapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day
Massage		from the 1-st to the 21-th day

The combined use of pharmacopoeial drugs, physiotherapy and dietetic therapy helps to suppress immunoallergic inflammatory, restores motor and secretory function of the nasal epithelium, enhances the natural immune resistance and normalizes the autonomic homeostasis.

The medical-preventive technology of the prevention of the progression of risk-associated bronchial asthma (magnesium, chromium, nickel) for patients, living in the territories with poor ambient air quality on the content of manganese and/or chromium, nickel

Technology of group D:

1) pathogenetic orientation – correction of specific disorders at the level of cellular and subcellular structures of the respiratory system, the restoration of morpho-functional state of the bronchial system, pathogenetic correction of the main types of exchange, neuroendocrine regulation, immunoreactivity, etc. taking into account the nature and extent of health harm;

2) clinical orientation is risk-associated bronchial asthma with progredient progression and resistance to basic therapy, occurring against the background of persistent sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target treatment and prevention programmes;

4) the form of realization – individual;

5) the frequency of application – individually;

6) implementation base – day hospital, hour stay hospitals, outpatient care health facilities, clinical subdivisions of specialized scientific centers.

The level of criteria evidence

Clinic criteria

The signs of persistent broncho-obstructive syndrome occurring against the deterioration of ambient air quality in content of metal allergens in the territory of residence of the patient; combination with epipharynx allergic diseases, atopic dermatitis, astenoneurotic/neurosis-like syndrome with a predominance of parasympathetic symptoms, decreased activity of cognitive functions and resistance to basic therapy – *Level of evidence B*.

Table 3.31

The diagnostic criteria of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel) (J45.9)

Criteria	Criteria characteristic
Hygienic	1. Poor ambient air quality in content of manganese and/or chromium, nickel in the territory of residence of the patient. 2. The presence of an unacceptable risk of respiratory diseases caused by inhalation intake of chromium and/or manganese, nickel. 3. The higher level of population morbidity in the territory of residence of bronchial asthma patient (compared to the average Russian and/or average sub-central, territorial, regional indicators).
Clinical	1. Year-round recrudescent nature of the course. 2. Disease recrudescence association with the worsening of ambient air quality in content of metal allergens in the territory of residence. 3. Persistent attack-like inefficient cough, worsening in the evening and at night, after the physical and psycho-emotional stress. 4. The abundance of different moist rales, wheezes, elongated breath, suppressed breath sounds in the period of recrudescence; dry scattered, individual moist rales in the period of remission. 5. Constant nasal congestion by "blocking nose" type. 6. Persistent epipharynx allergic diseases 7. Lymphadenopathy, hypertrophy of palatine tonsils and adenoids of II–III degree. 8. Atopic dermatitis 9. Presence of moderate symptoms of chronic intoxication. 10. Asthenoneurotic/neurosis-like syndrome with a predominance of parasympathetic symptoms. 11. The cognitive functions activity reduction. 12. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 13. Resistance to basic therapy
Functional	1. The reduction of the curve "flow – volume" of FEV1, PEF, MEF 75–85% during the disease recrudescence; preservation of reduced indicants of MEF 75–85% during remission (at spirography). 2. Great reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, retention of moderate reduced indicators of airflow and transnasal resistance (at rhinomanometry) during remission. 3. Positive tests with bronchodilators during the recrudescence (at spirography). 4. Negative functional tests with decongestants (at rhinomanometry). 5. Vagotonic type of initial autonomic tone and asimphatic-tonic version of autonomic reactivity (at cardiointervalography)
Laboratory	1. Levels of chromium and/or manganese, nickel in the blood ≥ 2RL. 2. General blood analysis: leukopenia with considerable limphomonocytic shift, decreased hemoglobin. 3. Biochemical blood analysis: reduction of serum ferrum, increase of total and unsaturated Fe-binding capacity of the blood: increase of the content of malondialdehyde in plasma, lipid hydroperoxides, glutathione peroxidase; increase/decrease of antioxidant activity, superoxide dismutase. 4. Immune blood analysis: increase of total IgE and specific IgE to manganese, chromium, nickel; reduction of the absolute content and functional activity of phagocytes, $CD4^+$-lymphocytes, γ-interferon level, total and secretory IgA; increase of $CD8^+$, $CD19^+$, leukotrienes, interleukins IL-4, IL-6, IL-10. 5. EIA increase of adrenocorticotropic hormone, cortisol, cyclic adenosine monophosphate, glutamate; reduction of serotonin, cyclic guanosine monophosphate and γ-aminobutyric acid. 6. Genetic typing: presence of pathological alleles CPOX, CYP1A1

Table 3.32

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of persistent broncho-obstructive syndrome occurring against the deterioration of ambient air quality in content of metal allergens. 2. The diagnostics of epipharynx allergic diseases, atopic dermatitis; symptoms of variable immunodeficiency; frequent acute respiratory diseases. 3. The detection of chronic intoxication symptoms. 4. The diagnostics of astenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 5. The assessment of the level of cognitive functions progression. 6. The assessment of the efficacy of basic therapy
2	Spirography	1. Functional study of external respiration (FEV1, PEF), including at the level of MEF 75–85% in the period of recrudescence and in the period of remission. 2. Functional test with bronchodilators during the recrudescence
3	Rhinomanometry	1. The assessment of the state of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional test with decongestants during the disease recrudescence
4	Cardiointervalography	The assessment of initial autonomic tone and autonomic reactivity during stress tests
5	Chemicoanalytical analysis of the blood	The investigation of chromium and/or manganese, nickel content in the blood
6	General blood analysis	The analysis of the number of leukocytes and leukogram, hemoglobin level
7	Biochemical blood analysis	The analysis of serum ferrum, total and unsaturated Fe-binding potency of the blood, malondialdehyde, lipid hydroperoxides, glutathione peroxidase, superoxide dismutase, antioxidant activity state.
8	Immune blood analysis	The analysis of the content of total and specific IgE to manganese, chromium, nickel; $CD4^+$, $CD8^+$, $CD19^+$- lymphocytes level; total and secretory IgA content; absolute content and functional activity of phagocytes
9	Genetic typing	The identification of pathological alleles CPOX, CYP1A1

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication, clinical signs of variable immunodeficiency – *Level of evidence C.*

Functional criteria

The reduction of spirography (MEF 75–85%) during the disease recrudescence and vagotonic type of initial autonomic tone with symptom-free-tonic variant of autonomic reactivity (cardiointervalography) – *Level of evidence A*.

The reduction of spirography (FEV1, PEF), reduction of air flow rate and increase of transnasal resistance at rhinomanometry, positive tests with bronchodilators and negative with decongestants during the disease recrudescence – *Level of evidence B*.

Laboratory criteria

The elevated content of manganese, chromium, nickel in the blood; leukopenia with limphomonocytic shift, decreased hemoglobin, serum ferrum, increase of total and unsaturated Fe-binding capacity of the blood; increase of total IgE level to manganese, chromium, nickel; reduction of $CD4^+$-lymphocytes, indicators of absolute content and functional activity of phagocytes; elevated levels of $CD8^+$, $CD19^+$, glutathione peroxidase; pathological alleles CPOX, CYP1A1 – *Level of evidence A*.

Table 3.33

Additional diagnostic measures

Diagnostic measure	Result
Rhinomanometry	The assessment of the state of nasal breathing in terms of airflow and transnasal resistance.
Immune blood analysis	The investigation of the level of γ-interferon, interleukins IL-4, IL-6, IL-10
Enzyme immunoassay of the blood	The analysis of the level of adrenocorticotropic hormone, cortisol, cyclic adenosine monophosphate, cyclic guanosine monophosphate, glutamate, serotonin, γ-aminobutyric acid
Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The reduction of total and secretory IgA, increase of malondialdehyde, lipid hydroperoxides, increase/reduction of antioxidant activity, superoxide dismutase – *Level of evidence B*.

The level of criteria evidence

Functional criteria

The saving of moderate reduced indicators of airflow and transnasal resistance during remission – *Level of evidence B*.

Laboratory criteria

The increase of adrenocorticotropic hormone, cortisol, cyclic adenosine monophosphate, glutamate, content of γ-interferon, serotonin, cyclic guanosine monophosphate, γ-aminobutyric acid – *Level of evidence B*.

The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of epipharynx allergic diseases, atopic dermatitis, symptoms of chronic intoxication, neurosis or astenoneurotic syndromes with a predominance of symptoms of parasympathetic nature, features of variable immunodeficiency, frequent acute respiratory diseases, cognitive function disorders) are diagnosed in patients with broncho-obstructive syndrome, living in conditions of ambient air contamination by metal allergens (magnesium and/or chromium, nickel); assess efficacy of basic therapy during *clinical research*.

The chemicoanalytical analysis of the blood is performed in patients with broncho-obstructive syndrome, the presence of epipharynx allergic diseases, atopic dermatitis, symptoms of chronic intoxication, asthenoneurotic or neurosis-like syndromes with a predominance of symptoms of parasympathetic nature, features of variable immunodeficiency, frequent acute respiratory diseases, cognitive function disorders and resistance to basic therapy for the determination of metal allergens content (manganese and/or chromium, nickel).

Functional analysis (spirography, rhinomanometry, cardiointervalography) and a *complex of laboratory diagnostics* (general, biochemical, immunoenzymatic, immunological blood analysis, genetic typing) are conducted at determination of high concentration of manganese and/or chromium, nickel in the blood (≥2 RL).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria for the diagnostics of bronchial asthma associated with impact of metal allergens (manganese and/or chromium, nickel).

Table 3.34

The pathogenetic orientation of the medical and preventive measures of the technology of progression prevention of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel)

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	The elevated levels of manganese and/or chromium, nickel in the blood (2 RL and more)	Reduced to 1 RL	The activation of natural elimination mechanisms. Enterosorption therapy
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The depression of immunopathological reactions, immune inflammation, reduction of vessel wall permeability, inhibition of bronchus mucosa hyperresponsiveness, subepithelial fibrosis, restoration of damaged epithelium	Inhaled corticosteroids. Leukotriene receptor antagonists. Systemic action antihistamines. Immunomodifiers. Physiotherapeutic procedures
3	Bronchial spasm	Bronchial apparatus recovery	Beta-adrenergic agonists Leukotriene receptor antagonists. Physiotherapeutic procedures
4	Expectoration hyperviscosity, disorder of nasal muco-ciliary clearance transport	An increase of functional activity of ciliated epithelium, expectoration viscosity reduction, restoration of muco-ciliary clearance transport, activation of surfactant generation	Secretolytics and stimulants of respiratory airways motor function
5	The activation of free radical oxidation, depletion of antioxidant protection	Restoration of oxidative-anti-oxidative process homeostasis	Antihipoxants and antioxidants
6	The functional disorders of the central and autonomic nervous system in parasympathetic form	The restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens

Differential diagnostics with bronchial asthma J45.0 shall be performed upon receipt of the results of primary diagnostic measures corresponding by less than *49 %* of criteria for the diagnostics of bronchial asthma associated with impact of metal allergens (manganese and/or chromium, nickel).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel).

The form and timing of technology

Specialized program for the prevention of risk associated bronchial asthma (manganese, chromium, nickel) is designed for implementation on the basis of day hospitals and day and night clinics, clinical outpatient departments of health care facilities, clinical subdivisions of specialized scientific centers.

The frequency of medical and preventive measures of technology is determined individually.

The total duration of the course – 21 days.

Individual contraindications for medical and preventive measures of technology of prevention of bronchial asthma associated with impact of metal allergens (manganese, chromium, nickel) inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy

of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; hepatic and renal insufficiency; chronic somatic diseases in recrudescence and decompensation stage.

Table 3.35

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
Glucocorticosteroids for inhalations 04.005 ATX: R03BA02	Pulmicort	1.5–6.0 months
Beta-adrenergic agonists 12.001 ATX: R03AK03	Berodual	In the period of recrudescence
Leukotriene receptor antagonists 13.008 ATX: R03DC03	Singulair	from the 1-st to the 21-th day
Secretolytics and stimulants of respiratory airways motor function ATX: R05CB06	Ambrobene	from the 1-st to the 10-th day
Antihistamines for systemic administration ATX: R06AX	Telfast	from the 1-st to the 21-th day
Immunostimulants ATX: L03	Imunofan	from the 10-st to the 21-th day
Antihipoxants and antioxidants ATX: C01EB09	Reamberin	from the 10-st to the 21-th day
ATX nootropics: N06BX	Pantogamum active	from the 10-st to the 21-th day
Physiotherapy methods		
Sinusoidal modulated current therapy		7–8 times
Electric tranquilization		7–8 times
Speleotherapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day
Massage		from the 1-st to the 21-th day

The use of pharmacopoeial drugs with physiotherapy, climatic factors, recreative gymnastics and therapeutic exercises, organization proper dietary regime, balneotherapy, provides detoxification effect, restoration of autonomic homeostasis and natural immunological resistance of the patient, and at the level of the target organs has anti-inflammatory, immunomodulatory action, restores motor and secretory functions of the bronchial system.

The medical-preventive technologies of the prevention of the development and progression of risk-associated bronchial asthma in patients with recurrent acute bronchitis, living in the territories with poor ambient air quality on the content of formaldehyde

The medical-preventive technology of the prevention of the development of risk-associated bronchial asthma in patients with recurrent acute bronchitis (J20.9), living in the territories with poor ambient air quality on the content of formaldehyde.

The technology of group A:

1) pathogenetic orientation – an increase of functional activity of homeostasis adaptation and balance systems, given the low potential risk of harm to the health;

2) clinical orientation – deconditioning syndrome, manifesting by recurrent acute bronchitis and impaired functional state of organs and systems of transient nature;

3) scope – health-improving programs;

4) the form of realization – organized groups;
5) the frequency of application – annually, biannually;
6) implementation base – children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities.

Table 3.36

The diagnostic criteria of moderate risk of the development of bronchial asthma associated with impact of formaldehyde in children with recurrent acute bronchitis (J20.9), living in the territories with poor ambient air quality on the content of formaldehyde

Criteria	Criteria characteristic
Hygienic	1. Poor ambient air quality in content of formaldehyde in the territory of the patient residence. Moderate risk of the development of respiratory diseases caused by inhalation impact of formaldehyde. 3. The higher level of acute bronchitis in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recurrent nature of the course, lack of disease recrudescence association with the worsening of ambient air quality on the content of formaldehyde. 2. The occurrence of the disease after acute respiratory viral infections, hypothermia. 3. Effective cough, subfebrile/febrile temperature; duration of thr disease episodes (about 2 weeks). 4. In the period of disease – an abundance of different moist rales, harsh breathing, in remission – harsh breathing. 5. The absence of episodes of bronchial obstruction. 6. No symptoms of hypokinetic biliary dysfunction. 7. The development of intoxication syndrome during disease. 8. Sensitivity to basic therapy
Functional	1. Predominantly restrictive respiratory disorders in the period of the disease; absence of respiratory disorders during remission (at spirography). 2. Normal speed of the airflow and transnasal resistance during disease recrudescence (at rhinomanometry). 3. The eitonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography). 4. The physiological indicators of morphofunctional state of the biliary tract
Laboratory	1. The content of formaldehyde in the blood is up to 2.0 times higher than the background level. 2. General blood analysis: leukocytosis with neutrophilic shift, physiological level of eosinophils, accelerated ESR, physiological level of hemoglobin. 3. Biochemical blood analysis: increase of malondialdehyde level, increase/reduction of antioxidant activity, physiological level of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase. 4. Immune blood analysis: physiological level of specific IgE to formaldehyde; increase of the absolute content and functional activity of phagocytes; increase of secretory IgA; moderate decrease of $CD4^+$-lymphocytes, insignificant increase of $CD8^+$ and $CD19^+$-lymphocytes, interleukins IL-4, IL-10. 5. EIA the physiological level of cortisol, glutamate, γ-aminobutyric acid, cyclic adenosine monophosphate, cyclic guanosine monophosphate. 6. Genetic typing: Absence of SULTIA1 gene polymorphism

The level of criteria evidence

Clinic criteria

The clinical signs of simple bronchitis, development of the disease against the background of acute respiratory diseases, hypothermia; lack of disease recrudescence association with the worsening of ambient air quality on the content of formaldehyde in the territory of the child residence/pre-school educational institution location. No symptoms of hypokinetic biliary dysfunction, astenoneurotic syndrome with a predominance of parasympathetic symptoms, the efficacy of basic therapy – *Level of evidence A.*

Frequent acute respiratory diseases, moderately severe symptoms of intoxication in the period of disease recurrence – *Level of evidence B.*

Functional criteria

Minor restrictive respiratory disorders during recrudescence and lack thereof in remission; eitonic type of initial autonomic tone with hypersimphatical-tonic autonomic reactivity, physiological indicators of the biliary tract state – *Level of evidence A*.

Laboratory criteria

The moderately increased content of formaldehyde in the blood. Leukocytosis with neutrophilic shift, accelerated ESR; physiological level of eosinophils, specific IgE to formaldehyde; increase in the absolute content and functional activity of phagocytes; increase of $CD4^+$, $CD8^+$, $CD19^+$, interleukins IL-4, IL-10; the absence of SULTIA1 gene polymorphism – *Level of evidence A*.

Table 3.37

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of recurrent acute bronchitis. 2. The association of the disease development with acute respiratory viral infections, hypothermia. 3. The identification of the average duration of the disease. 4. The diagnostics of intoxication syndrome and asthenic syndrome. 5. The diagnostics of biliary dysfunction. 6. The assessment of the efficacy of basic therapy
2	Spirography	The assessment of the function of external respiration in terms of FEV1 and PEF in the period of disease recrudescence and remission
3	Rhinomanometry	The assessment of the functional state of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence
4	Ultrasound scanning of the biliary tract	The investigation of morphofunctional state of the biliary tract
5	Cardiointervalography	The assessment of initial autonomic tone and autonomic reactivity during stress tests
5	Chemico-analytical analysis of the blood	The analysis of formaldehyde content in the blood
6	General blood analysis	The analysis of the number of leukocytes, eosinophils, leukogram, and ESR
7	Biochemical blood analysis	The analysis of activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, malondialdehyde level, antioxidant activity state
8	Immune blood analysis	The analysis of the content of specific IgE to formaldehyde; $CD4^+$, $CD8^+$, $CD19^+$- lymphocytes, secretory IgA, absolute content and functional activity of phagocytes
9	Genetic typing	The identification of SULTIA1 gene polymorphism

The increase of secretory IgA, increase of malondialdehyde, increase/reduction of antioxidant activity, physiological level of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase activity – *Level of evidence B*.

Table 3.38

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Enzyme immunoassay	The investigation of the content of cortisol, glutamate, γ-amino-butyric acid, cyclic adenosine monophosphate, cyclic guanosine monophosphate
2	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Laboratory criteria

The physiological level of cortisol, glutamate, γ-aminobutyric acid, cyclic adenosine monophosphate, cyclic guanosine monophosphate – *Level of evidence A.*

The absence of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of symptoms of chronic intoxication, biliary hypotonic dysfunction, astenoneurotic syndrome with a predominance of parasympathetic symptoms, frequent acute respiratory diseases of infectious origin, sensitivity/resistance to basic therapy are diagnosed in patients with clinical signs of recurrent simple bronchitis living in conditions of ambient air contamination by aldehydes (*formaldehyde*), during clinical research.

The chemicoanalytical analysis of the blood is performed in patients with recurrent simple bronchitis with symptoms of moderate intoxication and asthenic syndrome during the recurrence, efficacy of basic therapy for the determination of formaldehyde content.

Functional analysis (spirography, rhinomanometry, ultrasonic scanning of biliary tract, cardiointervalography) and a *complex of laboratory diagnostics* (general, biochemical, immunological blood analysis, genetic typing) are conducted at determination of high concentration of formaldehyde in the blood (1.5–2.0 RL times higher than background level).

The medical and preventive measures of the technology shall be performed when the results obtained correspond to 80% or more criteria of chronic bronchitis (J41).

An additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to at least *80%* of the criteria of chronic bronchitis (J41) diagnosis.

Medical and preventive measures shall be performed when the results of additional diagnostic measures correspond to *80%* or more criteria of chronic bronchitis (J41).

The technology of prevention of risk-associated bronchial asthma in patients with recurrent acute bronchitis (J20.9) is based on the existing standard approaches to the prevention of bronchopulmonary pathology in children. Combined use of pharmacopoeial drugs, physiotherapy, climatic factors, diet can prevent progression of the process, the formation of chronic bronchitis associated with impact of aldehydes (formaldehyde), stops the process of nonspecific inflammation in the bronchi, increases immunoresistance of the child body.

The form and timing of technology

The technology of prevention of risk-associated bronchial asthma in children with simple bronchitis (J20.9) and elevated content of aldehyde (formaldehyde) in the blood at the level of up to 1.5 RL is designed for implementation on the basis of children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities.

Table 3.39

The pathogenetic orientation of medical and preventive technologies of prevention of risk-associated bronchial asthma in patients with recurrent acute bronchitis (J20.9) and elevated levels of aldehyde (formaldehyde) in the blood

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	The elevated content of formaldehyde in the blood (up to 2.0 times higher than the background level)	The reduction to background levels	The activation of natural elimination mechanisms. Increase of functional activity of the hepatobiliary system
2	The disorder of nasal mucociliary clearance transport	An increase of functional activity of ciliated epithelium, restoration of muco-ciliary clearance transport	The stimulants of motor function of the respiratory tract. Physiotherapy measures
3	Inflammatory process	Inflammatory reactions depression	Antibiotics. Antiphlogistic
4	The reduction of activity of natural resistance mechanisms	The increased activity of nonspecific and specific resistance factors	Physiotherapeutic procedures. General tonic preparations, adaptogens

The treatment and preventive measures of technology are implemented annually or biannually.

The total duration of the course – 21 days.

Individual contraindications for treatment and prevention: inconformity to clinical criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

Table 3.40

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
Drugs with mucolytic, expectorative action. ATX: R05CB10	Ascoril expectorant	from the 1-st to the 14-th day
Stimulants of motor function of the respiratory tract. ATX: R05CB06	Bronchobos	from the 11-st to the 21-th day
Immunostimulants ATX: L03AX	Bronchomunal	from the 10-st to the 18-th day
Multivitamin Complex. ATC: A11BA.	Jungle	from the 1-st to the 21-th day
Antimicrobials. ATX: J01FA10; ATX: J01GB06; J01BA02;	Thiamphenicol glycinate atsetiltsisteinat	In the period of the recrudescence (for the main indications)
Drugs for bile ducts diseases treatment. ATX: A05AX	Hepabene	from the 1-st to the 21-th day
Physiotherapy methods		
Electrophoresis with potassium iodide to the root zone of the lung		7–8 times
Electroaerosol therapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day
Massage		from the 1-st to the 21-th day

The medical-preventive technology of the prevention of the development of risk-associated bronchial asthma in patients with allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of formaldehyde

The technology of group B:

1) pathogenetic orientation is an increase of functional upper airway resistance to the effects of living environment risk factors, restoration of functional activity of homeostasis adaptation and sustention systems with regard to the average level of the potential risk of health harm;

2) clinical orientation is chronic allergic rhinitis with transient sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target prevention programmes;

4) the form of realization – organized groups, individual preventive measures;

5) the frequency of application – biannually;

6) implementation base – children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities, day hospitals.

Table 3.41

The diagnostic criteria of high risk of the development of bronchial asthma associated with impact of formaldehyde in patients with allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of formaldehyde

Criteria	Criteria characteristic
1	2
Hygienic	1. Poor ambient air quality in content of aldehyde in the territory of the patient residence. 2. The high risk of the development of allergic rhinitis caused by inhalation impact of formaldehyde. 3. The higher level of allergic rhinitis morbidity in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recrudescent nature of the course, disease recrudescence association with the worsening of ambient air quality on the content of formaldehyde. 2. Rheum and nasal congestion, sneezing attacks in the period of disease recurrence. 3. The duration of episodes of disease recrudescence – from several days to several months. 4. Nasal congestion in the period of remission. 5. Combination with chronic inflammatory diseases of nasal pharynx. 6. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 7. The clinic features of hypokinetic biliary dysfunction. 8. The sympttoms of moderate intoxication. 9. Asthenoneurotic syndrome with a predominance of parasympathetic symptoms. 10. Resistance to basic therapy
Functional	1. The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, retention of reduced indicators of airflow and increase of transnasal resistance (at rhinomanometry) during remission. 2. Negative functional tests with decongestants (at rhinomanometry). 3. The features of hypokinetic biliary dysfunction (at ultrasound scanning of liver). 4. The vagotonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography)

Continuation of Table 3.41

1	2
Laboratory	1. The content of formaldehyde in the blood is up to 2.0–3.0 times higher than the background level. 2. General blood analysis: normocytosis, eosinophilia with limphomonocytic shift, increased eosinophil-lymphocytic index. 3. The rhinocytogram increase of the content of eosinophils, neutrophils in nasal secretions; increase of the eosinophils index 4. Biochemical blood analysis: Increase of activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, malondialdehyde level, lipid hydroperoxides, increase/reduction of antioxidant activity. 5. Immune blood analysis: increase of formaldehyde specific IgE, interleukins IL-4, IL-10, $CD19^+$, $CD8^+$-lymphocytes; reduction of $CD4^+$-lymphocytes, secretory IgA, functional activity of phagocytes. 6. EIA increase of glutamate, cyclic adenosine monophosphate, reduction of γ-aminobutyric acid, cyclic guanosine monophosphate. 7. Genetic typing: SULTIA1 gene polymorphism

Table 3.42

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of allergic rhinitis. 2. The association of disease recurrence development with the worsening of ambient air quality in content of formaldehyde in the territory of residence. 3. The determination of the disease recurrence duration. 4. The diagnostics of chronic inflammatory diseases of the nasal pharynx, frequent acute respiratory diseases; symptoms of hypokinetic biliary dysfunction, symptoms of chronic intoxication; astenoneurotic syndrome with a predominance of parasympathetic symptoms. 5. The assessment of the efficacy of basic therapy
2	Rhinomanometry	1. The assessment of the functional state of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional tests with decongestants
4	Cardiointervalography	The assessment of initial autonomic tone and autonomic reactivity during stress tests
5	Ultrasound scanning of the biliary tract	The assessment of morphofunctional state of the biliary tract
6	Chemicoanalytical analysis of the blood	The analysis of formaldehyde content in the blood
7	General blood analysis	The analysis of the number of leukocytes, eosinophils, leukogram, assessment of eosinophil-lymphocytic index.
8	Rhinocytogram	The investigation of the content of eosinophils, neutrophils in nasal secretions, eosinophils index assessment
9	Biochemical blood analysis	The analysis of activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase
10	Immunological blood analysis	The analysis of formaldehyde specific IgE, secretory IgA, $CD8^+$, $CD19^+$, $CD4^+$-lymphocytes, functional activity of phagocytes
11	Genetic typing	The identification of SULTIA1 gene polymorphism

The kevel of criteria evidence

Clinic criteria

The clinical signs of allergic rhinitis; disease recrudescence associated with the worsening of ambient air quality in content of formaldehyde in the territory of the patient residence; long-term (up to several months) recurrence duration; chronic inflammatory diseases of pharynx, larynx; hypokinetic biliary dysfunction; asthenoneurotic syndrome with a predominance of parasympathetic symptoms, resistance to basic therapy – *Level of evidence B*.

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication – *Level of evidence C.*

Functional criteria

The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, negative functional tests with decongestants, vagotonic type of initial vegetative tone with hypersimphatic-tonic autonomic reactivity variant, ultrasound features of hypokinetic biliary dysfunction – *Level of evidence B*.

Laboratory criteria

The increased content of formaldehyde in the blood; normocytosis, eosinophilia with limphomonocytic shift; increase of the activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase; increase of formaldehyde specific IgE, $CD8^+$, $CD19^+$-lymphocytes; reduction of secretory IgA, functional activity of phagocytes, $CD4^+$-lymphocytes; increase of eosinophils in nasal secretions, increase of eosinophil-lymphocytic index; SULTIA1 gene polymorphism – *Level of evidence A*.

Table 3.43

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Rhinomanometry	The assessment of the functional state of nasal breathing in terms of airflow and transnasal resistance during disease remission
2	Biochemical blood analysis	The analysis of the content of malondialdehyde in plasma, antioxidant activity in serum, lipid hydroperoxides, glutathione peroxidase
3	Immunological blood analysis	The analysis of the content of interleukins IL-4, IL-10
4	Immunoenzymatic blood analysis	The investigation of the content of γ-aminobutyric acid, glutamate, cyclic adenosine monophosphate, cyclic guanosine monophosphate
5	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Functional criteria

The saving of moderate reduced indicators of airflow and high transnasal resistance during remission – *Level of evidence B*.

Laboratory criteria

The increase of malondialdehyde, lipid hydroperoxides, glutamate, cyclic adenosine monophosphate; increase/decrease in the antioxidant activity of blood serum – *Level of evidence A.*

The increase of the levels of interleukins IL-4, IL-10; reduction of the content of γ-aminobutyric acid, cyclic guanosine monophosphate – *Level of evidence A*.

The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymerphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of chronic inflammatory diseases of the nasal pharynx, frequent acute respiratory diseases; symptoms of hypokinetic biliary dysfunction; moderate symptoms of chronic intoxication; asthenoneurotic syndrome with a predominance of parasympathetic symptoms; resistance/sensitivity to basic therapy are diagnosed and assessed in patients with clinical symptoms of allergic rhinitis living in conditions of ambient air contamination by aldehydes (*formaldehyde*), during *clinical research*.

Chemicoanalytical analysis of the blood is performed in patients with allergic rhinitis in combination with chronic inflammatory diseases of the nasal pharynx, frequent acute respiratory diseases, hypokinetic biliary dysfunction, moderate chronic intoxication, astheno-neurotic syndrome with a predominance of parasympathetic symptoms and resistance to basic therapy for the determination of formaldehyde content in the blood.

Functional analysis (rhinomanometry, functional test with decongestants, cardio-intervalography, ultrasonic scanning of biliary tract) and a *complex of laboratory diagnostics* (rhinocytogram, general, biochemical, immunological blood analysis, genetic typing) are conducted at determination of high concentration of formaldehyde in the blood (2.0–3.0 RL times higher than background level).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of allergic rhinitis associated with impact of aldehyde (formaldehyde).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria for the diagnostics of allergic rhinitis associated with impact of aldehyde (formaldehyde).

Differential diagnostics with allergic rhinitis (J30.2 Other seasonal allergic rhinitis) shall be performed upon receipt of the results of primary diagnostic measures corresponding to *no less than 50 %* of criteria for the diagnostics of allergic rhinitis associated with impact of aldehyde (formaldehyde).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of allergic rhinitis associated with impact of aldehyde (formaldehyde).

The medical and preventive measures of technology of prevention of risk-associated bronchial asthma in children with allergic rhinitis associated with impact of aldehyde (formaldehyde) is designed based on common approaches to the prevention of upper respiratory airways allergic diseases (standards and protocols) with regard to the features of disease processes associated with impact of formaldehyde and serve to prevention of progression of allergic rhinitis and development of bronchial asthma associated with impact of formaldehyde.

The joint action of used pharmacopoeial preparations and physiotherapeutic methods is directed to the main pathogenetic links of the pathologic processes induced by the impact of formaldehyde (immunopathological and cytotoxic responses) that prevents/interrupts the progression of the pathological process.

The form and timing of technology

The medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in patients with allergic rhinitis associated with impact of aldehyde (formaldehyde) are designed for implementation on the basis of children's camps of summer holiday, summer school grounds, pre-school institutions, sick rooms at schools, health centers at enterprises, sanatorium-preventorium, clinical outpatient departments of health care facilities, day hospitals.

When the content of formaldehyde 2.0–2.5 times higher than the background level, events are held annually, when the content 2.5–3.0 times higher than the background level – biannually.

The total duration of the course – 14 days.

Table 3.44

The pathogenetic orientation of the medical and preventive technologies of the prevention of risk-associated bronchial asthma in children with allergic rhinitis associated with impact of aldehyde (formaldehyde)

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	The elevated content of formaldehyde in the blood (2.0–3.0 times higher than the background level)	Reduction to background levels	The activation of natural elimination mechanisms. The increase of the functional activity of the hepatobiliary system
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The depression of immunopathological reactions, immune inflammation, the reduction of vessel wall permeability, the inhibition of mucosa hyperresponsiveness, the restoration of damaged epithelium	Local action glucocorticosteroids. Immunomodifiers. Physiotherapeutic procedures
3	Bile ducts dyskinesia of hypokinetic type	The restoration of the functional state of bile ducts, anti-inflammatory effect	Drugs for bile ducts treatment with hepatoprotective action
3	The activation of free radical oxidation, depletion of antioxidant protection	The restoration of oxidative-anti-oxidative process homeostasis	Antihipoxants and antioxidants
4	The functional disorders of the central and autonomic nervous system in parasympathetic form	The restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens

Individual contraindications for treatment and prevention: inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

The combined use of pharmacopoeial drugs and physiotherapy suppresses immunoallergic inflammatory, restores motor and secretory function of the nasal epithelium, enhances the natural immune resistance and normalizes autonomic homeostasis and functional state of biliary tract; prevents the disease progression.

Table 3.45

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
1	2	3
GC for intranasal use ATX: R01AD08	Flixonase	from the 1-st to the 5-th day
Drugs with mucolytic, secretomotor and anti-inflammatory action ATX: R07AX	Sinupret	from the 7-st to the 14-th day
Antihistamines for systemic administration. ATX: R06AX	Aerius	from the 1-st to the 14-th day
Immunostimulants ATX: L03AX	Polyoxidonium	from the 7-st to the 14-th day
Drugs for ATX bile ducts diseases treatment: A05AX	Hepabene	from the 1-st to the 21-th day

Continuation of Table 3.45

1	2	3
Multivitamin Complex, ATC: A11BA.	Jungle	from the 1-st to the 21-th day
Physiotherapy methods		
Variable magnetic field on paranasal sinus		7–8 times
Electroaerosol therapy		7–8 times
Speleotherapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 14-th day

The medical-preventive technology of the prevention of the development of risk-associated bronchial asthma in patients with chronic obstructive bronchitis (J44.8) and allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of formaldehyde

The technology of group C:

1) pathogenetic orientation is a restoration of respiratory organs morphofunctional resistance to the effects of living environment risk factors, increase of functional activity of homeostasis adaptation and sustention systems with regard to the high level of the potential risk of health harm;

2) clinical orientation is chronic obstructive bronchitis (J44.8) and allergic rhinitis against the background of persistent sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target treatment and prevention programmes;

4) the form of realization – individual, group;

5) the frequency of application – biannually, triannually;

6) implementation base – day hospital, hour stay hospitals or outpatient care health facilities.

The level of criteria evidence

Clinic criteria

The combination of chronic bronchitis with obstructive syndrome and allergic rhinitis; the recurrence of disease against the deterioration of ambient air quality in content of formaldehyde; chronic inflammatory diseases of the nasal pharynx, hypokinetic biliary dysfunction, astenoneurotic syndrome with a predominance of parasympathetic symptoms, resistance to basic therapy – *Level of evidence* B.

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication – *Level of evidence C.*

Functional criteria

Restrictive dysfunction of external respiration during the disease remission; vagotonic type of initial autonomic tone with hypersimphatical-tonic autonomic reactivity; signs of hypokinetic biliary dysfunction – *Level of evidence A*.

The dysfunction of external respiration (obstructive and restrictive types; reduction of air flow rate and increase of transnasal resistance, positive tests with bronchodilators, negative test with decongestants during the disease recrudescence – *Level of evidence B*.

Laboratory criteria

The elevated levels of formaldehyde in the blood, normocytosis, eosinophilia with limphomonocytic shift; increase of the activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase; increase of formaldehyde specific IgE, increase of the content of CD8+, CD19+, reduction of CD4+, functional activity of phagocytes; SULTIA1 gene polymorphism – *Level of evidence A.*

The reduction of secretory IgA, the increase of malondialdehyde, lipid hydroperoxides, glutathione peroxidase, increase/reduction of antioxidant activity, superoxide dismutase in serum – *Level of evidence B*.

Table 3.46

The criteria of very high risk of the development of bronchial asthma associated with impact of formaldehyde in patients with chronic obstructive bronchitis (J44.8) in combination with allergic rhinitis (J30.4), living in the territories with poor ambient air quality on the content of formaldehyde

Criteria	Criteria characteristic
Hygienic	1. Poor ambient air quality in content of formaldehyde in the territory of the patient residence. 2. Very high risk of the development of respiratory diseases caused by inhalation impact of formaldehyde. 3. The higher level of chronic bronchitis and allergic rhinitis morbidity in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The recrudescent nature of the course, the recrudescence association with the worsening of ambient air quality on the content of formaldehyde. 2. Inefficient cough, worsening in the evening and at night, after physical and psycho-emotional stress; duration of disease recurrence – more than 2 weeks. 3. Wheezing episodes. 4. The abundance of different dry and moist rales, elongated breath in the period of recrudescence; individual dry scattered rales in the period of remission. 5. Profuse rheum and nasal congestion, sneezing attacks with a duration of 2–3 weeks to several months. 6. Combination with chronic inflammatory diseases of nasal pharynx. 7. The clinical signs of hypokinetic biliary dysfunction (right hypochondrium pain, nausea, episodic vomiting, unstable stool, etc.). 8. Asthenoneurotic syndrome with a predominance of parasympathetic symptoms. 9. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 10. Chronic intoxication symptoms. 11. Resistance to basic therapy
Functional	1. The reduction of the curve "flow – volume" during the disease recrudescence on obstructive and restrictive type; retention of restrictive disorders in the period of remission (at spirography). 2. Positive functional tests with bronchodilators during the recrudescence (at spirography). 3. The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, retention of reduced indicators of airflow and increase of transnasal resistance (at rhinomanometry) during remission. 4. Negative functional tests with decongestants (at rhinomanometry). 5. The vagotonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography). 6. The features of hypokinetic biliary dysfunction (at ultrasound scanning of biliary tract).
Laboratory	1. The content of formaldehyde in the blood is 3.0 and more times higher than the background level. 2. General blood analysis: normocytosis, lymphomonocitosis, eosinophilia 3. Biochemical blood analysis: Increase of activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, malondialdehyde in blood plasma, lipid hydroperoxides, glutathione peroxidase, increase/reduction of antioxidant activity, superoxide dismutase in serum. 4. Immune blood analysis: increase of formaldehyde specific IgE, a moderate decrease of CD4+-lymphocytes, content of secretory IgA, functional activity of phagocytes; increase of $CD8^+$, $CD19^+$-lymphocytes, interleukins IL-4, IL-6, IL-10. 5.EIA: the increase of cortisol, cyclic adenosine monophosphate, glutamate; reduction of cyclic guanosine monophosphate and γ-aminobutyric acid. 6. Genetic typing: SULTIA1 gene polymorphism

Table 3.47

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of chronic bronchitis with periodically originating broncho-obstructive syndrome. 2. Disease development association with the worsening of ambient air quality in content of formaldehyde in the territory of residence. 3. The diagnostics of chronic inflammatory diseases of the nasal pharynx, frequent acute respiratory diseases; hypokinetic biliary dysfunction; symptoms of chronic intoxication; astenoneurotic syndrome with a predominance of parasympathetic symptoms. 4. The assessment of the efficacy of basic therapy
2	Spirography	1. The assessment of the function of external respiration in terms of FEV1 and PEF in the period of disease recrudescence and remission. 2. Functional test with bronchodilators during the recrudescence
3	Rhinomanometry	1. The assessment of the functional state of nasal breathing in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional test with decongestants during the disease recrudescence
4	Cardiointervalography	The assessment of initial autonomic tone and autonomic reactivity during stress tests
5	Ultrasound scanning of liver and biliary tract	The assessment of morphofunctional state of the hepatobiliary system
6	Chemicoanalytical analysis of the blood	The analysis of the formaldehyde content in the blood
7	General blood analysis	The analysis of the number of leukocytes, eosinophils, leuko-gram
8	Biochemical blood analysis	The analysis of activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, malondia-ldehyde, lipid hydroperoxide, glutathione peroxidase, superoxide dismutase, condition of antioxidant activity
9	Immunological blood analysis	The analysis of the content of formaldehyde specific IgE; $CD4^+$, $CD8^+$, $CD19^+$-lymphocytes; secretory IgA, functional activity of phagocytes
10	Genetic research	The identification of SULTIA1 gene polymorphism

Table 3.48

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Rhinomanometry	The investigation of the functional state of nasal breathing in terms of airflow and transnasal resistance during remission
2	Immune blood analysis	The analysis of the content of interleukins IL-4, IL-6, IL-10
3	Enzyme immunoassay of the blood	The analysis of the level of cortisol, cyclic adenosine monophosphate, cyclic guanosine monophosphate, glutamate, γ-aminobutyric acid
4	Genetic typing	The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Functional criteria

The saving of reduced indicators of airflow and increase of transnasal resistance during remission (rhinomanometry) – *Level of evidence B*.

Laboratory criteria

The increase of the content of interleukins IL-4, IL-6, IL-10, cyclic adenosine monophosphate, cortisol, glutamate; reduction of cyclic guanosine monophosphate, γ-aminobutyric acid – *Level of evidence A*.

The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymerphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of chronic inflammatory diseases of the nasal pharynx, hypokinetic biliary dysfunction, symptoms of chronic intoxication, astenoneurotic syndrome with a predominance of parasympathetic symptoms, frequent acute respiratory diseases, resistance/sensitivity to basic therapy are diagnosed in patients with chronic obstructive bronchitis and allergic rhinitis in conditions of ambient air contamination by formaldehyde during during clinical research.

The chemicoanalytical analysis of blood for the determination of formaldehyde shall be performed if a patient with chronic obstructive bronchitis and allergic rhinitis has symptoms of chronic inflammatory diseases of the nasal pharynx, hypokinetic biliary dysfunction, symptoms of chronic intoxication, parasympathetic astenoneurotic syndrome and resistance to the basic therapy.

Functional analysis (spirography, rhinomanometry, functional tests with bronchodilators and decongestants, cardiointervalography, ultrasonic scanning of liver and biliary tract) and a *complex of laboratory diagnostics* (general, biochemical, immunological blood analysis, genetic typing) are conducted at determination of high concentration of formaldehyde in the blood (3.0 RL and more times higher than background level).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of chronic bronchitis with broncho-obstructive syndrome and allergic rhinitis associated with impact of aldehyde (formaldehyde).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria for the diagnostics of chronic bronchitis with broncho-obstructive syndrome and allergic rhinitis associated with impact of aldehyde (formaldehyde).

Differential diagnostics with chronic bronchitis (J42 chronic bronchitis, unspecified) and allergic rhinitis (J30.2 Other seasonal allergic rhinitis) shall be performed upon receipt of the results of primary diagnostic measures corresponding to less than *50%* of the criteria of diagnostics of chronic bronchitis with broncho-obstructive syndrome and allergic rhinitis associated with exposure to aldehyde (formaldehyde).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of chronic bronchitis with broncho-obstructive syndrome and allergic rhinitis associated with impact of aldehyde (formaldehyde).

Specialized program for the prevention of bronchial asthma in patients with chronic obstructive bronchitis and allergic rhinitis associated with impact of aldehydes (formaldehyde), is aimed to prevention of disease recurrence, development of bronchial asthma and its complications. The program was developed bases on generally accepted approaches to prevention of bronchopulmonary pathology (standards and protocols), with regard to pathogenetic effects of aldehydes (cytotoxic, immunopathological, immunosuppressive and hepatotoxic effects).

The form and timing of technology

The medical and preventive measures of the technology of the prevention of risk-associated bronchial asthma in patients with chronic obstructive bronchitis and allergic rhinitis associated with impact of aldehydes (formaldehyde) are designed for implementation on the basis of outpatient care health facilities, day hospitals and day and night clinics.

Table 3.49

The pathogenetic orientation of the medical and preventive measures of the technology of prevention of risk-associated bronchial asthma development in patients with chronic obstructive bronchitis and allergic rhinitis associated with impact of ofrmaldehyde

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	Increased formaldehyde content in the blood (3.0 and more times higher than the background level)	Reduction to background level	The activation of natural elimination mechanisms. The increase of functional activity of the hepatobiliary system
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The suppression of immunopathological reactions, immune inflammation, subepithelial fibrosis, the restoration of damaged bronchial epithelium	Antihistamines for systemic administration. Immunomodifiers. Physiotherapeutic procedures
3	Bronchial spasm	Bronchial apparatus recovery	Beta-adrenergic agonists Physiotherapeutic procedures
4	The disorder of nasal mucociliary clearance transport	The reactivation of nasal mucociliary clearance transport	The stimulants of motor function of the respiratory tract
5	The activation of free radical oxidation, the depletion of antioxidant protection	The restoration of oxidative-anti-oxidative process homeostasis	Antihipoxants and antioxidants
6	Bile ducts dyskinesia of hypokinetic type	The restoration of the functional state of bile ducts, anti-inflammatory effect	Drugs for bile ducts treatment with hepatoprotective action
7	The functional disorders of the central and autonomic nervous system in parasympathetic form	The restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens

When the content of formaldehyde 3 times higher than the background level, events are held biannually, when the content 3 times higher than the background level – triannually.

The total duration of the course – 21 days.

Table 3.50

Pharmacological and physical therapy support program

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
1	2	3
ATX Beta-adrenergic agonists: 03AK03	Berodual	In the period of recrudescence
GC for intranasal use ATX: R01AD08	Flixonase	from the 1-st to the 10-th day
Antihistamines for systemic administration, ATX. R06AX	Aerius	from the 1-st to the 21-th day
Drugs with antiinflammatory and antibronchoconstrictive activity ATX: R03DX03	Erespal	from the 1-st to the 10-th day

Continuation of Table 3.50

1	2	3
Drugs with mucolytic, expectorant and broncholytic action ATX: R05CB10	Ascoril expectorant	from the 1-st to the 10-th day
ATX Immunoamplifiers: L03AX05	Imunorix	from the 10-st to the 21-th day
Drugs for ATX bile ducts diseases treatment: A05AX	Hepabene	from the 10-st to the 21-th day
Multivitamin Complex, ATC: A11BA	Jungle	from the 1-st to the 21-th day
Physiotherapy methods		
Electrophoresis with potassium iodide to the root zone of the lung		7–8 times
Electric tranquilization		10 times
Electroaerosol therapy		10 times
Variable magnetic field on paranasal sinus		7–8 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day
Massage		from the 1-st to the 21-th day

Individual contraindications for treatment and prevention: inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy of drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

The combined use of pharmacopoeial drugs, physiotherapy and dietetic therapy helps to suppress immunoallergic inflammatory, restores motor and secretory functions of the bronchial system, desintoxication and elimination function of hepatobiliary system, enhances the natural immune resistance and autonomic homeostasis.

The medical-preventive technology of the prevention of the progression of risk-associated bronchial asthma (formaldehyde) for patients living in the territories with poor ambient air quality on the content of formaldehyde

The technology of group D:

1) pathogenetic orientation – the correction of specific disorders at the level of cellular and subcellular structures of the respiratory system, the restoration of morpho-functional state of the bronchial system, pathogenetic correction of the main types of exchange, neuroendocrine regulation, immunoreactivity, etc. taking into account the nature and extent of health harm;

2) clinical orientation is risk-associated bronchial asthma with progredient progression and resistance to basic therapy, occurring against the background of persistent sub- or decompensation of the functional state of homeostasis adaptation and sustention systems;

3) scope – target treatment and prevention programmes;

4) the form of realization – individual;

5) the frequency of application – individually;

6) implementation base – day hospital, hour stay hospitals, outpatient care health facilities, clinical subdivisions of specialized scientific centers.

The level of criteria evidence

Clinic criteria

The clinical signs of persistent broncho-obstructive syndrome occurring against the deterioration of ambient air quality in content of formaldehyde in the territory of the patient residence; allergic or chronic inflammatory diseases of the nasal pharynx; hypokinetic biliary dysfunction; distention, palpatory density and soreness of the liver; asthenoneurotic syndrome with a predominance of parasympathetic symptoms, resistance to basic therapy – *Level of evidence B.*

Frequent acute respiratory diseases, moderately severe symptoms of chronic intoxication, clinical signs of variable immunodeficiency – *Level of evidence C.*

Table 3.51

The diagnostic criteria of bronchial asthma associated with impact of formaldehyde (J45.9)

Criteria	Criteria characteristic
Hygienic	1. Poor ambient air quality in content of formaldehyde in the territory of the patient residence. 2. The unacceptable risk of the development of respiratory diseases caused by inhalation impact of formaldehyde. 3. The higher level of bronchial asthma morbidity in the territory of patient residence compared to the average Russian and/or average sub-central, territorial, regional indicators
Clinical	1. The year-round recrudescent nature of the course. 2. Disease recrudescence association with the worsening of ambient air quality in content of formaldehyde in the territory of residence. 3. Choking spells and cough in the evening, at night, after physical stress. 4. Different moist rales, wheezes, suppressed breath sounds, elongated breath in the period of the disease recrudescence; dry scattered, individual dry scattered rales in the period of remission. 5. Upper respiratory airways allergic diseases and chronic inflammatory diseases of the nasal pharynx. 6. The clinic features of hypokinetic biliary dysfunction. 7. The distention, palpatory density and soreness of the liver. 8. The clinical features of asthenoneurotic or neurosis-like syndrome with a predominance of parasympathetic symptoms. 9. Frequent acute respiratory diseases with manifestation duration of more than 10 days. 10. The moderate symptoms of chronic intoxication. 11. The resistance to basic therapy
Functional	1. The reduction of the curve "flow – volume" of FEV1, PEF, MEF 75–85% during the disease recrudescence; preservation of reduced indicants of MEF 75–85% during remission (at spirography). 2. The reduction of air flow rate and increase of transnasal resistance during the disease recrudescence, retention of moderate reduced indicators of airflow and increased transnasal resistance (at rhinomanometry) during remission. 3. Positive tests with bronchodilators during the recrudescence (at spirography). 4. Negative functional tests with decongestants (at rhinomanometry). 5. The vagotonic type of initial autonomic tone and hypersimphatic-tonic version of autonomic reactivity (at cardiointervalography). 6. The signs of moderate diffuse liver disease, hypokinetic biliary dysfunction (at ultrasound)
Laboratory	1. The level of formaldehyde in the blood above the background level more than 3.0 times. 2. General blood analysis: normocytosis, lymphomonocitosis, eosinophilia 3. Biochemical blood analysis: Increase of activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase; increase of malondialdehyde level, lipid hydroperoxides, glutathione peroxidase; increase/reduction of antioxidant activity, superoxide dismutase. 4. Immune blood analysis: increase of total and specific IgE to formaldehyde; a moderate decrease of CD4+-lymphocytes, content of γ-interferon, functional activity of phagocytes, increase of secretory IgA; increase of CD8+, CD19+ – lymphocytes; increase of content of interleukins IL-4, IL-6, IL-10, leukotrienes. 5. EIA increase of cortisol, cyclic adenosine monophosphate, glutamate; reduction of cyclic guanosine monophosphate and γ-aminobutyric acid. 6. Genetic typing: SULTIA1 gene polymorphism

Table 3.52

Primary diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Clinical research	1. The clinical diagnostics of persistent broncho-obstructive syndrome. 2. Disease recurrence association with the worsening of ambient air quality in content of formaldehyde in the territory of patient residence. 3. The diagnostics of allergic and/or chronic inflammatory diseases of the nasal pharynx; hypokinetic biliary dysfunction; distention, palpatory density and soreness of the liver; moderate chronic intoxication; astenoneurotic syndrome with a predominance of parasympathetic symptoms; symptoms of variable immunodeficiency. 4. The assessment of the efficacy of basic therapy
2	Spirography	1. The study of external respiration in terms of FEV1, PEF, MEF 75–85 % in the period of disease recrudescence and remission. 2. Functional test with bronchodilators during the disease recrudescence
3	Rhinomanometry	1. The investigation of nasal breathing function in terms of airflow and transnasal resistance during disease recrudescence. 2. Functional tests with decongestants
4	Cardiointervalography	The investigation of initial autonomic tone, and autonomic reactivity during stress tests
6	Ultrasound scanning of liver and biliary tract	The investigation of morphofunctional state of the hepatobiliary system
7	Chemicoanalytical analysis of the blood	The analysis of formaldehyde content in the blood
8	General blood analysis	The analysis of the number of leukocytes, eosinophils, leukogram,
9	Biochemical blood analysis	The analysis of the activity of aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, malondialdehyde, lipid hydroperoxide, glutathione peroxidase, superoxide dismutase; condition of antioxidant activity
10	Immune blood analysis	The analysis of the content of total and specific IgE to formaldehyde; $CD4^+$, $CD8^+$, $CD19^+$-lymphocytes, γ-interferon; secretory IgA, functional activity of phagocytes
11	Genetic typing	The identification of SULTIA1 gene polymorphism

Functional criteria

The reduction of spirography (MEF 75–85%) during the disease remission; vagotonic type of initial autonomic tone with hypersimphatical-tonic autonomic reactivity; signs of moderate diffuse liver disease, hypokinetic biliary dysfunction – *Level of evidence A.*

The reduction of spirography (FEV1, PEF, MEF 75–85 %) and rhinomanometry (reduction of air flow rate and increase of transnasal resistance), positive tests with bronchodilators and decongestants during the disease recrudescence – *Level of evidence B*.

Laboratory criteria

Increased formaldehyde content in the blood; normocytosis, eosinophilia with limphomonocytic shift, eosinophilia; increase of the activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase; increase of total and specific IgE to formaldehyde; reduction of CD4+-lymphocytes, γ-interferon, absolute content and functional activity of phagocytes; increase of CD8+, CD19+- lymphocytes, SULTIA1 gene polymorphism – *Level of evidence A.*

The reduction of total and secretory IgA, increase of malondialdehyde, lipid hydroperoxides, glutathione peroxidase, increase/reduction of antioxidant activity, superoxide dismutase – *Level of evidence B*.

Table 3.53

Additional diagnostic measures

Ser. No.	Diagnostic measure	Result
1	Rhinomanometry	The investigation of nasal breathing function in terms of airflow and transnasal resistance during disease remission.
2	Enzyme immunoassay of the blood	The analysis of the level of cortisol, cyclic adenosine monophosphate, cyclic guanosine monophosphate, glutamate, γ-aminobutyric acid.
3	Immune blood analysis	The analysis of interleukins IL-4, IL-6, IL-10
4	Genetic typing	The identification of "zero" gene GSTM1 genotype both in co-mbination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A)

The level of criteria evidence

Functional criteria

The saving of moderate reduced indicators of airflow and increase of transnasal resistance during remission – *Level of evidence B*.

Laboratory criteria

The increase of cortisol, cyclic adenosine monophosphate, glutamate, interleukins IL-4, IL-6, IL-10; reduction of cyclic guanosine monophosphate, γ-aminobutyric acid – *Level of evidence A*.

The identification of "zero" gene GSTM1 genotype both in combination with GSTT1+ genotype, and in combination with a heterozygous genotype of CYP2E1 gene (polymorphism 7632T>A) – *Level of evidence B.*

The algorithm of diagnostic measures

The presence/absence of allergic and/or chronic inflammatory diseases of the nasal pharynx, hypokinetic biliary dysfunction, distention, palpatory density and soreness of the liver, symptoms of chronic intoxication, astenoneurotic syndrome with a predominance of parasympathetic symptoms, signs of variable immunodeficiency, frequent acute respiratory infections are diagnosed in patients with broncho-obstructive syndrome, living in conditions of ambient air contamination by aldehydes (*formaldehyde*); assess the efficacy of basic therapy during clinical research.

Chemicoanalytical analysis of the blood for the determination of formaldehyde shall be performed in patients with broncho-obstructive syndrome and the presence of allergic and/or chronic inflammatory diseases of the nasal pharynx, hypokinetic biliary dysfunction, distention, palpatory density and soreness of the liver, symptoms of chronic intoxication, astenoneurotic syndrome with a predominance of parasympathetic symptoms, signs of variable immunodeficiency and resistance to basic therapy.

Functional analysis (spirography, rhinomanometry, cardiointervalography, ultrasonic scanning of the liver and biliary tract) and a *complex of laboratory diagnostics* (general, biochemical, immunoenzymatic, immunological blood analysis, genetic typing) are conducted at determination of high concentration of formaldehyde in the blood (3 and more times higher than background level).

Medical and preventive measures shall be performed when *the results obtained correspond to 80%* or more criteria of bronchial asthma associated with impact of aldehyde (formaldehyde).

Additional diagnostic measures shall be performed upon receipt of the results of primary diagnostic measures corresponding to *only 50–79%* of criteria for the diagnostics of bronchial asthma associated with impact of aldehyde (formaldehyde).

Differential diagnostics with bronchial asthma J45.0 shall be performed upon receipt of the results of primary diagnostic measures corresponding by less than *49 %* of criteria for the diagnostics of bronchial asthma associated with impact of aldehydes (formaldehyde).

Medical and preventive measures shall be performed when *the results of additional diagnostic measures correspond to 80%* or more criteria of bronchial asthma associated with impact of aldehyde (formaldehyde).

Table 3.54

The pathogenetic orientation of the medical and preventive measures of the technology of prevention of bronchial asthma associated with impact of aldehydes (formaldehyde)

Ser. No.	Pathogenetic link	The orientation of exposure	The types of exposure
1	The elevated content of formaldehyde in the blood (3.0 times higher than the background level)	Reduction to background level	The activation of natural elimination mechanisms. Increase of functional activity of the hepatobiliary system
2	The development of immunopathological reactions, immune inflammation of respiratory airways	The depression of immunopathological reactions, immune inflammation, the reduction of vessel wall permeability, the inhibition of bronchus mucosa hyperresponsiveness, subepithelial fibrosis, the restoration of damaged epithelium	Inhaled corticosteroids. Antihistamines for systemic administration. Immunomodifiers. Physiotherapeutic procedures
3	Bronchial spasm	Bronchial apparatus recovery	Beta-adrenergic agonists Physiotherapeutic procedures
4	The disorder of nasal mucociliary clearance transport	An increase of functional activity of ciliated epithelium, restoration of muco-ciliary clearance transport, activation of surfactant generation	The stimulants of motor function of the respiratory tract
5	The activation of free radical oxidation, depletion of antioxidant protection	The restoration of oxidative-anti-oxidative process homeostasis	Antihipoxants and antioxidants
6	The functional disorders of the central and autonomic nervous system	The restoration of the central and autonomic nervous system functional state homeostasis	Physiotherapeutic procedures. General tonic preparations, adaptogens
7	Hepatotoxic action	The restoration of functional activity of hepatocytes	Hepatoprotectors

The medical and preventive measures of the technology of the prevention of bronchial asthma associated with impact of aldehydes (formaldehyde), are aimed at preventing the progression of the disease, preventing the formation of uncontrolled forms of the disease and its complications; developed on the basis of existing standard approaches to the prevention of asthma with regard to additional pathogenesis links mediated by the impact of aldehydes (formaldehyde).

The form and timing of technology

Technology for the prevention of bronchial asthma associated with impact of aldehydes (formaldehyde) is designed for implementation in day hospitals and day and night clinics, clinical outpatient departments of health care facilities, clinical subdivisions of specialized scientific centers.

Frequency and timing medical and preventive measures shall be determined individually.

The total duration of the course – 21 days.

Individual contraindications for medical and preventive measures of prevention technology: inconformity to hygienic and medicobiologic criteria complex; idiosyncrasy of

drugs and physiotherapy procedures included in the prevention programme; age under 4 years; acute infectious diseases; acute mental disorders; chronic somatic diseases in recrudescence and decompensation stage.

Table 3.55

Pharmacological and physical therapy support scheme

Pharmacological groups and physiotherapy methods	The drugs of choice	The duration of use
Glucocorticosteroids for inhalations 04.005 ATX: R03BA02	Pulmicort	1.5–6.0 months
Beta-adrenergic agonists 12.001 ATX: R03AK03	Berodual	In the period of recrudescence
Leukotriene receptor antagonists 13.008 ATX: R03DC03	Singulair	from the 1-st to the 21-th day
Secretolytics and stimulants of respiratory airways motor function ATX: R05CB06	Ambrobene	from the 1-st to the 10-th day
Antihistamines for systemic administration ATX: R06AX	Telfast	from the 1-st to the 21-th day
Immunostimulants ATX: L03	Imunofan	from the 10-st to the 21-th day
Antihipoxants and antioxidants ATX: C01EB09	Reamberin	from the 10-st to the 21-th day
ATX Hepatoprotectors: A05AA02	Ursofalk (suspension)	from the 1-st to the 21-th day
Physiotherapy methods		
Sinusoidal modulated current therapy		7–8 times
Electric tranquilization		7–8 times
Speleotherapy		10 times
Therapeutic exercises, respiratory gymnastics		from the 1-st to the 21-th day

The combined use of pharmacopoeial drugs, physiotherapy and dietetic therapy helps to suppress immunoallergic inflammatory, restores motor and secretory functions of the bronchial system, desintoxication and elimination function of hepatobiliary system, enhances the natural immune resistance and autonomic homeostasis.

3.6.4. Practical recommendations for the implementation of the basic efferent actions of medical-preventive technologies prevention programs

The detoxication and elimination actions of the basic block of prevention programs include: high water schedule, thermotherapy, physiotherapy, diet, massage, speleotherapy and in some cases the administration of enterosorbents, choleretic drugs, infusion detoxification therapy.

Enterosorbents shall be included in the complex of efferent actions of the programs of prevention of diseases associated with impact of metals at their concentrations in the patient's blood above 2 RL. The most appropriate enterosorbents: Enterosgelum, Polysorb, Polyphepanum, Lactofiltrum (Table 3.89); average duration of the course – 10 days. Drugs shall be administered in age dosage.

The efficacy of recommended drugs (according to the criteria of reduction of metal concentration in the blood relating to the initial level) is as follows: Enterosgelum – 50–60 %; Polysorb – 20–60 %; Polyphepanum – 30–50 %; Lactofiltrum – 20–40 %.

Contraindications for enterosorbents efferent therapy: the idiosyncrasy of the drug, ileus, gastrointestinal bleeding, galactosemia. Avoid using enterosorbents at recrudescence of gastric ulcer and dodecadactylon ulcer, intestinal atony.

Table 3.56

The recommended complex of efferent actions with regard to chemical class

The class of chemical substances	The set of measures	The mechanisms of action
Metals and their compounds	Enterosorbents	The absorption and evacuation of metals through the gastrointestinal tract
	High water schedule	The stimulation of urodynamics, the activation of renal mechanism of elimination
	Physical therapy, heat therapy, massage	The activation of microcirculatory processes, removal from the pool
	Dietary nutrition	The partial sorption of metals, the activation of peristalsis, the acceleration of elimination through the gastrointestinal tract
	Choleretics	The acceleration of muco-ciliary clearance transport
Aromatic hydrocarbons	High water schedule	The stimulation of urodynamics, the activation of the renal mechanism of metabolites elimination
	Physical therapy, swimming pool, massage	The activation of microcirculatory processes, the acceleration of substances biotransformation, removal from the pool
	Respiratory gymnastics	The acceleration of substances and their metabolites elimination with expired air
	Speleotherapy	The acceleration of substances and their metabolites elimination with expired air
	Dietary nutrition	The restoration of fat-soluble compounds enzymatic biotransformation in water-soluble compounds; the restoration of antioxidant, conjugation and elimination functions of glutathione system
Oxygen-bearing compounds	High water schedule	The stimulation of urodynamics, the activation of the renal mechanism of substances and their metabolites elimination
	Physical therapy, heat therapy, massage	The activation of microcirculatory processes, acceleration of biotransformation
	Respiratory gymnastics	The acceleration of substances and their metabolites elimination with expired air
	Dietary nutrition	The restoration of enzymatic biotransformation processes, antioxidant, conjugation and elimination functions of glutathione system
	Speleotherapy	The acceleration of substances and their metabolites elimination with expired air
	Choleretics	The acceleration of biotransformation and muco-ciliary clearance transport
Suspended substances	Respiratory gymnastics	The acceleration of substances and their metabolites elimination with expired air
	Physical therapy, heat therapy, massage	The activation of microcirculatory processes, the acceleration of substances and their metabolites elimination with expired air
	Speleotherapy	The acceleration of substances and their metabolites elimination with expired air

Table 3.57

Enterosorbents recommended for efferent therapy in the prevention of respiratory diseases associated with impact of man-made metals

Trade name of drug	International non-proprietary name. Release form and registration form	Active surface area per 1 g of sorbent	Traumatic particles to the intestinal mucosa	Recommended dosages	Age limit	Potential side effects
Enterosgelum	Polymethylsiloxane polyhydrate (methylsilicic acid hydrogel). Medicinal product	150 m^2 per 1 g	None	22.5 g 3 times per day or 1–2 caps	No age limits	Usually well tolerated
Polysorb	Silicon dioxide. Medicinal product	300 m^2 per 1 g	None	150–200 mg/kg 3–4 times per day	Recommended for children over 1 year	Rarely retention of feces
Polyphepanum	Natural polymer lignin. Medicinal product	16–20 m^2 per 1 g	None	0.5–1.0 g/kg, 3 administrations	Recommended for children over 1 year	The retention of feces, hypo-vitaminosis at prolonged use vitamin, malabsorption of nutrients
Lactofiltrum	Natural polymer lignin. Synthetic disaccharide-lactulose. Medicinal product	16–20 m^2 per 1 g	None	0.5–3 pilles 3 times per day	Recommended for children over 1 year	Possible allergic reactions to components of the drug, rarely - meteorism, diarrhea

Diet is an integral part of medical-preventive technologies prevention programs used in patients with diseases associated with impact of man-made environmental factors, and provides:

– the restoration of the activity of nonspecific resistance factors and immune defense;

– membrane protective and cytoprotective effect;

– increase in the activity of antioxidant protection factors;

– the enhancement of the liver detoxification function;

– the normalization of the motor-evacuation function of bile ducts;

– the normalization of fat-soluble compounds enzymatic biotransformation in water-soluble compounds;

– the restoration of antioxidant, conjugation and elimination functions of the glutathione system;

– the restoration of biotransformation coenzyme systems by compensation of B and C vitamins deficit.

The daily diet of patients with diseases associated with impact of technology-related living environmental factors, should include foods that have targeted mechanism of action (Tables 3.58, 3.59).

High water schedule. High water schedule assumes an increase of the volume of fluid consumed daily by adult patients by 1.0–1.5 liters, by children – 500 ml.

The main forms of water schedule for prevention activities:

– use of boiled purified tap water;

– use of bottled water.

Table 3.58

Food recommended for inclusion in the diet of patients with diseases associated with the impact of the chemical factors of living environmental

Ser. No.	Product features	Product types
1	Products with antioxidant properties	*Berries:* blueberry, black/red grapes, cranberries, black chokeberry, cherry, strawberry, blackberry, raspberry. *Fruits:* winter apples, plums, peaches, apricots, oranges. *Vegetables:* eggplants, red cabbage, radish, turnip, pumpkin, red sweet pepper
2	fibrous and pectin foods	*Berries:* raspberries, strawberries, cranberries, cherries, melon, watermelon. *Fruits:* plums, apple-quince, figs, dates, plums, pears, citrus fruits. *Vegetables:* potatoes, carrots, cabbage, peas, eggplants, sweet peppers, pumpkin. *Grains:* buckwheat, pearl, peeled barley, oats, pea. *Fruit and vegetable pulpy juices* (apple, carrot, apple and carrot, apple-cranberry, quince, peach). *Nuts* Marshmallows, paste, marmalade contain pectins
3	Products with antioxidant properties	Liver, wild rice, wheat, buckwheat, melon, watermelon, pumpkin, nuts, almonds, halva

Table 3.59

The food sources of biologically active substances that enhance the biotransformation of chemicals

The direction of correction	Biologically active substances	Food sources
1	2	3
The restoration of the activity of nonspecific defense factors and immune defense	B_1, B_2, B_6, B_5, C, B_{12}, K_3, B_3, carnitine, PP, biotin, inosine, citric acid, succinic acid, malic acid, fumaric acid, L-aspartic, L-glutamic, γ-aminobutyric acid, methionine, iron, copper,	Vegetables, fruits, grains, raspberries, strawberries, vegetables, lemons, barberry, apples, animal and vegetable proteins, nuts, vegetables, liver
The support of fat-soluble aromatic hydrocarbons enzymatic conversion to soluble compounds at physiological level	Native proteins – the sources of glutamic, sulfur-containing amino acids, glutathione; linoleic, linolenic fatty acids, complex of fat- and water-soluble vitamins, minerals	Beef, chicken, cod, eggs, fish, farmer cheese, milk and dairy products, soybean oil, potatoes, sweet peppers, white cabbage, beets, onions, tomatoes, cucumbers, fresh fruits, sweet briar, dried fruits, instant vitamin and mineral drinks
The normalization of conjugation and elimination functions of the glutathione system	Methionine, cysteine, glutathione, glutamic acid, betaine, linoleic, linolenic fatty acids, complex of fat- and water-soluble vitamins, lipoic acid	Beef, liver, heart, eggs, fish, farmer cheese, milk and dairy products, soybean oil, potatoes, sweet peppers, white cabbage, cauliflower, beets, onions, tomatoes, cucumbers, fresh fruits, sweet briar, dried fruits, instant vitamin and mineral drinks
The normalization of the energization of biotransformation processes and the	Methionine, omega-3 fatty acids, phospholipids, inulin, complex of fat- and water-soluble vitamins, lipoic acid	Meat, liver, heart, eggs, fish, farmer cheese, milk and dairy products, cheese, butter, flax-seed, soybean oil, buckwheat, oats, potatoes, sweet

Continuation of Table 3.50

1	2	3
compensation of the increased consumption of food substances; liver cells membrane protective effect; the increase of protein synthesis function of the liver; the normalization of the motor-evacuation function of bile ducts		peppers, white cabbage, brussels sprouts, broccoli, kohlrabi, cauliflower, beets, onions, tomatoes, cucumbers, fresh fruits, dried fruits, nuts, instant vitamin and mineral drinks
The increase of nonspecific organism immunoresistance	Native proteins – the sources of glutamic, sulfur-containing amino acids, glutathione; linoleic, linolenic fatty acids, phospholipids, melatonin, complex of fat- and water-soluble vitamins, minerals	Meat, liver, heart, egg, fish, seafood, farmer cheese, milk and dairy products, linseed oil, soybean oil, grits, oatmeal, fresh fruits, potatoes, sweet peppers, white cabbage, beets, onions, tomatoes, cucumbers, instant vitamin and mineral drinks

Instant (rapidly dissolving) vitamin drinks enriched with essential micronutrients (vitamins, minerals) allowed in the prescribed manner by the State sanitary and epidemiological supervision authorities to be used in the nutrition of the children of appropriate age should be used at water schedule organization along with drinking water (Table 3.60).

Table 3.60

Mineral waters recommended for high water schedule in patients with diseases associated with the impact of technology-related living environmental factors

Ser. No.	Trade name	The composition of water
1	Borjomi	Hydro carbonate sodium water
2	Smirnovskaya	Carbonated, slightly mineralized (3–4 g/l) sulfate-hydrocarbonate calcium-sodium water
3	Slavyanovskaya	Sulfate-hydrocarbonate calcium-sodium natural drinking mineral water of low salinity
4	Essentuki No. 4	Carbonate hydro-chloride-sodium mineral water of moderate concentration
5	Essentuki No. 17	Carbonate hydro-chloride-sodium mineral water of strong concentration
6	Essentuki No. 20	Sulfate-hydrocarbonate -calcium-magnesium water of low concentration.
7	Narzan	Carbonate hydrocarbonate -sulphate-calcium water
8	Naftusya (Truskavetska)	Low-mineralized calcium-magnesium hydrocarbonate water
9	Berezovskaya	Ferrous hydrocarbonate-calcium-magnesium water of low concentration
10	Atsyluk	Hydrocarbonate-sodium water

The individual control of water schedule should be provided at the implementation of preventive measures.

Boiled purified tap water schedule shall be carried out in accordance with current sanitary requirements.

The organization of bottled water schedule. Water schedule can be organized with the use of bottled water with different types of its filling. Pumps or coolers can be used for the analysis of water. In accordance with GOST R 51074-2003 "Food products. Consumer

information. General Requirements" (approved by the Resolution of the State Standard of the Russian Federation No. 401-st dated December 29, 2003) the label of packaged (bottled) drinking water must include the following information:

– product name;
– kind (artesian, well (spring), river, lake glacier);
– type (carbon dioxide-free);
– category – the first or higher;
– the name and address of the manufacturer;
– the name and location of the water source;
– total mineralization (mg/l or g/l);
– total hardness (mg-eq./L);
– nominal volume;
– instructions for use (for water for special purposes);
– the content of basic anions (mg/l) for the identification of specific products (determined by the manufacturer);
– the trademark of the manufacturer (if available);
– the date of bottling;
– expiry date;
– storage conditions;
– the indexing of the document in accordance with which the product was produced and can be identified;
– information on conformity assessment.

Respiratory gymnastics. The elimination through the lungs is most effective in the case of chemicals with high volatility and low solubility in the blood (oxygen-containing substances, aromatic hydrocarbons, etc.).

Respiratory gymnastics increases the functional reserves of the respiratory system, provides the increased supply of oxygen, stimulates the central blood and lymph flow, the receptor zones of upper respiratory airways, ensures the elimination of chemicals and their metabolites with expired air, removes excess carbon dioxide, activates metabolic processes and biotransformation, helps to eliminate stagnation in the respiratory tract, facilitates expectoration, preventing the development of respiratory and lung infections, at regular use increases the strength of respiratory muscles. Breathing exercises improve the neuro-psychological state of sick children, have a general revitalizing action, activate the body defenses.

Exercises shall be held in the daytime by specialists in physical therapy during the whole period of preventive measures realization. The duration is 15–20 minutes.

The room for breathing exercises should be relatively spacious, well ventilated, clean, with good lighting. The temperature in the room should be 20–22°C, relative humidity - 40–60%. If possible, the room shall be equipped with filters, ozonizers or air ionizers.

The complex of respiratory gymnastics shall be carried out according to standard procedures.

Speleotherapy. Salt microclimatic chamber creates healing environment due to natural multicomponent aerosols of fine salt (represented by potassium chloride, sodium, magnesium), light negative air ions, radiation background, original microflora. The temperature of the chamber should be 18–20°C, relative humidity 40–70%, the total concentration of light bipolar air ions ranges from 2000 to 5000 in 1 cm^3, while there is a consistent relationship between positive and negative ions. The power of g-emission created by sylvinite does not go beyond 17 mR/hr; β-particles flux density on the surface of the salt blocks is on the average 28 cm^2/min. Speleotherapy has anti-inflammatory and secretolytic effect, normalizes osmolarity and rheological properties of bronchial secretions, stimulates the mucociliary apparatus, restores the functional activity of ciliated epithelium and improves the drainage function of bronchi (the activation of monoamine oxidase and serotonin metabolism by negative ions), all of which contributes to the elimination of chemicals. The parameters of pulmonary ventilation are rised by 35–40% (the activation of acetylcholine by air ions), the levels of lysozyme in

saliva are increased, the content of opportunistic pathogenic microflora in mucous upper airways is reduced, the level of general and local immune defense is increased against the background of speleotherapy.

Heat therapy. The stimulation of blood and lymph circulation, metabolism improvement, which contribute to the natural elimination of chemicals and their metabolites, take place under external heat exposure. This leads to decrease in the activity of inflammatory process, as well as the emergence of biodegradable and analgesic effect. Baths and saunas are the best known methods of heat therapy. The protective functions of the body are increasing during bath visit, under the influence of temperature in the range of 80°C. Alongside with local actions, heat therapy has a general effect on the cardiovascular, the respiratory and the digestive systems.

The optimum temperature in the sauna room for children under 5–7 years of age should be set to 55–65°C, for children under 8–14 years of age – up to 60–75°C, for adults – 90°C. The relative humidity should not exceed 20%, and usually maintained in the range of 5–15%. Higher temperature and humidity can lead to hyperthermia.

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4. THE METHODOLOGICAL BASIS OF RISK COMMUNICATIONS

4.1. General principles, methods, and the model of risk communications

Today, the expression "we live in a risk society" proposed by German sociologist U. Beck, 1992, is familiar to almost everyone and is almost commonplace in nature. However, rethinking of the conceptual scientific views on the risk category in all fields of knowledge was required before it appeared and passed into spoken language. In the 1960s, according to the philosopher A. Algin (1989), the risk ceases to be subject only to specific sciences and transforms into an object of interdisciplinary researches, acquiring the status of a general scientific notion. This was due to the fact that the extraordinary paces of industrial development in the XX century led to contradictory consequences: outstanding results in electronic, nuclear, space, energy technology, in chemistry, biology, genetic engineering were obtained, which put humanity forward to fundamentally new frontiers in all spheres of life, but on the other hand, unprecedented potential and actual threats to man, its local and global environment were created. In recent decades, these threats have been realized under the influence of the largest technology-related disasters on different facilities [Beck U., 1992; Giddens A., 1990; Luhmann N., 1993; Perrow S., 1984 et al.]. It results in a new scientific paradigm, the so-called "ecological paradigm" [Dunlap R., 1980] (as opposed to the anthropocentric), the achievement of which was the refusal of the opposition of nature and society and the emergence of the term "risk society" as an understanding of the production risks that is inherent to any kind of public production [Yaanitsky O.N., 2003]. Risk overcoming is possible at the combined activity of science and the public as equal partners. According to U. Beck, the role of the social sciences is to change the forms of interaction between science and society. U. Beck insists on the democratization of science, its greater attention to the needs of particular social groups and stratum, on the right of non-professionals to act as a "civilian experts" and media those who have local knowledge needed for the calculation of risk at a given place and time [Koroleva E.V., 2007].

Development of **risk communication theories** begun with awakening the enormous difference between the expert knowledge of the risk and common ideas of it, as well as the insufficient mastery of information about the risk by decision-makers [Fischhoff B., 1995]. This resulted in the idea of the need to build communication risk models, allowing all interested parties to participate equally in the discourse [Leiss W., 2004].

Currently, one of the key theories of risk communication in the field of health is the approach of V. Covelo [Covello V.T., 1986], which allows to characterize the communication as a task-oriented exchange of information about the values and levels of health risks, and how to reduce them between interested parties. This assumes that all subjects of communication have any information regarding the risks and are interested in its transmission to others and receiving the response, feedback.

We can distinguish five groups as subjects of the communication process:

1. Expert community – individuals possessing the most objective data on the presence of health risks and their levels. This group includes risk assessors, scientists, representatives of the health care system.

2. Population as a whole and its individual groups that are subject to risk.

3. Mass media.

4. Decision makers (DM) – public authorities, local government, the heads of enterprises, whose function is to manage health risks and to minimize them.

5. Non-profit organizations, whose task is to promote a healthy lifestyle (HLS).

In the communication process expert community has the aim to overcome the information barrier between science and society, inform all interested parties on the presence and level of health risk and how to reduce it in an intelligible form. It should be noted as **the first problem** faced by all the subjects of communication. Except for the expert community, with the same purpose, or "hiding behind" it, the so-called "pseudo-experts" who are not really experts on the issues under consideration, but who are presented as ones enter the communication process. They are, for example, masters of health dedicated talk-shows. They have become very popular among the population and give some recommendations concerning health risks. Another example are commercialized media reports / Internet (Network). The emergence of "pseudo-experts" has become possible due to the phenomenon of society medicalization. On the socio-cultural point of view medicalization is regarded as the penetration of medicine in many spheres of society, which previously had no relationship to it. It is a process in which human state or behavior is increasingly beginning to be defined as a medical problem that requires medical decision [Boyazitova A.N., 2007]. This phenomenon creates a special type of humans awareness of its existence by medical terminology coming into speech, and medicine inherent ways of analyzing coming in thinking. Such phenomenon incredibly strengthens the role and authority of an expert physician who becomes necessary to implement a successful existence, which creates a kind of dependence on it. Thus, people become vulnerable to false information on the health risks obtained from semi-professionals or lay persons, playing the role of someone else, which in itself is a health risk because the distorted information may result in improper behavior.

In addition to information on the risks directly from the experts and "pseudo exerts" who broadcast data mainly through the media, people use the informal channels of communication: communication with relatives, friends, through social networks. And here it is appropriate to specify **the second problem**, which is closely related to the first and consisting in the formation of a certain perception of population risks ("perceived risk"), which is often different from the actual or set values of risk ("actual risk" or "calculated risk"). Communicators consciously or unconsciously interpret, edit, select, highlight the key points in their messages, depending on the format of television or radio broadcasting, newspaper, magazine or website, if communicator is mass media. In turn, individuals themselves also tend to give their evaluative judgments, rethink those information they have heard or seen and, ultimately, to share with each other some new information product. It is a bit like a children's game of "Telephone", which eventually leads to an inadequate perception of health risks: their value can be very underestimated or, conversely, overestimated. Distorted perception of risk in one way or another is referred to as "a sense of resentment" [Sandman P., 1993]. This situation can be explained, *on the one hand*, by the fact that the original theory of communication have been developed linear models, which showed solution to only one problem – inform the addressee in order to influence on him, and thus, communication is treated as a process of persuasion (communication model of H.D. Lasswell (1948). Such models eliminate feedback with the addressee and, despite the development of communication theory, are still the working tool of information broadcasters that is often caused by commercial interests or elementary incompetence of agents. Thus, the reaction of indignation is provoked intentionally or unintentionally when the message is crowded with negative characteristics of health risk (threat, danger, harm, damage, etc.), and the addressee perceives the risk as significant, "terrible" or, on the contrary, refers to objectively significant risks passively, indifferently if the message has hidden or understated its actual levels.

Secondly, now the boundaries between the media and consumers of its information is getting fuzzy (mass media democratization [Mosko V. Wasko J., 1988]), in particular due to their integration into the network. A huge number of forums, sites and groups in social networks are dedicated to health problems, the layman becomes a participant and creator of information space comparable to the space of traditional mass media.

Based on the foregoing, the model of risk communication in the field of health can be represented as follows (Fig. 4.1).

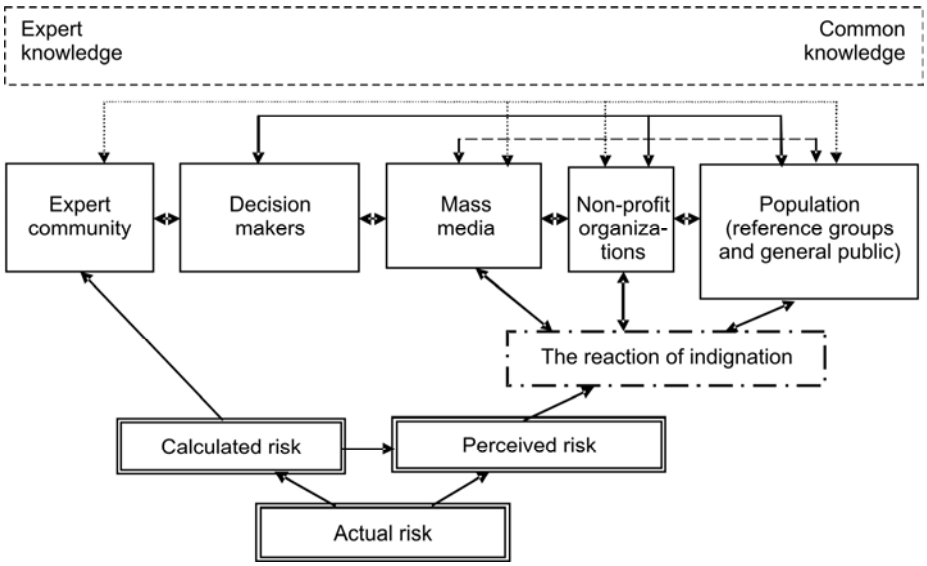

Fig. 4.1. The model of risk communication in the field of health
[Lebedeva-Nesevrya N.A., 2014]

Fig. 4.1 shows that all the participants of risk communication are the carriers of information and translaters at the same time. In determining whether there is any risk to health ("actual risk"), the expert community, which possesses special knowledge and skills sets its levels ("calculated risk"). It should be noted that experts and decision-makers tend to deal with the results of the risk assessment, which can not be said with respect to all other subjects of risk communication, which is already faced with a "perceived risk", i.e. information transmitted through informal interpersonal communications, different mass media and non-profit organizations edition. Therefore, messages reach the public through the prism of "reaction of indignation", amplifying or minifying risk values. A combination of socio-cultural values and stereotypes that are typical for society and social groups and formed by the subjects of the information and discursive field communication process, results in the reaction of indignation.

The sampled data of The All-Russian Public Opinion Research Centre (VTsIOM) may serve as an illustration[1]. For example, the theme of the consumption of foods containing genetically modified organisms (GMO), has recently been the subject of the general public and mass media. Such health risks at the use of GMO products as the occurrence of allergies, cancer, negative impact on the fetation and so on, which causes a very negative attitude of the population to this type of products are actualized in network. During the analysis of the results of VTsIOM research conducted in May 2014 (1,600 respondents in 130 settlements in 42 regions, territories and republics of Russia, the statistical error does not exceed 3.4%), it was found that 38% of respondents do not know what GMO abbreviation stands for, at that every second Russian (54%) would not buy products containing them. In the shop with two similar products 74% of respondents would rather buy a product without GMO, even if it is genetically modified analogue will be much cheaper. For comparison: in 2005 (All-Russian poll was conducted April 30 – May 1, 2005: 1,600 respon-

[1] VTsIOM official web-site: URL: http: //wciom.ru.

dents in 100 settlements in 40 regions, territories and republics of Russia, the statistical error does not exceed 3.4%), every fifth (21%) did not know what products are produced using GMO, but 68% of respondents expressed their unwillingness to consume them (including 45% – categorically not ready and 23% – more likely not ready)[1].

The above results of the studies give the evidence of the distorted perception of risk. The population is afraid of the possible harmful effects of genetically modified foods. Even people who do not know what a GMO is in reality are afraid of it. As a result, there is the formula "GMO → Hazard".

Concurrently with the mass survey in 2005 experts were interviewed (VTsIOM expert poll was conducted April 26 - May 4, 2005: interviewed 200 people by telephone interviews in 8 regions), and this additional data of All-Russian study is a specific example of the deep influence of the general orientation of the discussion among all communication parties on the reaction of indignation resulting in the inadequacy of risk perception. So, 200 experts were surveyed. They were asked one question: "Do you support a prohibition against the cultivation of genetically modified organisms in Russia until it will be finally found, whether it can have harmful effects on human health and ecology?" The experts were, firstly, farmers and agricultural workers. 68% of these respondents made affirmative reply, 14%, – negative. Secondly, the managers of grocery stores, made affirmative reply in 74% of cases (12% negative responses). Thirdly, doctors supported the prohibition in 86% of cases against 12% of those who had not supported the prohibition. Fourthly, deputies, civil servants (officials) in the field of health care and agriculture made such replies: 76% "fully support" and "more likely support".

It is necessary to draw attention to the choice of representatives of the expert community. It is obvious that the managers of grocery stores can not represent it, and their views are unlikely to differ from the position of a layman. Doctors and some representatives of the agricultural sphere are more competent, but we are surprised by the lack of genetic engineering specialists, microbiologists, etc. Nevertheless it can be seen as on a par with the broad masses of the population, people who are at a different level of awareness, lend themselves to general "panic" moods.

For decision-makers, the results of such studies are not only a marker of social attitudes and awareness about the risk, which serve as the basis for creation of informing programs, but also in general show how the process of communication is under way. Expert community (scientists, representatives of the risk assessment bodies, etc.) provides materials on decision-makers risk assessment and based on them strategies of risk mitigation measures and citizens, mass media and non-profit organizations informing about it are developed. The latest, in turn, realize the function of public informing. However, the public is not merely a passive recipient and consumer of obtained information. The public is actively involved in the process of risk communication through informal communication channels, creating discursive fields without institutional intervention. As the public reacts to information obtained from all risk communicators, it becomes the subject of feedback, acting as a social actor, which in turn addresses decision-makers through mass media and network.

The results of sociological studies show that on the whole the society is familiar with the discussion of the risks to health and formed a strong opinion as to their significance. Thus, according to another VTsIOM poll conducted in April 2014 (initiative All-Russian VTsIOM poll was conducted April 19–20, 2014: 1,600 respondents in 130 settlements in 42 regions, territories and republics of Russia; statistical error does not exceed 3.4%), aging is the main seeds of disease according to every third respondent (31%). Over the last decade, the relevance of this factor has increased significantly (in 2006 17% of respondents made a similar response). One in four believes that his health is deteriorating due to the unfavorable environment. 24% named stress as the main cause of poor health. One fifth of respondents (20%) complain about the lack of money for medicine, and 19% of respondents did not have enough time for treatment and recreation. Another 19% of respondents named heredity[2].

[1] Ibidem.

[2] VTsIOM official web-site: URL: http: //wciom.ru/index.php? id=459&uid=114815.

It is necessary to pay special attention to the acceptability of risk to society, social groups and individuals as a part of the development of risk communication strategies. The understanding of risk acceptability consists in the fact that its level does not cause the concern of the individual [Kuzmin I.I., 2005], and this can only be achieved taking into account social and economic considerations [Elokhin A.N., 2004], requires a decision on the acceptability of health risk as a social problem, essentially transforming the issue into a problem of the social acceptability of risk.

The acceptability of risk is perceived through the prism of benefits or losses that could be obtained or will be incurred by an individual or a group, assuming a certain level of risk.

Let us illustrate the acceptability of individual risk on the example of the results of the research on "The perception of health risk by Perm Krai population", conducted in 2010 by the experts of FBUN "Federal Research Center of medical-preventive technologies of public health risk management"[1].

The city of Perm is a major industrial center, characterized by a large number of industrial enterprises, as well as significant traffic congestion. Its population is exposed to health risks that are associated with the negative anthropogenic impact on the environment. Respondents know about the fact that the territory of citizens' living has negative environmental factors, that have effect on health, (*"it is very bad in the city, noise, exhaust fumes", "the environmental situation is not very good, city centre, cars, gassed, few trees", "our kindergarten is located next to the road, there's a lot of cars, children are running around, breathing this air ...", "life in the city with such production does a reasonably large harm to health"*). At that the risks associated with these factors are perceived as objective, independent of individual actions. The decision on the risk here is made only at the initial stage, for example, when someone selects the district to buy an apartment, then the events are no longer controlled by the individual. However, even at the stage of decision making the expected value of risk-taking behavior and the prospective yield from the safe behavior in relation to exogenous risks shall be assessed as low, while the expected costs of safe behavior shall be supposed as unreasonably high. These costs can be expressed in the need of the refusal of traditional way of life, additional time to move inside the city, increasing the financial costs of transportation, etc.. For example, a respondent B., 48 years old, living in the center of the city, her reaction to a possible offer to move to a more environmentally friendly, but secluded district, described as follows: *"I would have moved only if I drove the car*. *But since I do not drive a car, and public transportation annoys me, this is totally unacceptable for me".* So many people prioritize, partly showing the priority of their own psychological comfort to the probable changes in the state of physical health due to exposure to technology-related factors. Another respondent, K., 24 years old, also lives in the center of the city, responded to a hypothetical possibility to move as follows: *"No, I would not agree to move. It is important for me that everything is within my availability. I am very lazy person, I find it hard to get up even an hour earlier ... I have many friends in secluded districts, I see their problems with transport, etc., I do not want to live in secluded district! ".* The above statement makes assertions about the high value of the traditional way of daily life for the individual, which inevitably would have to change at the decision to move in an ecologically clean district. Thus, the motivational factors that determine the high level of acceptable risk in relation to exogenous risks can have not only economic but cultural, social, or psychological origin [Barg A.O., Lebedeva-Nesevrya N.A., 2010].

The acceptability of risk from the perspective of a social group or society as a whole is not only an assessment of the ratio of the risk level and economic and other costs on its reduction, but the assessment of the features of risk level perception by different social groups and the admissibility of possible damage from their point of view. This thesis is the

[1] Here and elsewhere, data of FBUN "FNTS UPRZN" social research conducted in 2010 by 2 stages: 1) 20 respondents, the method – semiformalized personal interview using semi-directive guide; 2) 1,068 respondents, the method – formalized personal interview at the place of residence and place of study.

basis of the concept of the integrated acceptability of risk. The term "integral" here reflects the consideration of interests and opinions of all the subjects of risk communication.

The efficacy of health risks communication is determined by the following parameters:

1) the readiness and propensity of subjects of risk communication to a constructive dialogue;

2) the ability of the expert community to provide information on the risks to various social groups and institutions;

3) the specificity of the reaction of indignation;

4) the ratio of the real risk, assessed risk and perceived risk.

4.2. The methods for the assessment and management of health risks perception by different social groups

Analyzing the data of sociological research on the health risks, the population awareness, the features of their perception, one can not forget the great work of the Austrian sociologist P. Berger and the American theologian T. Luckman "Social Construction of Reality". It discusses three dialectical moments of social reality: society as a human product, the society as an objective reality and man as a social product [Berger P., Luckmann T., 1995]. In this perspective, one can consider any social phenomena, including the risk.

Risk is produced by human. For example, a sedative "Thalidomide" made in Germany in 1954, which has not passed proper test, but widespread by pharmaceutical companies worldwide, has provoked a surge of children born with birth defects. Several years the drug was considered safe with no side effects, and the expert community supported the manufacturer's point of view. This makes it possible to say about health risk generated in the process of human interaction, which has acquired the character of objective reality. On the other hand, at the detection of heavy drug exposure on the fetus arising objective health risk become being perceived, filled with a variety of meanings and values, interpreted at the level of individual and group consciousness that allows us to describe it as a social construct.

That is the risk itself is no longer under consideration, but a kind of collective knowledge of it, which in turn forms the individual, subjective perceptions of the probability of an adverse event.

Not only individuals are the actors of the process of the health risks construction, but also social groups, organizations and institutions. For example, the formation of the reaction of indigation by mass media is an example of the risk construction.

Therefore, speaking about the perception of health risks, it is necessary to take into account the fact that a person has a set of judgments, assumptions and attitudes about risk and its consequences [Gavrilov K.A., 2007] that would determine whether an individual assesses the future situation as dangerous and how he/she calculates its probability. If the negative consequences are assessed as significant, the individual will behave in self-preserving way, but if the assessment of consequences, refracting through the particular features of the perception of a social subject (which often perceives risk inadequately, overstates or understates the probability of occurrence or value of negative consequences), comes to the conclusion of minor damage or lack thereof then the individual would be risk-oriented [Barg A.O., 2010].

Thus, in order to be able to talk about the methods for the assessment and consideration of health risks perception by different social groups, it is necessary to answer the question: what constitutes their opinions, views and attitudes? Firstly, belonging to the cultures and subcultures [Douglas M., Wildavsky A., 1982], secondly, the personal experience of the individual, the individual's social environment, the social contexts [Thompson M. et al., 1990] and thirdly, the existing system of values and preferences [Dietz T. et al., 1996] could be the source.

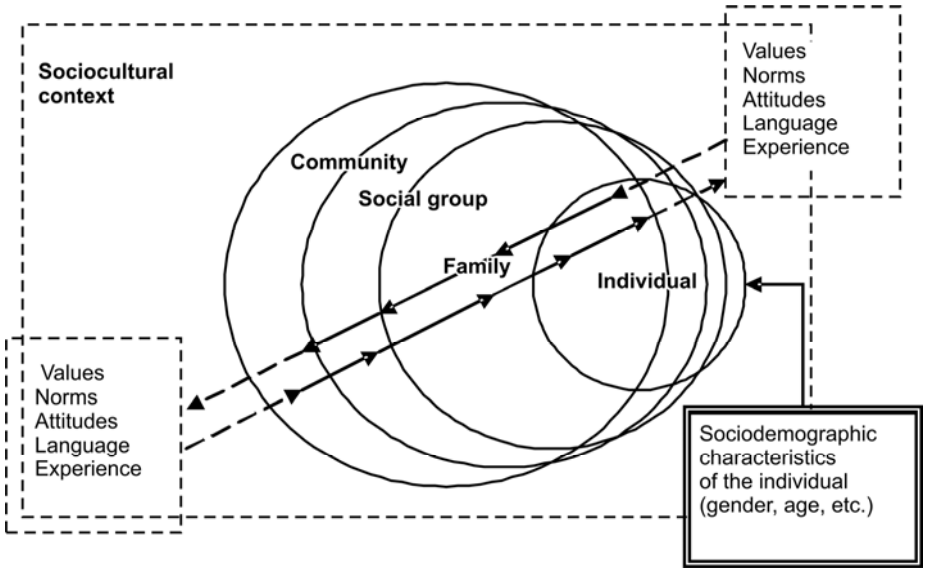

Fig. 4.2. Model of factors, which determine the perception of risk

If we analyze the bulk of approaches to the process of formation of the perception of risk, it is possible to present a model of factors, which determine them (Fig. 4.2).

On the basis of this model (Fig. 4.2), and based on the results of sociological researches, we can form a plan to build a research tool that will identify and make the account of perception features.

1. It is necessary to obtain information on socio-demographic characteristics of the individual (gender, age, education, occupation, marital status, presence/absence of children, income, nationality, ethnicity and religion). These objective parameters of the human who perceives risk show his/her social status, main roles, belonging to any culture, partly give the opportunity to present social environment, the membership of a particular social group.

Here are some examples of how some of these characteristics affect the perception of health risks. The data mentioned in the previous paragraph of sociological study of the perception of health risks by Perm Krai population imply that gender, age, education determine the significance of behavioral factors in the formation of the health for the individual.

Young people and people with the low levels of education are more likely to underestimate their importance in comparison to those who have higher or incomplete higher education and belong to the older age cohorts. In the group of respondents with a basic special education one third of respondents believe that smoking is not one of the leading risk factors of disease development, whereas in the group of respondents with higher education such a response made 12.7%. Among the students of specialized secondary educational institutions 28.6% think that the harm of smoking is greatly exaggerated, and among the working population this judgment expressed only 17%.

Another example shows that age affects the overall health value. Its value is increased with the age increment. Older respondents pay more attention to health, which is reflected in the responsible health behavior (preventive examinations, the implementation of the recommendations of doctors). Among people with children, the degree of their responsibility for the health of the child increases with the age increment. For example, older parents (regardless of the age of the children) often demonstrate competent health behavior (for example, regularly pass the necessary medical tests of a child for timely diagnosis of hereditary diseases).

2. It is necessary to identify the individual settings and the type of behavior with respect to health (the self-assessment of health, the degree of personal responsibility for it, activity/inactivity in the implementation of self-preservation behavior).

The same study also found the perception of behavior risks dependence on the settings and types of behavior. If the health is assessed as a good, and the key role in its support is assigned to individual actions, the behavioral risks are assessed as more dangerous and everyday life is dominated by active behavioral practices. On the other hand, at the low degree of personal responsibility for their own health and negative characteristics of its condition the perception of behavior risks is not quite adequate, the risks are underestimated, and the human is passive in the implementation of self-preservation behavior.

For example, the respondent Sh, 44 years old, satisfied with her health ("*I am absolutely healthy, 100%"*) and feeling a high degree of responsibility for her own health ("*My health depends on me almost completely*"), perceived behavioral risks as extremely important ("*to be healthy, we need exercise, sports, healthy food. We should fortify the immune system, take interest in disease causes, symptoms. Take measures timely*") and, as a consequence, implementing a healthy lifestyle ("*move a lot","do not drink, do not smoke", "I eat natural fortified food", "at work, when necessary, I always pass a medical examination timely")*. Another respondent S., 41 years old, talking about the weakness of her health (*"I am far from being a healthy person, because" it hurts here and there"*), is inclined to see the cause of the situation in the low efficacy of the Institute of Health (*"they consider that the prevention is a waste of time for themselves and for patients, and make no bones about it", "vaccinations ... administer wrong to observe formalities"*) and the impact of environmental factors (*"our city is rather messy, it can badly affect the health, running in the morning will not help", "clean air and good environment are necessary to be healthy"*), but underestimates the impact of her own actions on health ("*I smoke now, though gave up smoking. Not to say that it was better").*

3. It is necessary to conduct a comparative characterization of actualized human needs (i.e., determine what is more important – health, welfare, professional consistency, calmness, absence of changes, etc.).

An important determinant of the inadequate perception of health risks is the presence or absence of benefits associated with the risk that is associated with the satisfaction of a particular need. For example, exogenous risks associated with residence in a zone of high man-caused impact can be compensated subjectively by good transport accessibility of the district, its central location, proximity to social infrastructure, etc. When asked about the desire to move to a district with a more favorable environment, only one sixth of the surveyed residents of the territories with the high levels of anthropogenic impact expressly answered "yes", while the majority of respondents chose the option "yes, but under certain conditions." It is significant that the second group of respondents characterize the environmental situation in their place of residence as a more prosperous, compared with the first group of respondents.

4. It is desirable to determine the level of institutional trust (trust in the institutions of health care, mass media, education, etc.).

The high level of untreated diseases is largely due to the delayed visits of a doctor, insufficient treatment, the ignoring of preventive examinations, i.e. the low medical activity and irresponsible behavior of the population (*"I visit a doctor only in very neglected case and mostly it is gynecology" (K., 34 years old), "I do not visit doctors. Preventive medical examination was conducted, I did not visit any doctor" (D., 24 years old)).* The underestimation of the significance of risks generated in this type of behavior, is largely due to the low level of trust in the Institute of Health, which develops in the interaction with medical staff, doctors, presence in health care facilities *("I do not like to go to hospitals, I'm irritated by lines at polyclinics, I do not like the attitude of the doctors", "I trust in all doctors ... then realize that I should not do it ... Two doctors for 2 days made completely different diagnoses").*

5. It is necessary to provide the awareness of risk factors and anti-risk practice, which ensures human resistance to the harmful effects of external ecological and social environment.

The majority of respondents (72.5%) believe that the refusal of bad habits (smoking, alcohol overindulgence) will help to protect oneselves against cardiovascular diseases in the first place, while proper nutrition, the refusal of foods high in cholesterol as anti-risk factor are mentioned only by 33.6%, and the avoidance of stresses, nervous tension is mentioned by 37.0% of respondents. The perception of oncological diseases is more adequate: in 50.9% of cases the respondents believe that preventive examinations, timely visiting a doctor are the leading factors of the anti-risk of cancer, 56% of respondents mention refusal of bad habits (smoking, alcohol overindulgence). However, the population underestimates the proper nutrition, the refusal of foods high in cholesterol (mentioned only by 24.3% of respondents) and the avoidance of stresses, nervous tension (mentioned by 34.5% of respondents) as anti-risk factors.

6. It is necessary to find out the attitude of the individual to risk the factors of different nature.

A characteristic feature of the perception of health risks is a reassessment of the importance of environmental risk factors at underestimation of the importance of lifestyle factors. According to modern scientific ideas [Lisitsyn Yu.P., 2010], the total contribution of lifestyle factors to the performance of human health is 50–55%, and environmental factors (air, soil, water pollution, radiation, magnetic and other emission) – 20–25%. Among the surveyed residents of Perm Krai, only a quarter of respondents adequately assess the role of these factors in the formation of human health. The skewness of responses distribution at the assessment of the significance of environmental factors: (–) 0.511 (a shift towards higher values), at the assessment of lifestyle factors – 0.687 (a shift towards smaller values). The majority of respondents have the aberrant perception of the role of genetic factors in the formation of human health – 33.5% underestimate the importance of inherited predisposition in disease determining, 25.5% – inflate, 10.5% – find it difficult to assess the contribution of these factors. The observed discrepancy between objective and subjective judgments regarding the role of various risk factors is primarily caused by the nature of the risk – whether it is voluntary or compulsory, and what a degree of individual risk controllability. "Forced, uncontrollable risk is perceived as more dangerous" [N. Kogan, 2008].

The features of the perception of socially determined and exogenous risks to the health of children of preschool age were established based on the analysis of the results of another survey conducted by the employees of FBUN "Federal Research Center of medical-preventive technologies of public health risk management" in the spring and summer of 2010. [N.A. Lebedeva-Nesevrya, 2014] in 6 municipalities of Perm Krai (the city of Perm, Krasnokamsk, Chusovoi, Ilinskii, Uinskoye, Chastye). 642 respondents, the method – the dispensing survey of the parents of preschool children attending educational institutions for children. The type of sample – probabilistic, cluster (95% confidence probability, ±4% confidence interval).

The analysis of the results of the study showed preschool children parents' underestimation of the importance of behavioral health risks against the increased exogenous risks concern. Thus, the factor load index[1], which shows the direction of public opinion in assessing the potential of the impact of various risk factors on children's health, according to the factor of "water contamination" and "air contamination" is 0.94 and 0.91, respectively (at the maximum level 1). The value of the specified index of "unhealthy diet"

[1] Load factor index (I) indicates the ratio of the number of groups with opposing assessments of the significance of the potential impact of factors on the child health. It is calculated by the formula $I = \frac{(n_1 + n_2 - n_3 - n_4)}{n}$, where n_1 – number of respondents who specified an option "very strong effect», n_2 – "rather strong effect", n_3 – "rather mild effect", n_5 – "very mild effect», n – the total number of respondents who gave a valid response. The index value ranges [-1; 1]. A positive index value indicates the predominance of respondents in the studied group who believe that the factor has a negative effect with higher than the average intensity; negative – the predominance of those who believes that the negative impact of factors on the health of the child is rather or very mild; values close to 0 indicate a roughly equal number of the ratio of two groups.

was 0.76, "child breaches of personal and household hygiene" – 0.72, and "failure to comply with day regimen" – only 0.38 (Table 4.1).

At small proportion of respondents giving generally low assessments of the negative impact of ambient air and drinking water pollution on child health (4.5 and 2.8%, respectively), the percentage of parents who are prone to underestimate the possible negative effect of behavioral factors, is extremely disturbing. Thus, 12% of respondents believe that unhealthy diet is not able to impact on the child health significantly; 14.4% of respondents make similar conclusions about low motor activity, 19% – about relatively unfavorable living conditions.

Table 4.1

Factor load index values

Ser. No.	Risk factor	Index value
1	Water contamination	0.94
2	Air contamination	0.91
3	Unhealthy diet	0.76
4	The delayed visits of a doctor	0.76
5	Adverse family atmosphere	0.74
6	The breaches of personal and household hygiene	0.72
7	Insufficient access to fresh air	0.72
8	The lack of physical activity	0.71
9	Uncomfortable living conditions	0.59
10	Dirt and debris in the streets	0.58
11	The non-complience of day regimen	0.38
12	The high level of noise	0.37
13	Stay in a group of kindergarten	-0.63

The lowest potential of negative impact factor among the behavioral risk factors proposed to parents for assessment in the course of questionnaire survey has been set for "non-compliance of day regimen". Thus, 30.6% of respondents said that the possible impact of this factor is "very mild" (4.6%) or "rather mild" (26.1%). There is the insufficient awareness of parents that irrational day regimen can lead to intellectual and physical and psycho-emotional stresses. Among the responses to open-ended question: *"What are the negative consequences for the health of the systematic non-compliance of the day regimen by the child?"* – vague statements like *"onset of diseases", "various disorders", "health problems*" were prevalent, in rare cases, respondents suggested options such as *"nervousness", "irritability," "emotional instability"*, etc. A significant proportion of respondents could not answer the question.

The results of studies [Garbuzov V.I. et al., 1977] show that the adverse psychological atmosphere, negative intrafamilial climate, strained relationships between family members not only determine the mental illness of the child, but also affect the performance of its overall development, provoke sleep disorders, nutritional disorders, etc. In the survey, 13.2% of respondents, however, said that psychoemotional state in the family is not able to exert significant influence on the child's health, which indicates a lack of awareness about the psycho-hygienic aspects of preschool age child-rearing.

In families where at least one parent has a university degree, the potential of the negative impact of stress-filled psycho-emotional microclimate on child health is of higher value. Thus, in the group where both parents with higher (including incomplete) education, 84% believe that this factor can have a dramatic impact on the child's health, while "rather mild" and "very mild impact" were chosen by only 1.6% of respondents. In the group where both parents have less than incomplete higher education, the option, which marks the highest degree of factor impact was selected by 63% of the respondents, and options, which reflects the low and very low levels of impact were selected by 18.3% of respondents. The

correlation coefficient of "parental education" and "the assessment of the potential of the negative impact of adverse psycho-emotional climate in the family for the child's health" variables was 0.223 (weak correlation), $p<0.001$.

Despite the fact that the majority of parents (87.4%) are confident in unhealthy diet's ability to have a significant negative impact on the child's health (among them 53.5% characterize this impact as "very strong"), the level of the respondents awareness in the sensible nutrition of children can not be considered as fully adequate. Thus, 45.2% of respondents believe that bakery products should not be included in the daily diet of the child of preschool age; 47.8% of parents believe that cereal and pasta should be excluded from the daily diet; 54.5% believe that daily intake of eggs is excessive, 27.7% believe that daily intake of fish is excessive. Responses to open-ended question: *"What are the negative consequences for the health of the systematic eating disorder and non-compliance of the dietary structure by the child?"* – were rather general: *"health disorders", "various diseases", "diseases", "health problems"*, more concrete answers – *"diseases of the gastrointestinal tract," "digestive diseases", "disorders of the digestive system,"* etc.

The underestimation of the importance of particular risk factors impact on the child's health leads to the implementation of behavioral practices that do not conform to the principles of self-preservation behavior.

In the group of respondents, 29.7% of parents said they often or regularly fail to put baby to bed on time, another 28% said that they face similar difficulties, *"sometimes, from time to time".* The most common cause of sleep abnormality is hyperactivity, excessive restlessness of the child before bedtime (this cause was indicated by 46.3% of parents).

Over a third of parents (35.2%) noted the absence of a set diet out of kindergarten, stating that the child is fed *"when he/she wants,"* or *"at haphazard".* Many parents find that the systematic inclusion of "bad" foods in the child's diet is normal. Thus, 44.9% of respondents indicated that their child frequently or constantly eats sausage products, 39.6% – mayonnaise and ketchup, 16.2% – chocolate bars; 12.0% of parents regularly buy chewing gum, 9.3% – sweet carbonated water, 8.4% – the Chupa Chups. There is a weak negative correlation between the level of education of parents and the frequency of inclusion of "bad" foods in the child's diet. For example, in families where both parents have a higher education, sweet carbonated water is never included in the child's diet in 56.3% of cases and in families where both parents have no higher education, similar behavior is implemented only by 30.4% of respondents (r=(–) 0,199, p<0,001).

To characterize the prevalence of behavioral risk factors associated with physical activity, we have studied issues concerning the physical education of a child: morning exercises, physical exercises on the development of individual muscle groups, exercises in sports clubs. It was found that children in 43.5% of cases do not fulfill morning exercises at home (the parents themselves allow to neglect exercises). In 18.1% of cases, children are engaged in physical exercises at home with a frequency of more rarely than once a week and 17.3% – do not perform any exercises at home. The most common motive in refusing to engage with the child is the statement that *"children are already very active."* In this case, there is a low level of parents' awareness about the fact that while the growth the child losses mobility associated with the games, and the need for physical training may be unformed.

Despite the fact that the majority of respondents (97%) believe that namely parents have the primary responsibility for maintaining the health of the child, recognize their dominant role in shaping a child's healthy lifestyle skills, the basic ways to manage health risk are recognized and articulated by them rather weakly. Thus, 22% of respondents strongly agreed with the statement that "*parents can generate a child's healthy living habits, even if they do not live a healthy lifestyle*" still 33.2% of respondents rather supported this statement. This indicates a lack of the parents' understanding of the mechanisms of formation of the child's healthy living habits, which are based primarily on imitation and social stereotyping. Parents assign the wrong model of behavior, imposing negative attitudes. Only 11.3% describe their way of life as completely healthy, the others recognize that implement adverse behavioral practices in their daily lives (for example, 28% of adults smoke in the family room in the presence of a child).

The established features of the perception of socially determined and exogenous health risks require the construction of an effective system of risk communication, which shall include all interested parties.

4.3. The methods of health risk communication

Effective risk communication is based primarily on clearly and consistently stated quality information. It is brought to the recipient timely and actually defines the process of risk communication.

The first thing to consider at reporting on health risk – for whom the message is intended, i.e., the commutator must comply with the principle of information ***targeting***, realize its intent for a particular social group (the parents of preschool children, youth, high school students, etc.). This simplifies the choice of the means of communication (language, communication medium) and allows achieving greater efficacy of the communication process.

Relevance is the second point. The message should be timely, urgent, have value for a decision in the field of risk management at the time of its use. It is also important to determine the ***scope*** of material to be transferred to the recipient. In order the addressee (non-expert) fully understands the problem and has the opportunity to take a decision on the specified health risks, the information should be sufficient. The desired effect upon receipt of the message is the absence of questions from the recipient. In addition to the completeness of information the principle of its ***availability*** should be complied. Dissemination channels should first of all be familiar and in the confidence of the information object. For example, according to the analysis of survey results conducted in the spring and summer of 2010 by experts of FBUN "Federal Research Center of medical-preventive technologies of public health risk management" on the features of the perception of socially determined and exogenous risks to the health of preschool age children[1], it became known that with the need for information about risk factors to children's health, most parents turn to mass media rather than specialized publications and scientists. The immediate social environment – friends and relatives, kindergarten teachers and health workers in kindergarten, district pediatric physicians are reference figures in relation to the acquisition of information on health risks. The analysis of the survey results showed that 51.4% of respondents derive information on health risk factors mainly from TV, 45.7% of respondent get acquainted with publications on relevant topics in newspapers, magazines, 22.5% – in the Internet. In this case, more than a third of respondents believe that publicly available sources provide insufficient information on the exogenous and social risk factors on children's health [Lebedeva-Nesevrya N.A., Barg A.O., 2011].

A further aspect of literate information can be described as ***getability*** (cognitive accessibility). It is necessary to consider such socio-demographic characteristics of the recipient, as the level of education, age, gender, membership of a particular social group, etc. at the selection of the style of language and the explanation of special terms. This will increase the probability of a correct perception and understanding of the information received. The further ability of the recipient to use the data in decision-making in the field of self-preservation behavior is one of the tasks of health risk communication. To solve this problem the message should contain practical guidances on the development and implementation of health saving behavior strategies. Thus, the information takes ***practical significance.*** Data transmitted by the communicator must be ***reliable*** and objective. Personal assessments and judgments should not be brought in order to avoid the imposition of a point of view: the addressee should be allowed to form his/her own position.

[1] The method – dispensing survey of parents of under school age children attending educational institutions. The sample size is 642 people. Type of sample – probabilistic, cluster (95% confidence probability, ±4% confidence interval).

If you observe the stated principles of information, it will be possible to ensure the formation of systemic medical and hygienic knowledge of the population, improve the hygiene and medical literacy of information and develop sanitary and hygienic culture of the society. It will also reduce the prevalence of individually deterministic health risk factors and form commitment to health saving behavior models. The reduction of social tensions due to the high prevalence of unconfirmed (distorted, incomplete) information on the health risks might become an equally important result. The inclusion of persons responsible for maintaining and improving the population health in health risk management system is required for the implementation of effective communication.

With regard to the ***information content***, it can be structured according to the methodology of risk analysis, which assumes:

1) the identification of risk factors;

2) the proof of their role in human health disorders;

3) the quantitative characteristic of adverse effects dependences on the levels of specific factors impact;

4) the determination of effective ways to validate and select management decisions on the regulation of the impact of risk factors on human health.

Having the *information on the factors that may have a harmful effect on human health*, and the relationship between risk factors and health disorders provides an understanding of what increases the probability of disease. It is important to note that information on the risk factors of various etiologies shall be provided separately by selecting a channel for each message, and it is desirable to issue messages partially, but consistently and systematically. For example, the propagation of information on medical and biological risk factors for the child's health, which include, in particular, the features of antenatal, intrapartum and postnatal period, genealogical history burden, etc., is rather a function of the health care system. The district pediatric physician, general practitioner (family doctor) during the examination of a child is able to inform parents about available medical and biological health risk factors in qualified, targeted and purposeful way, with regard to the features of the recipient of information, and thus more efficiently than other social agents. If we talk about exogenous (chemical and physical) health risk factors, which include the chemical contamination of ambient air, drinking water, food, noise, vibration, etc., consideration must be given to the fact that these factors are usually not subject to management at the individual level, and as a consequence, dictate an increased level of anxiety. Although the World Health Organization confirmed that human health only to 20% depends on the state of the environment, according to the VTsIOM poll conducted in April 2014 (initiative All-Russian VTsIOM poll was conducted April 19–20, 2014: 1,600 respondents in 130 settlements in 42 regions, territories and republics of Russia; statistical error does not exceed 3.4%), 30% of respondents believe that bad environmental conditions are the main reason for health problems[1]. As a guideline to the authors of information material about the environmental factors of health risk, we shall note that the message must be scientific in nature, but it is better to avoid the abundance of special terms at choice of language and form of its presentation.

The list of health factors risk is significant and population should have an understanding of the full range of potential threats. However, due to the differential impact of risk factors on health, priority information should be to provide data on the priority factors of different nature.

Information on the health risk characterization is the most difficult for understanding. This applies either to decision-makers and the general public. The "risk" category is understood by specialists as the probability of a threat to life or health. This probability is quantitative and identifiable as well as the severity of adverse effects on the life or health of citizens in the implementation of procedures for health risks assessment. However, quantitative risk values will hardly mean something for a layman without some explanations.

[1] VTsIOM official web-site. URL: http: //wciom.ru/index.php?id=459&uid=114851.

This was confirmed in the framework of approbation and clarification of new tools for quantitative sociological research on "Risk communication in the field of health."[1]

The employees of FBUN "Federal Research Center of medical-preventive technologies of public health risk management" in May 2014 held a focus group study among psychology students of the Institute for Advanced Studies – RMTSPK GOO DPO. 11 women with higher education took part in a talk. The group was not homogeneous in age (23 to 58 years) and the professional composition of participants (1 lawyer, 1 doctor, 2 educators, 1 *PR*-manager, 4 housewives, 1 recruiter, 1 tourism manager). During the talk, it was found that none of the participants understand the meaning of the expression "the risk is $1 \cdot 10^{-6}$ or $1 \cdot 10^{-3}$," such a numerical expression of risk as 0.000001 or 0.001 also was difficult to grasp[2]. *"In general, I do not absorb such numbers! It is easier for me to percept words"* (respondent O., 36 years). Other respondents had similar reaction to the question: *"Why do not you explain normally? If I just hear that there is at least some risk of cancer, I'm scared, and the numbers do not make it clear, they obfuscate me"* (respondent K., 45 years). Consequently, the information on health risk characteristics will be more effective if it includes such components as a ranked list of risk factors on the level of danger and the list of critical organs and organism systems that fall under the influence of the priority risk factors. It is also important to identify the level of risk compared to an acceptable level (with an indication of the level of impact at which adverse effect is not observed). The task of Information is answer an addressee's question: "How does a risk factor operates?" and "What are the consequences of this action?" However, this is not enough, because if a person knows about the threat to his/her well-being and understands exactly the possible responses from health, but is not informed about how to deal with it, then comes a sense of increased anxiety, and in the process of risk communication – "the reaction of indignation ". Therefore, risk communication must include *information about* undertaken or planned (in the case of exogenous risk) or recommended (in the case of social risk) *health risk management methods*. This means that, in the case of exogenous risk factors in the process of informing the addressee should be given information about

a) the measures taken to reduce the risk ("what is being done to reduce the risk?")

b) the subjects of measures ("who implements these measures?")

c) the probable efficacy of risk reduction measures ("whether the measures taken are effective?")

d) the level to which the risk will be reduced ("will a threat remain in the future?").

In addition, at feasibility of actions to reduce risk at the group or individual level, it is necessary to include corresponding recommendations in the information message. Thus, the task of propagation of the information on the methods of health risk management is to form a clear idea about the fact that the risk can be reduced, to provide a sense of control over the event of risk. It is human's consciousness of himself/herself as a person who knows, understands the situation, and to some extent controls it, is the criteria for the success of the risk communication process [Zykova I.A., Arkhangelskaya G.V., 2007].

The risk is not only an objective and knowable fact, but always mediated by social and cultural attitudes and processes. Non-specialists in their perception of risk are oriented not only on its quantitative characteristics and possible health effects, but also on the already formed public opinion, the degree of confidence in propagated data about risk factors, because of their emotional impact [Onishchenko G.G. et al., 2002]. A person or group of people reaction to risk is defined by different determinants regarding both socio-psychological, value, emotional, and other characteristics of the individual or social group, and the risk or information about it (a source of hazard, potential consequences and their severity, a diversity of obtained information on risk, etc.). The account of risk perception by different target groups is intended to improve the efficacy of information process [Zaitseva N.V., Lebedeva-Nesevrya N.A., 2010].

[1] The research is supported by the Russian Foundation for Humanities ("Risk communication in the management of population health at the regional level" No. 14-16-59011a/(p)).

[2] The audience was asked: "How do you identify "cancer risk is $1 \cdot 10^{-6}$, or 0.000001?"'

The difference between risk assessment and risk perception is determined, firstly, by risk features. The risk may be *voluntary*, i.e. person knows about the health threat, but for various reasons takes the probability of an unfavorable outcome and does not change his/her risk behavior towards self-preservation. As an example, addictive behavior (smoking, alcohol overindulgence, etc.). Risk *forcibility* and *uncontrollability* are other signs (even knowing about it, person have no power to do anything). The examples are exogenous risks, talking about which people often say: *"What can I do? What can I change?"* With respect to ecological risks the passive acceptance of risk as an inevitable consequence of the non-free choice of the actions is typical ("that is ecology, we can not change it," "it [contamination] is normal for the city"). A low level of awareness about the ways to reduce the negative effects of anthropogenic impact through individual actions is also characteristic: *"I do not know how to protect myself from chemical emissions,", "I only know about the air ionizer, I read about it, but do not believe they will save me from this* [the harmful man-made effects]" [Barg A.O., 2010]. It is risk forcibility and uncontrollability that lead to person's increased concern and anxiety. Taking into account this feature of perception, the information materials should include the comparative risk characterization of different nature according to importance extent, emphasizing the seriousness of the impact of voluntary risks on health. We should also note such features of risk as *familiarity* or *non-familiarity*. On the one hand, it is known that everythig new is perceived as more dangerous. People treat any new information with caution and a certain degree of mistrust, on the other hand, well known information does not seem "scary." Familiarity becomes the equivalent of normality. Hence, any unknown risk is considered as higher regardless of its actual value. For example, according to the study conducted by the experts of FBUN "Federal Research Center of medical-preventive technologies of public health risk management" in December 2013 and aimed at studying Berezniki population's perception of health risks associated with the problem of Earth crust break in its territory, it became clear that a third of the population become concerned about Earth crust breaks less than 2–3 years ago. This is due to formed familiarity with the risks and their transformation from an emergency situation into something everyday [Barg A.O., Lebedeva-Nesevrya N.A., 2014]. This effect induces to include materials about the risks that are not typical for the object of information, comparison with usual risks of a similar nature, preventing the re-assessment of the importance of extraordinary risk by the target audience. The *presence* or *absence of benefits* associated with risk also determines the features of its perception. If the risk is associated with any benefits that from the individual point of view exceeds health problems, the risk is subjectively perceived as less significant and the level of concern regarding this risk is reduced. Benefits may take various forms – from material to psychological – and often connected with the satisfaction of certain wants and emotions. Needs do not exist independently of each other and often competitive with respect to each other [Simonov P.V., Ershov P.M., 1984]. Thus, it is impossible to simultaneously satisfy the actual need for health and smoking. At the same time the need for nicotine generates a strong negative emotion of abstinence along with the memory of the positive emotions of pleasure from smoking [Barg A.O, Lebedeva-Nesevrya N.A., 2010]. This feature of perception supposes the inclusion of emotionally colored component, which emphasizes the benefits and does not allow to underestimate the risk and overestimate the benefits in health risk information materials.

Secondly, the difference between risk assessment and risk perception is determined by the ***characteristics of risk information.*** At the selection of a channel and message translator in the process of health risk information it is necessary to pay attention to the degree of confidence in the source. There is a direct relationship of confidence in the message on reliance, which is formed both at institutional and individual level. For example, according to the Public Opinion Foundation (FOM) study data ("FOMnibus" – a poll of Russian citizens 18 years and older conducted in September 2, 2012, 43 subjects of the Russian Federation, 100 settlements, 1,500 respondents (home interview); statistical error does not exceed 3.6%), the level of confidence in the institute of health is quite high. So, 60% of our citizens trust in doctors and 28% do not trust. The half (52%) of the respondents

have more confidence in public health facilities, 18% – in private health facilities[1]. State media is in the confidence of 62% of the respondents of another survey conducted by the Public Opinion Foundation in March 2014 (FOMnibus is a survey of Russian citizens 18 years and older conducted in March 23, 2014, 43 subjects of the Russian Federation, 100 settlements, 1,500 respondents. Home interview. Statistical error does not exceed 3.6%), 16% of respondents trust in non-state media[2]. Thus, it is necessary to take into account the level of institutional trust at choosing a channel of information.

On a personal level, confidence is formed on the personal perception of the informant addressee, so honesty, openness and friendliness of the transmitter are necessary at the presentation of risk information. At personal provision of information to the audience you should not try to answer poorly understood or controversial questions; be prepared to answer "I do not know"; not express an unscientific point of view on issues related to the impact of risk factors on health [Onishchenko G.G. et al., 2002].

The relevance of information about the risks to the needs and interests of the target audience is also important. It is the desire to meet the needs that encourages people to act. If a message containing information about the risks to health, does not satisfy the actual needs of the audience, it is either looking for necessary information through other channels, or suppresses the need for this kind of information, and thus its activity. A layman is most interested in information about the probability of the occurrence of a disease due to the impact of risk factors, as well as forecasts of these factors impact. Thus, at health risk communication you should apprise the existing information needs, monitor the dynamics and promptly respond to their appearance. The content of information messages could be updated according to obtained data. The consideration of the needs and interests of the target audience can improve the efficacy of information process due to the effect of the psychological mechanism of selective perception, expressed in terms of the resonance principle: information, which meets the needs and values of the individual is perceived faster than information, which does not meet ones.

One of the most important points relating to information about health risks, on the one hand, is its *diversity* and often *multidirectionality*. There is a risk of the loss of recipients' confidence because of the mismatch of opinions and judgments in different sources. Thus it is necessary to take measures for the coordination of informants (actual and potential), so that they could appear with common science-based opinion concerning information on health risk assessment and its explanation. On the other hand, the lack of official information increases the probability of the emergence and propagation of unverified data by informal communication channels. At that the higher the uncertainty, the greater the confidence (positive attitude) in the informal sources of information, in order to reduce the level of anxiety of the recipient [Bezzubtsev S.A., 2003].

Thirdly, the difference between risk assessment and risk perception is determined by the *characteristics of the object of information.* This, above all, is the *psychological characteristic* of the individual, affecting the perception of information. Apart from the individual characteristics of a person, there are two psychological processes that certainly affect the perception of information by everyone without exception:

1. "Availability heuristic" (the person who makes the decision, "assesses the frequency or the possibility of events on the ease with which examples or cases come to mind") [Kahneman D., Tversky A., 1979]. If a person obtains information about the health risks, the first thing he/she does, is the intuitive sorting of anecdotal evidences in memory, that would confirm or deny the message being analyzed. For example, the message says that smoking increases the risk of lung cancer, but if the individual can not remind of any single example from his/her personal experience and confirming heard information, he/she will be inclined to assess this risk as less significant.

2. "Cognitive dissonance" (the existence of contradictory relations between the individual elements in a system of knowledge) [Festinger L., 1999]. For example, a message

[1] the Public Opinion Foundation official web-site. URL: http: //fom.ru/Zdorove-i-sport/10866.
[2] Ibidem.

about smoking harm to a smoker is unpleasant and comes into conflict with some of his/her attitudes and beliefs. When an individual desires to get rid of the discomfort, he/she always tries to somehow reconcile the conflicting elements of his/her knowledge, so in the case of smoking, he/she can rationalize his/her behavior by the thesis that the risk is not great because he/she is in good health, and that if he/she would give up smoking, he/she would put on weight. For all these reasons, it is necessary to consider this kind of psychological "trap" and include "work with the objections" into the process of the information on health risks.

Socio-demographic characteristics of the individual, such as education, gender and age are equally important for the perception of information. These parameters affect the degree of understanding of the message, and the confidence in the information translators and propensity to the critical assessment of new knowledge. Thus, the higher the level of education, the easier the recipient of information masters and understands it. Or the older the recipient of the message about health risks is, the more closely he/she relates to it. On the contrary, young people due to their special emotional sensitivity, desire to take risks and pursuance of "freedom", and also because of the prevailing social culture of the consumption of alcoholic beverages, which is quite contradictory, since, on the one hand, this demonstrates behavioral practices as the norm and on the other – condemns, in most implements negative behaviors, treating it as a normal phenomenon, not adequately assessing the risks [Barg A.O., 2011].

Thus, if you will take into account all the factors affecting the perception of information about the health risks at the formation of information strategies, it is possible to increase the efficacy of the process of risk communication in general.

Separately, it must be said about the great significance of an approach to *the selection of information channels*, which are divided into mass, group and individual. In respect to mass channel, it is necessary to understand that it is designed for the general public and there is no possibility to take into account any particular characteristics of recipients. A message sent through mass communication channel should be general in nature, focusing on the evidence material base. Material structuring should be done in such a way that minimizes the possibility of the translator evaluation comments.

Another option of substantive content of the information assumes the group transmission channel. Here it is possible to focus on a specific target audience, with its features, values and attitudes. Detailed information about health risk is achieved through individual propagation channels. The selection of channel depends on the goals and objectives assigned to the risk communicator and the following characteristics act as selection criteria:

1) accessibility (the addressee must be able to address the source, such as a web or television);

2) the ability to provide information as required (a time limit of broadcasting is possible);

3) channel typicality to the target audience (i.e. the recipient is used to refer to this source in the search of information on the matter of concernment);

4) the degree of "accountability" of the channel (the probability of the change of information, its commentation and assessment by the translator).

Table 4.2 presents the data on the assessment of the efficacy of risk communication channels.

The use of multiple communication channels simultaneously or sequentially with a focus on an assessment of their efficacy can contribute to achieving the goals of information (see Table 4.2).

The model of information efficacy assessment is a tool to determine the solution of the problem posed at the development of information activities, and make the necessary changes in the strategy and tactics of information (Fig. 4.3).

Fig. 4.3 shows the stages of the information process efficacy assessment.

The first stage of health risk communication is focused on the development of a general concept, the creation of materials and the verification of their content. The produced materials shall be approved prior to message broadcasting to general public, certain social groups or carrying out of individual risk communication. Qualitative study methods are the

Table 4.2

Risk communication channels efficacy assessment [Lebedeva-Nesevrya N.A. et al., 2012]

Ser. No.	Risk communication channels	Risk communication channel characteristics				
		Availability	Correspondence to scope and the form of information	The confidence of target audience	Typicality	The degree of accountability
1	Specialized publications*	Low	High	High	Low	High
2	External information	Average	High	Average	Low	High
3	Television	High	Average	Average	High	Average
4	Print press	High	High	Average	High	Average
5	Radio	High	Average	Average	Average	Average
6	Websites	Low***	High	Average	Low	High
7	Lectures, public presentations	Low	High	High	Low	High
8	Individual professional consultations	Low	High	High	Low	High
9	Informal communications	High	Average	High	High	Low

N o t e : * – Information and information-analytical bulletins, government reports, scientific journals, monographs, collections of articles, etc.;

** – flyers, brochures, posters, billboards, etc.;

*** – according to the "Public Opinion" Fund the weekly audience of the Russian Internet is 33% of the population, daily – 25%. The data from the 13 polls of summer of 2010. Total – about 26 thousand respondents. Stratified random (for large economic-geographical regions and urban / rural population), three-stage sample.

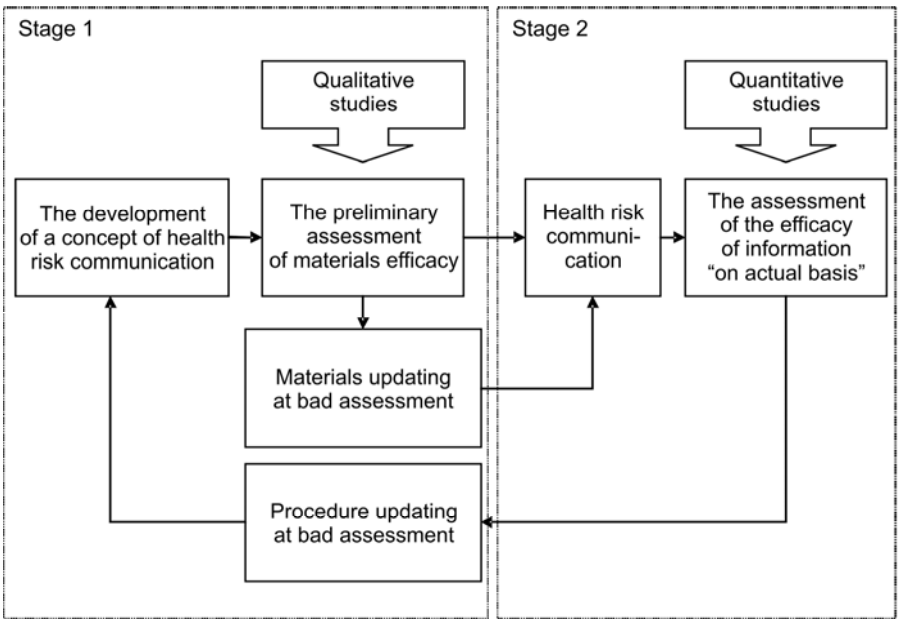

Fig. 4.3. The model of health risk information activities efficacy assessment [Lebedeva-Nesevrya N.A. et al., 2012]

most appropriate to do this. With the help of focus groups, individual in-depth interviews with the representatives of alleged social groups, etc. you can identify message deficiencies, such as a lack of information or difficulty to understand. This will allow timely correction and to prevent the recipients' perceptual aberration in the future.

At the second stage, the assessment of the efficacy of information "on actual basis" is carried out. It is advisable to do with quantitative study methods, the results of which will act as the markers of awareness and the response of addressees in the overall process of risk communication.

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5. THE LEGAL BASIS OF RISK ANALYSIS IN RUSSIA AND ABROAD

The state of modern society, which is characterized by complication and the instability of social relations and institutions, the use of hazardous industrial and social technologies, growing threats and dangers of different nature, omissions in management decision-making, crisis in the normal course of management, has led to the fact that a number of researchers believe that an assessment of modern society as a "risk society" is justified [Beck W., 2001; Rasmussen M.V., 2006].

The awareness of the situation, as well as the intensive development of the theory of the issue has led to a situation where a number of countries have consolidated risk assessment and management by legislative acts; economic entities are charged with the task to assess hazards and risks associated with their production activities, conformity assessment bodies are charged with the task of the results verification, and the control and supervisory authorities – performing monitoring compliance with legal requirements on risk assessment and minimization.

As of the current date, in the legislations of many countries risk assessment and management are featured as a part of environmental protection, population and territories protection against natural and man-made disasters, insurance, banking and credit sector, and technical regulation in a number of other activities. The Russian Federation is in the beginning of legislative and regulatory support of the analysis of population health risk. It is gradually taking over all the best that has been developed in other countries, and finding own approaches that take into account the specifics of national practices and socio-economic situation.

5.1. The legal basis of risk analysis in the field of living environment protection

For the first time the notion of risk as a criterion for environmental safety and consequently human living environment safety was introduced in the legislation of the United States of America.

An act of national policy in the field of the environment in 1969 (NEPA, 1969), which essentially became a major US law in the environmental field, formulated the basic principles, institutions and mechanisms of the state environmental policy. The law imperatively determined the binding analysis of the ecological sequences of various entities activity at the federal level. The basic principles have been developed in environment quality improvement, clean air, clean water, the preservation and restoration of resources, the control of toxic substances, etc. acts.

Clean Air Acts as of 1970, 1977 and 1990 and the amendments thereto have established a partnership to monitor air quality between the states and the federal government. At the same time it is indicated that the acceptable level standards, developed by the U.S.Environmental Protection Agency, use population health and well-being risks as a criteria.

The State is responsible for the implementation of these standards. Responsibility for the implementation of air quality control process management in the States comes first and allows federal control over the states, as well as making efforts to keep the achieved level.

If we consider the EU legislation, it should be noted that even the primary documents of EU law, such as International Treaties that establish the European Union and cooperation between the parties, consolidate the requirement to ensure a high level of population health protection, which is achieved at definition and implementation of all policies and actions of the Union. The legal base of the EU as to environmental protection, which is more than 80 acts, is permeated by a common idea to minimize life and health risks. Directive 96/61 / EC "On integrated pollution prevention and control", Directive 83/360/EEC "On air pollution by industrial enterprises", Directive 85/337/EEC, as amended (97/11/EEC) "Environmental impact assessment (ETA), Directive 76/464/EEC "On hazardous substances", Directive 91/689/EEC "On hazardous waste", Regulation 793/93/EEC "On the evaluation and control of the risks of existing substances", Regulation 1907/2006/EC concerning the Registration, Evaluation, Authorization and Registration of Chemicals (REACH), Directive 2008/50/EC "On ambient air quality and cleaner air for Europe, Directive 2001/82/EC "On the definition of a potential serious risk to human, and animals health or the environment – almost all of these documents deal with the aspects of risk analysis. At that the quality of the environment, population health and the quality of life are considered in a single system, and safety – as the absence of unacceptable health risk.

The EU legislation establishes the procedure for risk assessment, identifies persons involved in the risk assessment: business entities that are hazardous to the health of citizens, organizations in the field of conformity assessment and regulatory authorities. The aspects of the preparation of risk management measures, including risk communication are well-developed.

Directives are harmonized in terms of the notions of "safety" and "health risk".

The european standards of environmental quality are throughout focused on the assessment of health risks and broadly developed with due regard to the assessment of health risks (risk-based standards)

The requirement of a permanent reduction of the impact on the environment is the principal legislative provision of the EU legal system. Despite the fact that the implicit ideal – a complete lack of any impact – looks utopian and technically unachievable, this requirement has allowed European countries to significantly reduce environmental contamination while maintaining the competitiveness of the industry.

The issues of the assessment of population health risk associated with impact of the living environment, occupy an important place in health policy in many countries, as well as public organizations such as the World Health Organization, the International Labour Organization and others. The health of all people is fundamental in the realization of peace and safety and is dependent on the efficacy of cooperation of individuals and states. Governments are responsible for the health of their people, and this responsibility requires social measures in the field of the insurance of sanitary and epidemiological welfare of the world community.

In the states-members of the Eurasian Economic Community legal regulation in the field of analysis of human living environment favorability, including by means of health risk assessment is carried out by the legislative acts, which regulate the relations in the field of sanitary and epidemiological welfare, environmental protection, radiation safety.

The comparative analysis of the laws of the states-members of the Eurasian Economic Community (EurAsEC) in the field of the assessment of population health risk associated with the impact of living environment, showed that the risk assessment methodology is widely used for legal regulation of interested parties activity in the assessments of "environment – health". However, the level and breadth of use of these assessment criteria are very heterogeneous.

So, health risk assessment methodology is harmonized in the field of radiation safety in the legislative aspect to the fullest extent. The laws of the states-members of EurAsEC use nearly identical formulations and principles of the regulation of the permissible levels of radiation exposure which are based on the principles of health risk assessment.

As for the other factors of human living environment, there are significant differences evident both in the use of the term "health risk assessment", and on its place in the system of legal regulation.

Explicitly, the term "health risk assessment" is used in the legislative acts of the Russian Federation, Belarus and Kazakhstan. The Legislation of the Kyrgyz Republic and the Republic of Tajikistan uses terminology pairs of "danger – safety" and "harm – harmlessness," which imply human health risk assessment, but does not postulate it explicitly.

The risk assessment methodology is most commonly used in the legislation of the Republic of Kazakhstan, where, for example, in accordance with the Code of the Republic of Kazakhstan on people's health and the health care system, risk assessment, as a scientifically based methodology of assessment of the probability of entry and propagation of agents or transmitters of infectious and parasitic diseases, as well as the negative impact of environmental factors on health and related potential medico-biological and economic consequences, is also one of the tools of professional activity of sanitary-epidemiological service. A target of legal regulation in the field of environmental protection is to minimize population health risks. It should also be noted that in accordance with the law of the Republic of Kazakhstan on architecture, urban planning and construction activities in the Republic of Kazakhstan all possible risks to human life and health and the environment at all stages of the life cycle, including during normal operation, emergencies, alleged violations during the construction and installation works and inappropriate construction should be identified and taken into account at the design of structures. This approach is peculiar to the Republic of Kazakhstan and does not apply to other countries-members of the EurAsEC.

The legislation of the Republic of Belarus includes health risk assessment in the Law "On the sanitary-epidemiological welfare of population" as to the validation of sanitary regulations, as well as social-hygienic monitoring.

In the Russian Federation health risk assessment is included in the notion of ecological risk in the law on technical regulation and is an analytical tool of social and hygienic monitoring carried out in accordance with the Russian Federation Government Resolution "On the approval of provision for social-hygienic monitoring."

The legislation of the Kyrgyz Republic and the Republic of Tajikistan, as mentioned above, does not explicitly use the term "human health risk assessment", replacing it with terminology pairs "danger – safety" and "harm – harmlessness."

In the Russian Federation at the level of government regulations risk assessment is featured as part of socio-hygienic monitoring. However, the absence of legislative consolidation of the results of the risk assessment characterizes public health monitoring as information and recommendations. Only SanPiN 2.2.1/2.1.1.1200-03 "Sanitary protection zones and sanitary classification of enterprises, buildings and other facilities" provides the mandatory application of risk assessment.

Determination, an order of assessment and classification of "health risk" are considered in detail in the document P 2.1.10.1920-04 "Guidelines for public health risk assessment at impact of chemicals that pollute the environment."

However, a number of strategic documents uses the term "health risk" – "The concept of long-term socio-economic development of the Russian Federation for the period up to 2020", "Ecological Doctrine of the Russian Federation."

"Bases of the state policy in the field of environmental development of Russia up to 2030" approved by the President in April 30, 2012, make provision for the consideration of acceptable risk to the environment and public health at ecological regulation.

This provision may be the basis for the development of the legal framework in terms of the inclusion of the concept of public health risks into sanitary and ecological laws system and other provisions related to the procedure for risk assessment, risk management and information about public health risks.

In Russian legislation population health as a target at economic management and implementation of environmental protection measures is considered almost everywhere. The established criteria of living environment quality are used as health safety criteria. The definition of safety as the absence of unacceptable health risk, as well as the definition of

risk as a combination of the probability of harm from impact of living environmental factors and the severity of that harm has not yet been directly adopted in the Russian sanitary and ecological legislation.

Partially safety issues are related to the category of "health risk" in the Federal Law No. 3-FZ dd. 09.01.1996 "On the Radiation Safety of the population", which establishes the basic principles of radiation safety of the population. Thus, the law declares the requirement to prohibit all activities on the use of ionizing radiation sources, in which benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation. Effective dose is defined as the ionizing radiation impact value, which is used as a measure of the risk of long-term effects of the human body and organs exposure with regard to their radiation sensitivity.

According to the Constitution of the Russian Federation (Sec. 2, Art. 42) everyone has the right to a healthy environment, reliable information about its condition and to compensation for damage caused to his/her health or property by environmental offense.

This provision has been developed in a number of legislative acts. The Law No. 52 dated March 30, 1999 "On the sanitary-epidemiological welfare of the population of the Russian Federation" states that sanitary and epidemiological welfare of the population is a population health, human living environment in which no adverse effects of living environmental factors on human and provided favorable conditions of the life.

The sanitary and epidemiological welfare of the population (Art. 2) is ensured by a number of actions and procedures, including social and hygienic monitoring (Art. 2), and in accordance with the Government Resolution of the Russian Federation No. 60 dated February 2, 2006, "On Approval of provision for social and hygienic monitoring" (item 3), problems of identification of cause-and-effect relationships between population health and human living environmental factors impact based on systemic analysis and public health risk assessment are solved in the course of monitoring.

Despite the fact that the Federal Law "On Environmental Protection" has no direct references to the health risk assessment, it is assumed that the relations arising in the field of environmental protection, to the extent necessary to the insurance of sanitary and epidemiological welfare of the population, are regulated by the legislation on sanitary and epidemiological welfare of the population and the legislation on health care, yet there is a sufficient number of articles on the impact of living environment on health. In accordance with stated law verification of projects and other documentation proving the economic and other activities should be carried out with regard to the assessment of citizen life and health threat (art. 3). Noted law establishes the rights and obligations of public and other non-profit organizations operating in the field of environmental protection, including the right of acquisition of timely, complete and accurate information about the environment, measures for its protection, the circumstances and the facts of economic and other activities that pose a threat to the environment, life, health and property of citizens (Art. 12). The emplacement of production and consumption waste in a way that creates human health hazard is prohibited (Art. 51).

The Federal Law "On Technical Regulation" establishes the concept of the safety of products and related processes of production, operation, storage, transportation, marketing and utilization as a condition in which there is no unacceptable risk associated with the infliction of harm to life or health of citizens. The aims of standardization, one of which is to increase the level of safety of life and health of citizens, taking into account the risk of natural and man-made disasters, improve environmental safety, life safety and animal and plant health are determined (Art. 11).

Federal Law "On Radiation Safety" defines the effective dose as the amount of exposure to ionizing radiation, which is used as a measure of the risk of teh long-term effects of the human body and organs exposure with regard to their radiation sensitivity. The basic principles of radiation safety also include the principle of normalization – the non-exceedance of the limits of individual doses of citizens' exposure from all sources of ionizing radiation and the principle of validation – the prohibition of all activities on the use of ionizing radiation sources, in which a benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation.

The Constitution of the Republic of Belarus guarantees the right to health care that is provided by measures of living environment enhancement (Art. 45).

The law of the Republic of Belarus "On the sanitary-epidemiological welfare of population" determines that the sanitary rules establish the acceptable levels of risk of possible deterioration of health due to adverse effects of living environment and living conditions factors on the human health (Sec. 2, Art. 8). Socio-hygienic monitoring is held in the Republic in order to identify human health risks and the development of activities aimed at the prevention, reduction and elimination of adverse effects of living environment factors on human health (Art. 12). Socio-hygienic monitoring is organized and conducted by the Ministry of Health in collaboration with relevant government agencies in the manner determined by the Government of the Republic of Belarus.

Law of the Republic of Belarus "On Environmental Protection" establishes the following definitions:

– environmental safety is the condition of the protectiveness of environment, people's life and health from possible harmful influence of economic and other activities, natural and man-made disasters;

– environmental harm is a harm caused to the environment, as well as life, health and property of citizens, including individual entrepreneurs, corporate property and property owned by the state, as a result of the harmful effects on the environment;

– environmental risk is a probability of the occurrence of an event that has adverse effects on the environment and caused by adverse effects of economic and other activities, natural and man-made disasters.

The Law of the Republic of Belarus No. 122-Z dated January 5, 1998 "On Radiation Safety of the population" as amended in 2006 also defines the effective dose as the value of ionizing radiation exposure, which is used as a measure of the risk of long-term effects of the human body and organs exposure with regard to their radiation sensitivity. The basic principles of radiation safety also include the principle of normalization – the non-exceedance of the limits of the individual doses of citizens exposure from all sources of ionizing radiation and the principle of validation – the prohibition of all activities on the use of ionizing radiation sources, in which a benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation. Thus, in the legislation of the Republic of Belarus the term "ecological risk" is closely related to health risk. Law determines the composition, sources and types of environmental information, the form of its provision and propagation, states that the environmental information shall include information about the health and safety of citizens, about conditions of their life, cultural facilities and buildings condition to the extent that they are or may be affected by the environment or environmental factors (Art. 74).

In accordance with the Constitution of the Republic of Kazakhstan the citizens of the Republic of Kazakhstan shall have the right to health care (Art. 29), and the state aims to protect the environment favorable for life and health (Art. 31).

The Code of the Republic of Kazakhstan on people's health and the health care system provides the following definitions:

– "Risk assessment" is a science-based assessment of the probability of the entry and propagation of agents or transmitters of infectious and parasitic diseases, as well as the negative impact of environmental factors on health and related potential medico-biological and economic consequences (Art. 1);

– "Activities in the field of sanitary and epidemiological welfare of the population" is an activity of state authorities and organizations of sanitary-epidemiological service, aimed at protection of the health of citizens, which includes the state sanitary and epidemiological surveillance, hygiene training, sanitation and quarantine control, radiation control, sanitary and epidemiological valuation, risk assessment, sanitary and epidemiological monitoring, sanitary and epidemiological expertise (paragraph 115). It should be noted that the essential part of this definition is that the activities of State sanitary and epidemiological supervision authorities are aimed at risk assessment. The area of competence of the competent authority includes the definition of a common methodology for all organizations entitled to

conduct risk assessment and the establishment of procedures for risk assessment (Art. 7, par. 63), and the authorities exercising state control and supervision in the field of health, develop and approve departmental statistical reporting forms, checklists, risk assessment criteria (Art. 19, paragraph 5).

In this document a serious consideration is paid to the use of risk assessment in the prevention of communicable and non-communicable diseases, including professional and injuries. At that it is indicated that this work should include both the prevention of the behavioral risk factors of diseases and the improvement of health literacy, and the monitoring of the disease risk factors of attached population by the specialists of primary health care, the occupational diseases of workers – by the specialists of state authorities, which carry out activities in the field of sanitary and epidemiological well-being of the population, as well as the minimization of the operational factors of disease risk by public authorities within their powers, other authorities and organizations as well as individual entrepreneurs.

The Environmental Code of the Republic of Kazakhstan assigns environmental quality values to environmental quality target values. It is determined that the identification of the target values of environmental quality should provide (among them) ecological safety and the reduction of population health risks (Art. 24).

Documentation on environmental impact assessment (Art. 41) should include (p. 9) ecological risk and public health risk assessment. The chapter on industrial environmental control (Chapter 14), – On the aim and purpose of industrial environmental control, indicates that the purposes of industrial environmental control are to inform the public about the environmental performance of enterprises and population health risks (Art. 128, paragraph 2, section 7).

The law defines the task of risk assessment (Art. 303). The general requirements for hazardous waste landfills specify that the collection, processing and use of landfill gas must be carried out in a manner that minimizes harm to or deterioration of the environment and public health risk (p. 3).

In accordance with the Law of the Republic of Belarus No. 219-I dated 4/23/1998 "On Radiation Safety of the population" as amended in 2006, the effective dose is the value of ionizing radiation exposure, which is used as a measure of the risk of long-term effects of the human body and organs exposure with regard to their radiation sensitivity. The basic principles of radiation safety also include the principle of normalization – the non-exceedance of the limits of individual doses of citizens exposure from all sources of ionizing radiation and the principle of validation – the prohibition of all activities on the use of ionizing radiation sources, in which a benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation.

The Law of the Republic of Kazakhstan "On subsurface and subsurface use" determines the competence of the competent authority in the field of oil and gas, including the analysis and assessment of risk of harm to human life and health and the environment in the area of oil operations and oil transportation (Art. 18).

The Law of the Republic of Kazakhstan on industrial safety at hazardous production facilities indicates that the production control shall be carried out at hazardous production facilities for maximum possible reduction of risk of harmful effects of occupational hazards to production personnel, population and environment (Art. 16).

The Law of the Republic of Kazakhstan "On architectural, urban planning and construction activities in the Republic of Kazakhstan" indicates that the design of objects of architecture, urban planning and construction must ensure the safety of facilities for human life and health and the environment. All possible risks to human life and health and the environment at all stages of the life cycle, including during normal operation, emergencies, alleged violations during the construction and installation works and inappropriate construction should be identified and taken into account at the design of structures. The noise isolation of a facility shall be designed and developed in the absence of an unacceptable risk to human life and health (Art. 27.2).

If we consider the other CIS countries, the legislation of the Kyrgyz Republic should be noted, where, in accordance with the Constitution, everyone has the right to healthy life and healthy environment (Art. 48).

The Law of the Kyrgyz Republic on the sanitary and epidemiological welfare of the population establishes that the sanitary and epidemiological welfare of the population i.e., population health, human living environment in which no adverse effects of living environmental factors on human and provided favorable conditions of the life and safe conditions for people – state of living environment without the risk of its factors harmful effect on people.

Equally, it applies to the concept of "health standard", which is survey-defined permissible maximum or minimum quantitative and (or) qualitative value of the parameter, which characterizes this or that factor of the living environment in terms of its safety and (or) harmlessness to people. It also provides the concept of "social-hygienic monitoring", which is represented as a state system of population health and the environment surveillance, their analysis, assessment and forecasting, as well as the determination of cause-and-effect relationships between population health and the impact of living environmental factors.

The rights and responsibilities of citizens determine that citizens have the right to healthy living environment, the factors of which are not harmful to human, as well as obtaining information on sanitary and epidemiological situation, living environment state, quality and the safety of products for industrial purposes, food products, goods for household use, potential human health hazard of works and services (Art. 7).

Special attention should be paid to the chapter of this document, which defines the sanitary and epidemiological requirements to ensure living environment safety for human health. Here are both sanitary and epidemiological requirements for the planning and building of urban and rural settlements and other requirements with regard to other factors that have impact on the formation of human living environment (Chapter 3, paragraph 9).

The development, approval and implementation of sanitary regulations prescribes that the development of sanitary regulations should include (Art. 35):

– comprehensive studies to identify and assess the impact of living environmental factors on human health;

– the determination of sanitary and epidemiological requirements to prevent the harmful effects of environmental factors on human health;

– the setting of safety criteria and (or) harmlessness, hygienic and other norms of living environmental factors;

– the analysis of international experience in the field of sanitary and epidemiological regulation and a number of other actions.

The established task of social and hygienic monitoring: the assessment, identification of changes and the forecast of the population health and the environment condition, the identification and elimination of the harmful effects of environment factors on human. Social and hygienic monitoring shall be conducted at the state level, in urban and rural settlements by authorities and institutions of the State Sanitary and Epidemiological Service of the Kyrgyz Republic together with the executive authorities, local authorities, and the procedure for sanitary and hygienic monitoring is established by the Government of the Kyrgyz Republic (Art. 41).

The Law of the Kyrgyz Republic "On Environmental Protection" introduces the concept of "environmental damage", i.e. negative changes in the environment caused by human activity, as a result of environmental contamination, the depletion of natural resources, the damage, destruction of natural ecological systems, creating a real threat to the human health and life, plant and animal life, material valuables, and the maximum permissible harmful effects on the environment are treated as the indicators of permissible exposure limits of economic, recreational and other activities on the environment, which ensure the protection of the environment, the rational use of natural resources, society and human health environmental safety.

It should be noted in the law, but in a different article, the definition of environmental offenses as guilty of wrongful act that violates environmental laws and causing harm to the environment and human health, and environmental crime is socially dangerous act infringing

the established environmental law and order, the environmental safety of society, causing harm to the environment and human health (Art. 2).

The principle of priority is present among the basic principles of environmental protection: the insurance of human rights to environment favorable to human life, work and rest, which provides human life and health, as well as the principle of balance: the preservation of the stability of ecological systems, compliance with environmental regulations at the implementation of economic and other activities, the restoration of natural resources, the prevention of irreversible consequences for the environment and human health (Art. 3).

Citizens have the right to obtain complete and accurate information about the state of the environmental and public health (Art. 46).

In accordance with the Law of the Kyrgyz Republic On Environmental Impact Assessment, ecological risk is the probability of the adverse environmental and health consequences of any (deliberate or accidental, gradual and catastrophic) anthropogenic changes of natural objects and factors.

The Law of the Kyrgyz Republic "On Radiation Safety of the Kyrgyz Republic population" (Law of the Kyrgyz Republic No. 48 dated February 28, 2003, No. 168 dated August 1, 2003) states that the effective dose is the value of ionizing radiation exposure, used as a measure of the risk of long-term effects of human and particular organs exposure in accordance with their radiation sensitivity, and the principle of normalization (non-exceedance of the limits of individual exposure doses from all sources of ionizing radiation) and the principle of justification, i.e. the prohibition of all activities on the use of ionizing radiation sources, in which a benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation are some of the principles of radiation safety.

The Constitution of the Republic Tajikistan provides that everyone has the right to health care, and the government shall take steps to improve the environment (Art. 38).

The law of the Republic of Tajikistan On Public Sanitary and Epidemiological Safety in terms of health associated with the impact of living environmental factors is aligned with the similar document of the Kyrgyz Republic. Thus, in accordance with this document, sanitary and epidemiological safety of the population, i.e. population health, human living environment in which no adverse effects of living environmental factors on human and provided favorable conditions of the life and safe conditions for people – a state of living environment without the risk of its factors harmful effect on people.

Also this document defines hygienic standard i.e., the survey-defined permissible maximum or minimum quantitative and (or) qualitative value of the parameter, which characterizes this or that factor of the living environment in terms of its safety and (or) harmlessness to people and social-hygienic monitoring", which is represented as a state system of population health and the environment surveillance, their analysis, assessment and forecasting, as well as the determination of cause-and-effect relationships between population health and the impact of living environmental factors.

The citizens of the Republic of Tajikistan have the right to a healthy environment, to obtain complete and accurate information about the state of the environment, the quality and safety of products, potentially hazardous works and services (Art. 7).

The planning and building of settlements should provide for the creation of favorable conditions for public life and health, a comprehensive improvement of cities and other settlements, prevention and elimination of harmful and dangerous impact of factors of the environment and living conditions on human health (Art. 11).

Sanitary-epidemiological expertise and consultation on the assessment of the impact of living environmental factors on human health shall be held in the established order at the request of the chief state sanitary inspectors, as well as statements made by physical and legal entities (Art. 35).

The law states that socio-hygienic monitoring, which takes place at the national and local level by authorities and institutions of sanitary-epidemiological service of the Republic of Tajikistan together with local authorities and government is carried out for the assessment,

identification of changes and the forecast of the population health and the environment condition, identification and the elimination of the harmful effects of environment factors on human. Procedure for social and hygienic monitoring is established by the Government of the Republic of Tajikistan (Art. 42).

In accordance with the Law of the Republic of Tajikistan On the preservation of nature, harm to the environment i.e. negative changes in the environment caused by human activity, as a result of environmental contamination, the depletion of natural resources, the damage, destruction of nature ecological systems, creating a real threat to human health and life, flora and animal life, material valuables, and the maximum permissible harmful effects on the environment are established with regard to human health safety assurance.

The principle of priority of human life and health protection, favorable ecological conditions for life, work and rest of the population is implemented in the course of economic, administrative and other activities (Art. 49).

In accordance with these documents, environmental requirements at the designing, construction, reconstruction and commissioning of enterprises, structures and other facilities implies the carrying-out of the requirements of environmental safety and public health (Ch. 6). In addition, the law prohibits the development and implementation of national economic projects associated with the onset of irreversible effects for human health. Violation of the rules, which creates a threat to human health by chemical contamination of the environment, involves prohibition of production, storage, transportation, use of appropriate chemicals on the resolution of the specially authorized state bodies of the Republic of Tajikistan in the field of sanitary supervision, the environment protection, supervision over safe work procedures in industry and mining.

State control in the field of environmental protection assumes decision to suspend the activities of economic entities in order to prevent an imminent threat to life or health, the onset of man-made disaster, infliction of irreparable harm to natural objects or the environment. The decision is made in case of two or more violations of the requirements and conditions in the field of environmental protection and if the prevention of these disorders is impossible by other means (Art. 67).

The Law of the Republic of Tajikistan No. 42 dated August 1, 2003 "On Radiation Safety" defines the dose limit as the value of ionizing radiation exposure, which is used as a measure of the risk of long-term effects of human and particular organs exposure in accordance with their radiation sensitivity, and one of the basic principles of radiation safety is the principle of the prohibition of all activities on the use of ionizing radiation sources, in which a benefit for human and society does not exceed the risk of possible harm caused by additional exposure to natural background radiation.

Particularly noted should be the content of the article on the analysis of the impact on the environment and its problems. Thus, the analysis of the impact on the environment is a comprehensive check (analysis) of planned economic and other activities that affect the environment and living conditions, and is carried out before deciding on the implementation of this activity. The main objectives of the analysis of the impact on the environment is a development of effective environmental policies and ways of sustainable use and protection of natural resources, environmental quality and human health with the consideration of all viable alternatives, public involvement in the discussion of the benefits and risks of the proposed activity (Art. 90).

The analysis of the impact on the environment is mandatory for individuals and legal entities, which plan the implementation of potentially environmentally hazardous activities and precedes the state ecological expertise. The list of activities covered by the procedure of analysis of the environmental impact, and the procedure shall be defined by the Government of the Republic of Tajikistan.

According to the Law of the Republic of Tajikistan On Ecological Expertise, the objects subject to environmental review should contain, among others, validation of environmental safety of the proposed activity, the complex ecological and socio-economic assessment of the existing or anticipated impact on the state of the environment, assessment of the environmental risk and harm to human health, as well as alternative predictable options to reduce such impacts (Art. 17).

In general, the performed analysis allows making the following conclusions.

– health risk assessment methodology as a part of the procedures for risk analysis, which includes, in addition to the risk assessment and management, the dissemination of information about risk, is an effective tool for dealing with legal issues in the field of "living environment – human health", which should be enshrined in the relevant legal acts of member-states of the Eurasian Economic Community;

– it is necessary to develop a typical legal act for member-states of the Eurasian Economic Community, unifying procedure of the assessment of risk to public health due to the impact of living environment factors;

– it is relevant to regulatory approve health risk assessment procedure as an element of the validation of sanitary norms and rules;

– it is important to legalize mandatory assessment of residual risk to health in the development of project documentation for the construction or reconstruction of industrial plants or other facilities that are the source of the adverse effects on the human environment;

– it is necessary to establish procedures for the use of health risk assessment method for resolution of legal disputes in the field of causing (or likelihood of) damage to health by contamination or other adverse effects on the living environment;

– it is necessary to legislatively consolidate the rights and responsibilities of state authorities, local governments, business entities in terms of public health risk assessment and management.

5.2. The legal regulation of occupational risk assessment

Poor working conditions in most industrial facilities, the high level of injuries and diseases associated with the work, unfavorable demographic situation and extremely large economic losses of the state associated with the working conditions in the Russian Federation, which in 2013 amounted to 1.86 trillion rubles. (2.79% of GDP) (Council Directive 90/385/EEC dated 20.6.1990 on the approximation of the legislative acts of member-states in the field of active implantable medical devices), were the main reasons for a comprehensive reforming of the national labor protection system. The main element in the reforming system is to move from the concept of "react and rectify" to the concept of "anticipate and prevent", which is realized through the introduction of the system of assessment and management of occupational risks in practical activities of enterprises and organizations.

The term "occupational hazard" was first mentioned in the International Labor Organization Recommendation "On the health services in the enterprise" in 1959 (Recommendation No. 112 of the International Labor Organization). In this document, the term "occupational hazard" was used exclusively as an identifiable harmful occupational factor. In 1978, experts of the World Health Organization (WHO) has defined risk as a concept that reflects the expected severity and/or frequency of adverse reactions to this exposure [Malyshev D.V., 2008]. In other words, an occupational hazard is a predictive probability of the frequency and severity of adverse reactions on harmful factors of working environment and labor process.

In the legal acts of the Russian Federation, the term "occupational hazard" is found in four documents: Federal Law No. 125-FZ dated 24.07.1998 "On compulsory social insurance against job-related accidents and occupational diseases ", the Federal Law No. 197-FZ dated 30.12.2001" The Labor Code of the Russian Federation ", Federal Law No. 184-FZ dated 27.12.2002 "On Technical Regulation" and the Federal Law No. 426-FZ dated 28.12.2013 "On a special assessment of working conditions." The term "occupational hazard" in the above regulations is virtually identical to the definition of "likelihood of injury as a result of impact of harmful and (or) dangerous production factors in the performance of duties under an employment contract", but approaches to its assessment are quite different.

As a part of the system of social insurance against industrial accidents and occupational diseases, occupational risk class shall be set a priori, depending on the assignment to a particular type of economic activity, according to the Government Resolution of the Russian Federation №No. 713 dated 01.12.2005 "On approval of rules for economic activities assigning to the professional risk class." In particular, the class of occupational risk is established based on the level of industrial injury, occupational morbidity and the costs of insurance benefits, established on the economic activities of insurers. In accordance with the "Rules" we can calculate an integral index of occupational risk Ii (defined as the ratio of the total costs in the economic sector (sub-sector) to a compensation of harm in the past calendar year caused by the insured as a result of accidents and occupational diseases (temporary disability benefits, compensation for lost earnings, lump sum and monthly insurance payments, the cost of medical, social and vocational rehabilitation), to the amount of the wage fund in the economic sector (sub-sector), with assessed contribution to the Social Insurance Fund of the Russian Federation). The level of payments of the Social Insurance Fund of the Russian Federation is pegged to the level of wages of the injured person, and the duration of benefits depends on the severity of the injury (occupational disease).

According to this provision, the Order of the Ministry of Labor and Social Protection of the Russian Federation No. 625n dated 25.12.2012 "On Approval of classification of economic activities in classes of occupational risk", all economic activities are divided into 32 classes of occupational risk. The functioning of this system is carried out through the determination of the amount of insurance rates for each class of occupational risk and further certain contributions of the employer to Social Insurance Fund of the Russian Federation. The above-mentioned system was formed in Russia in 2000 and has an unconditional positive value in terms of the employee who received the economic mechanisms of protection in the event of disability due to an accident or occupational disease. However, the use of this methodology in the assessment of occupational risk has a number of disadvantages, namely: when determination of the class of occupational risk occurs. It leads to the averaging of the number of accidents and occupational diseases in homogeneous economic activities, and the direct assessment of the health status and working conditions at a particular enterprise is not carried out, in addition, a socially responsible employer under this provision is not stimulated virtually, as there is no transition to individual insurance rates, for a particular enterprise class of occupational risk is directly related to the level of industrial injuries and occupational diseases in the industry.

In 2011, the Labor Code of the Russian Federation also introduced the concept of "occupational hazard", at the same time it was found that the procedure for occupational risk level assessment is determined by the federal executive authority responsible for public policy and legal regulation of labor, taking into account the views of Russian Trilateral Commission for regulation of social and labor relations. However, the official procedure for occupational risk level assessment of the Ministry of Labor and Social Affairs of the Russian Federation, which is above mentioned federal executive body, has not been approved as of today. Recent years have seen active discussion of three basic concepts of occupational risks assessment.

The first concept. Hazard identification and risk assessment, used in international practice at the development of OSH management systems. In 2001, the International Labor Organization adopted the "Guidelines on OSH management systems" (ILO-OSH 2001/ ILO-OSH 2001). The Russian Federation on the basis of this document adopted GOST 12.0.230-2007 "Interstate standard. Occupational safety standards system. OSH management systems. General requirements." A series of OHSAS 18000 (Occupational Health and Safety Assessment Series) has laid down similar principles of hazard identification and risk assessment. OHSAS 18000 consists of two parts, OHSAS 18001 and 18002, and includes a number of other publications. OHSAS Standards, which apply to the management of occupational safety and health, are designed to provide organizations with the elements of effective management system of occupational safety and health, which can be integrated with other management requirements in order to assist organizations in achieving the goals of occupational health and safety and economic purposes. OHSAS 18001 is compatible with

ISO 9000 and ISO 14000 and is applicable to all sectors of production and services. OHSAS 18001 Certificate shows that the enterprise closely monitors factors of production and professional risks, concerns about the safety of personnel in the workplaces.

The basis of the above documents is a mechanism to ensure a continuous cycle of improvement of working conditions due to the risk assessment, planning and control of elimination or reduction measures. One of the key tasks is to conduct an initial analysis, which should serve as a basis for establishing an OSH management system in the organization.

Tools for risk assessment are proposed in the manual "Five steps to risk assessment" of the Executive Committee of the Health and Safety of Great Britain (HSE) (Health and safety executive. URL), in the overall assessment of risks to the sector of small and medium businesses of the Netherlands (Royal Association MKB Netherlands), as well as many industry-specific risk assessments.

According to the documents, the occupational risk assessment should be carried out by competent persons, with regard to consultations with workers and should include: identification and assessment of hazards and risks to health and safety, determination of the correspondence of planned or existing protective measures to eliminate hazards or control risks and analysis of the results of workers' health surveillance. Thus, in the frameworks of this concept, the risk assessment is carried out by expert assessment with priority in assessing the risk of injury. The acceptability (admissibility) or inacceptability of risks shall be determined at the final stage. The certainly positive aspect of this methodology is the maximum coverage of all the hazards and their further hierarchical alignment, which allows eliminating the highest hazards and optimizing costs for reduction of occupational risks. In addition, the risk assessment system is fairly simple for practical use and the employer does not bear high material costs for its application. The main disadvantages of the above concepts are: development of a model of occupational risk assessment based on subjective opinions of experts and the lack of an objective study of production factors impact on health of workers.

The second concept is the concept of risk assessment used in the authorities and institutions of Rospotrebnadzor and approved by the Federal Service for Supervision of Consumer Rights and Human safety Protection. In 2003, the Chief State Sanitary Doctor of the Russian Federation approved R 2.2.1766-03 "Guidelines for assessment of occupational health risks for workers. Organizational and methodological bases, principles and criteria of assessment." According to this methodology, all the factors of production, occupational injuries and other health disorders are subject to mandatory registration and assessment. Occupational risk assessment model follows two principles: a priori risk assessment involves the assessment of production risk factors based on hygienic criteria i.e., exceedance of maximum permissible concentration (maximum permissible level) and a posteriori assessment of risk, which is carried out based on medical and biological criteria i.e., occupational morbidity, morbidity with temporary disability, an increase of biological age relating to passport age, mortality, etc. [Izmerov N.F. et al., 2001; Denisov E.I., Chesalin P.V., 2007].

Based on this methodology highly reliable mathematical models for occupational risk calculation are being created, taking into account the three main components: factor level; the duration of its impact and effective feature, i.e., the indicators of the labor collective health status. On the basis of the principles of evidence-based medicine, clinical epidemiology in particular, we can determine the quantitative assessment of the cause-and-effect relationships of health problems with work, calculate the relative risk and etiological fraction of working environment factors contributing to pathologic behavior [R 2.2.1766-03].

In the development of this concept Rospotrebnadzor developed and approved a number of guidance documents, in particular, the Resolution of chief state sanitary doctor of the Russian Federation No. 79 dated 31.10.2007 "On approval of the concept of toxicological studies, risk assessment methodology, identification and quantification of nanomaterials", guidelines 1.2.0041-11 "System of decisions on nanosafety control based on assessment of production risks, use and disposal of nanomaterials based on the monitoring of these processes in nanoindustry enterprises" procedural guidelines1.2.3017-12 "Assessment of risk of the effects of pesticides on workers." At the same time this methodology forms the basis of a

number of local industry regulations, such as "Russian Railways" JSC (Order of "Russian Railways" JSC No. 2631 dated 21.12.2009 "On approval of guidelines "Criteria of assessment of occupational risks of "Russian Railways" JSC workers", directly related to trains movement").

At the same time the application of this model in its pure form is extremely difficult, since one of the main indicators taken into account in this system, is an occupational morbidity, which is revealed in industrial enterprises at an extremely low level for various reasons. Furthermore, disadvantages of this concept are: the duration of the hygienic studies of production factors and assessment of workers' health status, the relatively high cost of a posteriori assessment of occupational risk and the lack of assessment of injury free operation of equipment.

The third concept is the concept of evaluation and ranking of working conditions at assessment of workplaces. The assessment of workplaces was carried out in the Russian Federation since 1992. It was regulated by specific legal acts (Order of the Ministry of Labor and Employment of the RSFSR population No. 2 dated 08.01.1992 "On the procedure for assessment of workplaces according to working conditions", Resolution of the Ministry of Labor of the Russian Federation No. 12 dated 14.03.1997, "On assessment of workplaces according to working conditions," Order of the Ministry of Health Care and Social Development of the Russian Federation No. 569 dated 31.08.2007 "On approval of the Procedure for assessment of workplaces according to working conditions," Order of the Ministry of Health Care and Social Development of the Russian Federation No. 342n dated 26.04.2011, "On approval of the Procedure for assessment of workplaces according to working conditions"). At the same time assessment of workplaces was always based on the hygienic assessment of working conditions, which was carried out according to the "Guidance on the hygienic assessment of working environment and labor process factors" in various editions. It should be noted that the hygienic assessment of working conditions, in accordance with the guidance given above, allows an a priori assessment of occupational risk.

In our opinion the main disadvantage of this concept is that only a priori risk assessment can be carried out during the assessment of workplaces and, accordingly, the regulations have no mechanism of study of the implementation of identified occupational hazards impact on workers' health.

In 2013, with the adoption of the Federal Law No. 426-FZ dated 28.12.2013 "On special assessment of working conditions," the order of assessment of working conditions according to working environment factors has changed significantly. In connection with the exception of hygienic assessment of working conditions "Guidelines on hygienic assessment of working environment factors and labor process. The criteria and classification of working conditions "(R 2.2.2006-05) are not applied, also a number of production factors (natural lighting, pulsation factor, etc.) is excluded, as well as the approach to the assessment of risk factors (noise, weight, etc.) are changed. As a result, a priori risk assessment during a special assessment of working conditions is practically not applicable for today.

Thus, it is necessary to state that, despite the fact that the term "occupational risk" is already widely used among employers, security services and occupational medicine, there is no generally accepted and federal level-approved methodology for occupational risk assessment as of today.

Considering the fact that the risk assessment carried out in the Russian Federation according to the procedures requires special one-off studies and focusing on the international experience of occupational risk assessment, it is appropriate, in our opinion, to develop a qualitative assessment of the degree of risk (simplified system of risk assessment for small enterprises). This can be achieved through the development of an exemplary algorithm for risk assessment on the model of foreign documents with possible free access to the Internet.

It should be noted that the simplified system of risk assessment will not be a substitute for existing methodology used in the country, and it does not obviate the need to monitor the impact of production factors (production laboratory control). In fact, the Russian

Federation has a wealth of experience of instrumental measurements of an industrial environment factors, qualified specialists, well-established measurement methodologies.

Simplified risk assessment methodology can be further integrated into GOST 12.0.230-2007 "SSBT. OSH management systems. General requirements." They will have to identify and assess hazards and health and safety risks arising from the existing or proposed working environment and labor organization, and to determine whether planned or existing measures are adequate for hazards elimination or risks limiting.

5.3. Legal basis for risk assessment in the system of technical regulation: domestic and international aspects

The Federal Law of the Russian Federation "On Technical Regulation", which came into force on 1 July 2003, has the defined system of determination and application of the requirements for products, production processes, and services, which is an entirely new for the country.

The system assumes a consistency of approaches to the definition of mandatory requirements for products and related processes of design (including research), manufacturing, construction, installation, commissioning, operation, storage, transportation, sale and utilization, as well as to perform works or provide services and legal regulationof relations in the field of conformity assessment.

The manifestation of technical regulation system in the Russian Federation had substantially brought together the positions of the country and international approaches in the field of the standardization of requirements for goods and services. The separation of powers and responsibilities of the state and business for the safety and quality of products is provided on the basis of rational combination of free enterprise and government regulation, their harmonization with international practice. At that the state on the basis of a new category of regulations, i.e., technical regulations, claimed responsibility for the determination of socially acceptable safety requirements and regulations of confirmation of products compliance with these requirements.

It is the Federal Law "On Technical Regulation" that most clearly and unambiguously introduced the concept of "risk" in relation to human life and health into domestic law: "A risk is a probability of harm to life or health of citizens .... taking into account the severity of the harm. " The safety of products and related processes of production, operation, storage, transportation, marketing and utilizationare determined asa condition in "which there is no unacceptable risk associated with infliction of harm to life or health of citizens..."

Within the Customs Union legal documents, which have priority over national documents in a part of requirements to products (goods), life and health risk is also considered as a criteria of safety: *"Safety is the absence of unacceptable risk associated with the possibility of harm-doing and (or) impairment" (Art. 1 "Agreement on coordinated policy in the field of technical regulations, sanitary and phytosanitary measures"* dated 28.01.2008) and "a risk" is regarded as "a combination of the probability of harm-doing and consequences of the harm to human life or health, property, environment, life or health of animals and plants".

"Uniform sanitary and epidemiological and hygienic requirements for goods subject to sanitary and epidemiological supervision" / approved by the Decision of the Customs Union Commission number 299 dated May 28, 2010) and many of the technical regulations of the Customs Union operate on the concept of "risk", combining it with the characteristics of the goods.

Health risk is legally defined as the criteria of safety, which corresponds to the general international practice [Directive 2001/95/EC on general safety of products dated 03.12.2001; Regulation 178/2002 dated 28.01.2002; Guide ISO/IEC 51: 1999; Consumer Product Safety Improvement Act of 2008: US law "On the Consumer Product Safety Improvement" No. 4040; Risk Assessment and Cost Benefit Act, 1995, et al.].

However, in contrast to the Federal Law "On Technical Regulation", a number of basic documents of the Customs Union, the place and role of risk assessment procedures in the determination of product safety are adequately established in international law.

Thus, *Directive 2001/95/EC* is the source of "horizontal legislation" and establishes general requirements for all manufacturers, specifies the various provisions of the safety of products and defines the EU countries' obligations to supervise and control the EU market. Risk assessment is established within the procedure of safety norms(standards) establishing. At that art. 3, par. 5 of *Directive 2001/95/EC* states that "products compliance with criteria aimed at assurance of the overall safety, does not preclude the possibility to take appropriate measures to limit its marketing, recall or withdrawal in the event that, despite these compliance, this product is dangerous." Therefore, recognizes the possibility of a situation where at complying with all requirements and standards the products can be dangerous to life and health of the consumer under the actual conditions of use.

The manufacturer is obliged to comply with safety requirements and implement the procedures for assessment of risk of manufactured goods at design and manufacturing stage (art. 3, par. 1). It is indicated that a general duty of safety is used in respect to corresponding product and other risks if there is no special regulation for certain risks or certain categories.

Directive 2001/95/EC provides for the mandatory establishment of periodic updating and implementation of surveillance programs by categories of products or risks (Art. 9, p. *a*), check and updating of scientific and technical knowledge about product safety (art. 9, p. *b*), exchange of information on risk assessment, hazardous products, methods of control tests and (their) results (Art. 10, par. *b*), including through information systems RAPEX and RASFF[1].

Decision 768/2008/EC dated 09.07.2008 [EC, 2008] establishes a set of conformity assessment procedures for products and offers a set of modules[2], from which the legislator can choose the procedure that is best suited to the level of emerging risks. In this case, all the modules *(A-H)* contain requirements for the assessment of health risks: "... the manufacturer shall establish the technical documentation. Documentation allows assessing the product in terms of its compliance with the relevant requirements, and shall include an adequate analysis of one or more risks... ". The same document suggests that there may be a situation where the product that meets all the requirements, still poses a risk to consumers (Art. R33)[3].

The most fully issues of importance and place of risk assessment in the legislation of the European Union are covered by food documents. Regulation 178/2002/EC [EC, 2002] defines procedures to ensure food safety. The same Regulation sets up European Food Safety Authority (EFSA). The document defines the specific requirements, including those related to assessment of products risk, defines mechanisms for the exchange of information on hazard products and health risks. Thus, Regulation *178/2002/EC* states that "... food legislation makes suggestion to reduce, eliminate or avoid health risks" and "three interrelated components of risk analysis i.e., risk assessment, risk management and risk communication should serve as a systematic methodology for the determination of effective, proportional and targeted measures or other actions on health protection" It is shown that "... in order to ensure the credibility of the scientific basis of food legislation, risk assessment should be carried out independently, objectively, transparently and should be based on the available scientific information and scientific data" (Preamble to the Regulations, par. 16–18).

Regulation 178/2002/EC provides that, to ensure a high degree of the protection of human life and health, EU food legislation should be based on a system of risk analysis.

[1] RASFF is Rapid Alert System for Food and Feed.

[2] A) Internal control of production and controlled trials of products. B) standard sample "CE" study. C) Conformity to standard sample based on internal production control. D) Conformity to standard sample based on quality assurance of the production process. E) Conformity to standard sample based on product quality assurance. F) Conformity to standard sample based on product verification. G) Conformity based on product unit verification. H) Conformity based on full quality assurance.

[3] Art. R33 Related products that nevertheless poses health hazard and safety risk.

Certain technical regulations emphasize the significance and importance of consumer life and health risk assessment procedures. Thus, *Directive 2009/48/EC dated 18.06.2009* indicates that the toys and their parts must not bring a risk of physical harm, must not bring a risk of suffocation, burn (flame formation), noise, chemical exposure (Annex II. Special safety requirements). "... In order to study the risks posed by toys, and protect the health and safety of consumers, manufacturers shall be obliged to perform tests of samples of products, carry out the necessary investigations and, if necessary, keep a register of complaints against toys that do not meet the requirements, and their reviews and inform distributors about conduction of such monitoring" (par. 4, p. 4).

Council Directive 89/686/EEC dated 21.12.1989 indicates that personal protection equipment should come onto the market and put into service only if, "... they provide health protection and safety of users without compromising the health and safety of others persons, domestic animals or property ... ", and the safety of the PPE should be provided so as to eliminate the risks and other adverse factors in the stipulated conditions of use (paragraph 1.2 of Appendix 2).

Directive 2006/42/EC dated 17 May 2006 (as amended on Oct. 21. 2009) states that "a manufacturer of machinery or its authorized representative shall ensure the conduction of risk assessment to determine the requirements for health and safety applicable to machines and mechanisms"; "... machines and mechanisms must be designed and constructed with regard to the results of the risk assessment" (par. 1 of Annex I). Machine manufacturer or its authorized representative shall be obliged for identification of hazards that may be caused by machine and mechanisms and associated hazardous situations, assessment of risks, taking into account the severity of the possible injury or harm to health and the probability of their occurrence, and decision making on risk minimization based on the results of risk assessment through the iterative process of risk assessment and their reduction.

According to *Directive 89/106/EEC dated 21.12.1988*, "... building structures must be designed and constructed in such a way that they do not present an unacceptable risk of accidents or damages during service or use ..." (par. 4 of Annex 1).

Similar requirements are contained in *Directive 90/385/EEC dated 20.06.1990*, in *Directive 2006/95/EC dated 17.05.2006*, (as amended on 21.10.2009) on low-voltage equipment, electrical equipment designed for use at nominal voltage 50 to 1000 V AC and 75 to 1500 V and a number of others. In this case, all the directives orient manufacturers to the assessment of life and health risks in the designing, manufacturing and use of products.

The issues of the safety of chemical products are separately and deeply addressed in the EU legislation. *Regulation 1907/2006/EC* concerning Registration, Evaluation and Authorisation of Chemicals (REACH)[1], which entered into force on June 1, 2007 requires that according to the Directive of Council of Ministers 67/548 EU dated 16.08.1967, all "new "substances presented to the market after 1981 (about 3000 compounds with the volume from 10 kg per year and above) were examined " ...on the assessment of potential risks to public health and the environment as a result of their production and use ... ". It is stated that the volumes of public-available information on the assessment of harmful effects and risks of "existing" substances which make up more than 99% of the total available on the market, are not sufficient. In accordance with the requirements of REACH "existing" and "new" substances will have to go through the same risk assessment procedures.

REACH holds the enterprises fully responsible for the manufactured or imported chemicals, responsible for risk assessment at chemical products handling, risk management and risk communication, as well as the stimulation of innovations and the development of the alternative methods of risk assessment of chemicals (including the assessment of human life and health risks). A Chemical Safety Assessment (CSA) should be carried out for substances that are classified as hazardous or persistent and those, which have the ability to bioaccumulation. This assessment shall include evaluation of intrinsic hazards, determination of hazard classification, obtainment (if possible) of DNEL (Derived No-Effect

[1] REACH (from the Registration, Evaluation, Authorisation, Restriction of Chemicals).

Level) / PNEC (Predicted No-Effect Concentration), an assessment of persistence, potential to bioaccumulation and toxicity of a substance, etc. (if necessary). Requirements of REACH Regulation to CSA conduction are defined in the technical annexes to the Regulation, as well as in the manuals developed by the Agency of ECHA.

The assessment of chemical substances safety carried out by the manufacturer or importer shall include an assessment of the risk associated with the various uses of the substance, including all consumers of the substance in the supply chain.

CLP Regulation – *Regulation 1272/2008/EC on classification, labeling and packaging of chemical substances and mixtures* [EC, 2008], adopted within the framework of the transfer of a global system of classification and labeling of substances (UN GHS), under the jurisdiction of the European Union came into force on January 20, 2009 and to June 1, 2015 will completely replace *Directive 67/548/EEC on hazardous chemicals and the Directive on Dangerous Preparations* (1999/45/EC). Mandatory compliance with criteria of CLP/GHS Regulation on classification and labeling of chemicals will be required since December 1, 2010, and classification and labeling of mixtures will need to meet the requirements of CLP since June 2015.

According to the GHS recommendations, chemical substances and mixtures shall be classified on the basis of the risks associated with human health effects (toxicity, mutagenicity, carcinogenicity, etc.). At that, mandatory risk assessment (with different levels of priority) shall be established for certain substances. GPS study result is a formalized document (a report on GPS), which contains a description of the chemical, personal hazard, the results of risk characterization and assessment of acceptability of the risk.

The same approach to the classification is set out in the UN Recommendations on the Transport of Dangerous Goods *"Orange Book" – Model Regulations on the Transport of Dangerous Goods. List of UN* [Recommendation number 112, 1959].

Decision 768/2008/EC [EC, 2008] establishes the conformity assessment procedure correspondence to type and significance of risks (Art. 4, par. 1). *Regulation 852/2004/EC "Special rules for the organization of official control over products of animal origin intended for human consumption," dated 29.04.2004* states that "... the nature and intensity of official control should be based on an assessment of human health risks... where appropriate, on the assessment of type and performance of production process being conducted ... ".

It is important, that almost all the EU legislative documents emphasize the significance of scientific evidence of safety criteria of products and transparency of information on hazard (safety) of products. *Thus, Regulation 854/2004/EC dated 29.04.2004*, which establishes specific rules for the organization of official control over products of animal origin intended for human consumption, clearly indicates that the "legislation of the Community on food safety should have a sound scientific basis ... ". A number of documents directly link given criteria with research results, including risk assessment. *The European Commission Regulation 2073/2005* On microbiological indicators for food (Preamble, para. 9) *dated 15.11.2005* refers directly to the scientific reports (Opinions) of the Scientific Committee on Veterinary Measures relating to public health. It is outlined the main conclusions and recommendations made by scientists, with reference to the results of the assessment of health risks and the opinion of the scientific expert working group on biological hazards (Working Group of Experts BIONAZ); the Regulation establishes microbiological parameters for food.

The determination of mandatory requirements for products is not the main way to ensure consumer safety in US legislation. The special features of the technical regulation in the United States include minimum valuation; minimal restrictions for business and maximum informativity of a society. The emphasis is on the stringent regulation of requirements for information about products rather than the establishment of products requirements. Fundamental starting point that defines this approach is the assumption that the awareness of the general public, business community and consumers about the risks of products directs manufacturers to voluntarily assessment and minimization of life and health risks. RACBA, for example, provides that a report on danger to life, health and the environment shall be prepared before the preparation of other documents on the products. At the same time it is pointed out that such a report should contain relevant information on

laboratory and epidemiologic studies, evidence for the presence or absence of a relationship between the human health and life risk and potential activities.

Thus, the legal framework, particularly of the United States and the European Union, on the assessment of products risk to health is well developed, covers almost all areas of the product mix and a wide range of organizational aspects.

Procedures for the assessment of products risk to health that were originally developed in some countries, are gradually integrated into the coordinated activities of international assessment of hazards. Thus, the problems of hazardous chemicals handling were addressed in the "Agenda for the XXI Century", adopted by the United Nations Conference on Environment and Development in 1992 [Review, 2010]. Issues of sound management of chemicals is reflected in 17 different multilateral agreements, in particular *the International Code of Regulations on the Distribution and Use of Pesticides of the Food and Agriculture Organization of the United Nations (FAO)* [UNEP, 1987, 2007]*, the Basel Convention on the Control of Transboundary Movement of Hazardous Wastes and Their Disposal* [UNEP, 1989]*, the Montreal Protocol on Substances that Deplete the Ozone Layer, the Convention of the International Labour Organization (ILO) No. 170 on safe at use of chemicals at the place of production, the Rotterdam Convention on the prior Informed Consent Procedure for Certain hazardous Chemicals and Pesticides in International Trade* [UNEP/FAO/PIC/CONF/2, 1998]*, the International Convention of the International Maritime organization (IMO) for the prevention of vessel-source pollution* [International Convention, 1973], *the Stockholm Convention on Persistent Organic Pollutants* [Stockholm Convention, 2001] *and the International Medical and Sanitary Regulations* [WHO, 2005].

The international community has developed and globally agreed the System of Classification of hazard and Labelling of Chemicals (GHS) [UN, 2005]. At present, the implementation of the recommendations of the UN – GHS is held in more than 60 countries, including the US, Canada, Japan, China, India, CIS and EU countries.

In the Russian Federation and the Customs Union aspects of the organization, the use of risk assessment, the persons responsible for the implementation of risk assessment, risk communication and management are highlighted significantly weaker.

In general, Russia has significant potential to improve its own legal framework, including rich experience of foreign countries and communities and analysis of problems related to safety of products (goods) and services.

With regard to the legal framework for risk assessment in the field of product safety and technical regulation, it is necessary to address the issues of risk assessment institutionalization. Obligation to assess the risk in this sphere has led to the creation of a network of national and international scientific, research and practice, information structures that perform certain types of work in the field of risk assessment.

GHTF (Global Harmonization Task Force) is an organization that deals with the harmonization of regulatory requirements for medical devices at the international level and is designed to support the approximation of these requirements worldwide.

The European Chemicals Agency (ECHA) operates in accordance with the REACH regulation.

Project Committees ISO/PC 243 and ISO/PC 240 were specifically established within the framework of the International Organization for Standardization (ISO) on the initiative of the working group of the ISO Committee on consumer policy (ISO/COPOLCO) in order to reduce the risks associated with consumer products.

Commission Codex Alimentarius, established in 1961 at the 11th session of the Conference of the Food and Agriculture Organization (FAO) and the World Health Organization, is composed of a number of specialized committees (such as the Codex Committee on Food Additives (CCFA), the Codex Committee on contaminants in food products (SSSF) and the Joint Committee of FAO/WHO experts on Food additives (JECFA)

A whole network of specialized organizations responsible for maintaining the safety of products, for example, the European agency for food safety (EFSA), in the framework of which – the assessment of risks associated with all stages of the food chain was created

within the European Union framework in order to implement the provisions of the technical regulation system.

In the United States Consumer Product Safety issues are administered by the Consumer Product Safety Commission (CPSC), which is an independent federal authority responsible for protection of the population against the risks associated with consumer products, and involved, in addition to a risk assessment to determine the need for different "corrective actions" and their feasibility in the development of voluntary standards with industry; publication and implementation of mandatory standards or prohibition against the use of consumer products, if possible standard can not provide adequate protection of the population; submission of claims to manufacturers for product recall or organization of its repair; prosecution of researches to identify potential risks of products; information and education of consumers through mass media, state and local governments, private organizations and submission of responses to the questions of consumers, etc.

Special organizations focused on the scientific support of risk assessment, including products risk assessment (Institute for Risk Assessment of the Federal Republic of Germany, the Center for Food Safety and Applied Nutrition Risk Analysis (USA), Center for managing the risks associated with the production of grain (Uganda), Central Institute for Scientific Research in the field of food in Budapest (Hungary), and others.) are established in a number of countries.

International organizations also entrust universities and medical centers with the scientific researches on health risks assessment.

For example, within the framework of food safety in the Federal Republic of Germany, the European Commission makes legislative decisions in the field of product safety, including safety standards, among them risk assessment; EFSA – consults and provides scientific support to the European Commission; Bureau of Food and Veterinary Office of the European Commission (FVO) coordinates the activities of federal and international authorities and controls safety systems of the EU Member States and third countries; Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) adopts legal acts at the national level, develops risk management measures; The Federal Institute for Risk Assessment (BfR) and 4 departmental institutions provide scientific-methodological and informational support to the Federal Ministry of Food; Ministries of federal lands coordinate activities in the field of supervision and co-operate with the Federal Ministry of Food (BMELV); the Federal Office of Consumer Protection and Food Safety (BVL) coordinates activities between the federal, provincial authorities and the EU authorities; representatives of the regulatory authorities of federal lands (city and district authorities carry out random checks of products and quality management systems, owners of business entities ensure compliance with the goods safety requirements.

Similar systems in one form or another exist in other European countries.

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6. THE OPTIMIZATION OF SOCIAL AND HYGIENIC MONITORING BASED ON HEALTH RISK ASSESSMENT

6.1. The place of health risk assessment in the system of social and hygienic monitoring

The identification of priority national issues and strategic objectives requires reliable information and analytical framework. The system of social-hygienic monitoring (SHM), introduced in the country by the Government Resolution of the Russian Federation No. 1146 dated 06.10.1994, is the basis for the sanitary and epidemiological assessments and identification of factors that may have the most significant impact on the health and demographic indicators of the country.

SHM had been intended to accumulate information that enable the determination of cause-and-effect relationships between Russians health and factors that have influence on it, and perform a number of deep science-based analytical tasks for the benefit of decision-makers at various levels of statehood.

Currently valid "Regulations on the social-hygienic monitoring", approved by the Government of the Russian Federation No. 60 dated February 2, 2006, defines the purpose of social-hygienic monitoring as support of sanitary and epidemiological welfare of the population, which is achieved by successive solution of the main tasks:

- the hygienic assessment (diagnosis) of living environmental factors and human health;
- the identification of cause-and-effect relationships between public health status and the impact of living environmental factors on human is based on systemic analysis and public health risk assessment;
- the determination of the causes and identification of conditions for the occurrence and propagation of infectious and mass non-infectious diseases (poisoning);
- preparation of proposals on the necessary measures to address the identified harmful effects of human living environment for adoption by federal executive authorities, executive authorities of subjects of the Russian Federation and local authorities.

Each task requires relevant initial information and an adequate methodological support. Health risk assessment methodology is fully consistent with the appointment SHM according to its principles, methods and logical structure. As a consequence, it is within the social-hygienic monitoring health risk assessment has received the greatest distribution.

The introduction of health risk assessment methodology in social-hygienic monitoring began with the Resolution of the chief state sanitary doctor of the Russian Federation and the Chief State Inspector of the Russian Federation for the Protection of Nature, dated November 10, 1997 "On the use of risk assessment methodology for environmental and health of the Russian Federation population quality management" [the Resolution "On the use of the methodology ..." dated 10.11.1997]. The document was strategic in nature and had practical significance, and led to a series of effective steps for the implementation of risk assessment methodology in the practice of living environment and health quality management, including through the SHM system [Onishchenko G.G., 2005].

The tasks of risk assessment were included in the list of main priority actions of the "National Environment and Health Action Plan of the Russian Federation (NEHAP) for 2001–2003", approved by the government commission for the protection of the citizens health. The National Plan was provided to develop and strengthen the legislative and methodological framework for work on health risk assessment. It was prepared the legislative initiative "On risk assessment and management of public health risk and compensation of damage from the harmful effects of environmental pollution on human health." The chief sanitary doctor in the subjects issued the Order of the Ministry of Health of Russia No. 157 dated 21.05.2002 "On additional measures to improve the sanitary and epidemiological situation in the Russian Federation in 2002," according to which it was instructed to take effective measures for the introduction of monitoring of public health and living environment and the introduction of methodology of risk assessment of living environment adverse effects on health in 2002. At that risk assessment methodology in the system of social-hygienic monitoring was focused on the following problems solution:

– qualitatively and quantitatively assess the probability of adverse effects on the population health in a particular exposure to living environmental hazards;

– determine risk contingents among population groups exposed to harmful effects;

– allocate the types of health problems that are associated with the impact for the conditions of the specific impact;

– assess the risk structure (factors contribution to the total risk), with highlighting of priority hazards that have the most significant negative impact on the population health status;

– allocate territories (zone, areas) with the highest levels of health risks and, on the contrary, most favored territories;

– justify the lines of research on evidence of actual harm to the health and related economic loss;

– predict negative or positive changes in the health of the population based on forecasts of living environment quality changes.

For the formation of information files that were supposed to be the basis of hygienic analytics and risk assessment, there was created the Federal Information Fund (FIF) that collects national statistics and the results of aimed laboratory studies of the authorities and organizations of Rospotrebnadzor, Federal Service for Hydrometeorology and Environmental Monitoring of Russia and other competent executive authorities. The list of data accumulated in the system is quite significant and covers measures of quality of living environment, public health, workers' health, a number of indicators of socio-economic development of regions. This allows us to assess the risk of health problems under the influence of macro- and microsocial factors and factors of external and working environment, consider the combined effect of factors. Long time series of data collected in the FIF in relation to all subjects of the Russian Federation, make it possible to make risk assessment and deep science-intensive analysis on the level of the Russian Federation as a whole and at the level of individual regions in particular.

The expanding of the use of risk assessment methodology in the framework of social-hygienic monitoring has required scientific validation and development of relevant guidance documents. The relevance of this problem was highlighted in the decision of the board of the Ministry of Health of Russia dated May 28, 2002. "On work on social-hygienic monitoring in 2000–2001 and tasks to improve it." At the moment, more than a dozen of documents relating to risk assessment problems, including the "Guidance for the assessment of risk for public health when exposed to chemicals that pollute the environment" [R 2.1.10.1920-04], "Guidelines for the assessment of occupational risks for worker's health. Organizational and methodological foundations, principles and criteria of assessment" [R 2.2.1766-03], procedural guidelines "Food stock and food products contamination by chemicals: collection, processing and analysis of indicators" [procedural guidelines 2.3.7.2125-06]," Determination of exposure and assessment of risk of food chemical contaminants impact on the population" [procedural guidelines 2.3.7.2519-09], a number of guidelines [guidelines 5.1.0029-11; guidelines 2.1.10. 0031-11; guidelines 2.1.4.0032-11; guidelines 5.1.0030-11;

guidelines 2.1.10.0057-12, etc.] have been already developed within the SHM. Documentally confirmed approaches are widely used in the practice of social-hygienic monitoring of the country regions. Large-scale studies are performed in Voronezh region [Pichuzhkina N.M., 2006], Sverdlovsk region [Gurvich V.B., Kuzmin S.V. et al., 2004; Kornilkov A.S., 2006], Tula region [Grigoriev Yu.I., Liapina N.V., 2013] Perm Krai [Zaitseva N.V., May I.V. et al., 2009]; St. Petersburg [Kiselev A.V. et al., 2001], Moscow [Avaliani S.L., Mishina A.L., et al., 2001-2010; Bobkova T.E., 2009], Samara [Tsunina N.M., Ayupova L.V., 2014], Orenburg [Boev V.M., 2009; Boev V.M. et al., 2006], etc. In these studies, the risk assessment is mainly associated with the study of effects of chemical factors on the population and is to establish the probability of oncology diseases during lifetime (cancer risk) or semi-quantitative assessment of noncarcinogenic effects (determination of hazard factors or indexes). Air, drinking water, soil, food, and working environment pollutants are considered as risk factors [Zadiran A.V. et al., 2012; Trukhina G.M., 2008]. The results of the risk assessment as part of social-hygienic monitoring are used to validate management decisions regarding environmentally friendly and hygienic measures on specific impact sources, architectural and planning measures for facilities output from the dwellings zone, creation of buffer zones, development and implementation of preventive health assistance to the population, etc. [Gurvich V.B. et al., 2013; Mehantev I.I. et al., 2012; Kuzmin S.V. et al., 2010; Fokin S.G., 2011]. Optimal diets are developed, measures of targeted rehabilitation and preventive care to people living in areas of unacceptable risk are implemented, proposals to optimize the supervisory activities are formed based on the results of health risks assessment within the SHM.

In addition, the risk assessment methodology can be considered as a tool for the improvement of the system of laboratory researches within the SHM. Health risk criteria validated the optimal networks of positions and observation programs allow obtaining the

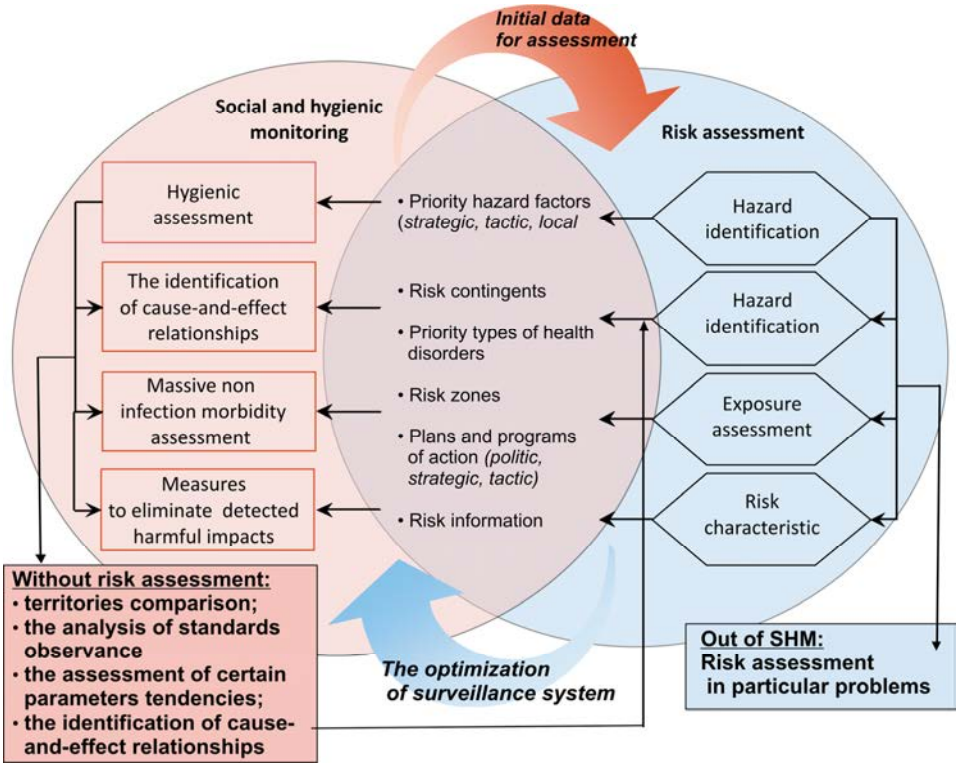


Fig. 6.1. Risk assessment in the system of social and hygienic monitoring

most correct information about health hazard and risk levels, including in the dynamics. Such "self-improvement" of the SHM provides the maximum value of laboratory tests of the real situation at minimum required measuring volume. In conjunction with the modern computer geographic information systems (GIS), spatial interpretation of the results of risk assessment as part of the SHM enables to assess the number of people exposed, and features of the spatial distribution of risks.

At the same time, for wider application of the methodology in the frameworks of the SHM, a more developed methodological support for all stages of risk assessment is required: hazard identification, "exposure – response" relationships determination, exposure assessments, etc. A number of developments is presented in sections 6.2–6.4.

6.2. Methodological approaches and practices to optimize the network and programs of laboratory researches within the system of social and hygienic monitoring using a health risk assessment methodology

The effectiveness of the decisions made based on the social and hygienic monitoring is determined primarily by the quality of the initial information about the risk factors and associated disorders of population health.

In this context, the selection of the points of laboratory measurements within the SGM system and the observational programs correspondence to the actual population exposure conditions is the key to the accurate assessments of hygiene and the reliability of information and the analytical base of decisions made.

The selection of the zones (areas) of the territories in which the population is exposed to the greatest health risks is extremely important to optimize the SGM observation network [Zaitseva N.V. et al., 2010]. In this case, the calculation should include the different routes of harmful factors intake, acute exposure and chronic non-carcinogenic effects, as well as the probability of cancer under the influence of carcinogenic factors, etc. Despite the fact that the instrumental researches of living environment facilities quality are quite costly procedure, the criterion of field studies optimization in the SGM is the minimum number of sampling points and studied factors that ensure the availability of data on population exposure and potential health risks.

Especially important is the Optimization of the stations network and programs of instrumental measurements within SGM in the largest industrialized settlements, where the spatial variability of living environment quality, and hence the threats to the health of citizens is quite high and is determined by a large number of hazards.

Methodical approach based on the sequential allocation of zones, which are characterized by health risk factors different in number and intensity, risk assessment for each zone and the choice of the factors forming the maximum contribution to this risk is proposed in order to validate minimally sufficient number of monitoring points of the chemical air pollution in large settlements.

For example, zoning can be done on the basis of dispersion calculations using a consolidated database on the most affordable list of stationary and mobile sources of air pollution. Estimated regular grid is formed so as to be able to assess the exposure of the population of all the residential areas of the city. Calculations are performed for all chemical contaminants for which there is evidence of harmful health effects and which may be included in the assessment of acute and/or chronic carcinogenic and non-carcinogenic risk (N). Each point (x; y) located in the residential area is characterized by the N-th set of of hazardous contaminants concentrations as a result of a series of calculations.

The resulting data matrix is subjected to cluster analysis that can be performed by various means. Analysis is tested and found reliable using the software package SAS,

Statistika, etc. Clusters – the group of points in an area which has a homogeneous concentrations of polluting components – are obtained as a result of analysis.

The number of clusters in the territory can be significant if the territory is large enough, and the hazards nomenclature is high. The number of clusters can be set based on the expert advice of the existing regulation documents[1].

The average characteristics of the levels of carcinogenic, acute, chronic, and non-carcinogenic risk are calculated based on the results of cauterization, for each group of points (clusters) that characterize a certain territory. At that, exposure levels in the cluster are specified by average (MEEN) characteristics of exposure factors $k_x(l+n+m)$ (6.1):

$$[M]^T = \begin{bmatrix} \overline{CR_1^1}, & \overline{HI_{ac1}^{\,1}} \ldots \overline{HI_{acn}^{\,1}}, & \overline{HI_{cr1}^{\,1}} \ldots \overline{HI_{crm}^{\,1}} \\ \overline{CR_1^2}, & \overline{HI_{ac1}^{\,2}} \ldots \overline{HI_{acn}^{\,2}}, & \overline{HI_{cr1}^{\,2}} \ldots \overline{HI_{crm}^{\,2}} \\ \ldots & \ldots & \ldots \\ \overline{CR_1^k}, & \overline{HI_{ac1}^{\,k}} \ldots \overline{HI_{acn}^{\,k}}, & \overline{HI_{cr1}^{\,k}} \ldots \overline{HI_{crm}^{\,k}} \end{bmatrix}, \quad (6.1)$$

where [*M*] – cluster medium matrix;

CR – chronic carcinogenic risk level;

HI_{ac} – hazard index with respect to *n*-critical organs and systems in acute exposure;

HI_{cr} – hazard ratio with respect to *n*-critical organs and systems in chronic exposure;

k – the number of clusters;

l – the number of substances used in the calculation of individual carcinogenic risk;

n – the number of critical organs and systems, for which the hazard index is estimated under acute exposure;

m – the number of critical organs and systems, for which the chronic non-carcinogenic risk is estimated;

Clusters are ranked according to the criteria of acceptable risk. Ranking criteria and clusters characterization from the perspective of the instrumental studies organization within the SGM are the following:

– I rank (high risk level unacceptable to the working conditions and the public): $CR>10^{-3}$, $HI_{ac}>1$ (one index, and more), $HI_{cr}>1$ (one index, and more). The constant monitoring of the full program in the mode of a stationary monitoring station is obligatory. It is recommended to perform monitoring in the on-line mode;

– II rank (average risk level acceptable to the working conditions and unacceptable for the public): $10^{-4}<TCR<10^{-3}$, $HI_{ac}>1$ (one index, and more), $HI_{cr}>1$ (one index, and more). Constant monitoring of the full program in the mode of a stationary monitoring station is obligatory. Monitoring according to the reduced program in the mode of route monitoring station is allowed;

– III rank (low (acceptable) risk level): $10^{-6}<TCR<10^{-4}$, $THI=1$ (one index, and more). Sample reconnaissance observations according to the incomplete measurement program, including under adverse weather conditions are recommended. The mode of route monitoring station or under plume research is allowed;

– IV rank (minimum (preferable, target) risk level): $TCR<10^{-6}$, $HI<1$ (each index). Monitoring is not required. It is possible to conduct sample surveys in a changing hygienic situation, the emergence of new sources of exposure, etc.

Optimal monitoring station placement point is selected and a program of instrumental measurements is formed for clusters of I-III ranks.

Clusters location is matched with the spatial distribution of the residence density for the exposed population number assessment to highlight a placement point of air quality

[1] In accordance with the RD "Guidelines for the air quality control": 1 station – up to 50 thousand inhabitants, 2 stations – up to 100 thousand inhabitants, 2–3 stations – 100–200 thousand, 3–5 stations – 200–500 thousand, 5–10 stations – more than 500 thousand, 10–20 stations (stationary and route) – more than 1 million inhabitants.

monitoring station for SGM within a cluster. The performance of such operations in an environment of geographic information system based on the vector map of the territory is optimal. For example, if the computational grid covers the entire residential area, population number can be defined as a residence density function for each segment. As a consequence, reference points within the cluster boundaries can be selected to accommodate the monitoring station (stations), they belong to the segments with the highest residence density. As measurement results, this will allow obtaining data that are representative for the entire cluster and to the greatest extent characterizing the living environment of the larger population.

The formation of monitoring programs is carried out on the basis of the estimates of the individual chemical impurities contribution to the formation of unacceptable health risks. In this regard, the average values of risk parameters for each cluster ([M]) rank separate impurities according to the criteria given in Table 6.1.

Table 6.1

Criteria to rank substances – health risk factors for the SGM programs formation

The degree of contaminants priority	Population Health Risk Value	Recommendations for incorporation in the monitoring programs
High	Contribution to the unacceptable carcinogenic and non-carcinogenic acute or chronic risk is more than 50%	Mandatory inclusion to a full program of observation programs
Average	Contribution to the unacceptable carcinogenic and non-carcinogenic acute or chronic risk of 25–50%	Inclusion to the complete, incomplete, or reduced observation programs is recommended
Low	Contribution to the unacceptable carcinogenic and non-carcinogenic acute or chronic risk of 10–25%	Inclusion of under plume and reconnaissance observations in the program is recommended
Non-priority	There are no unacceptable risks or contribution to the unacceptable carcinogenic and non-carcinogenic acute or chronic risk is less than 10 %	Are not included in the programs of instrumental studies

The final amount of monitoring programs is determined by an expert, taking into account economic and other parameters, as well as instrumental observations carried out in the framework of environmental monitoring in the territory, production control, researches in the course of control and surveillance activities. If there are measurements that are performed by other organizations, SGM programs are formed to avoid thr duplication of researches and opportunities for data exchange between public services.

In general, the optimal reasonable programs of air quality monitoring in the minimum required number of sampling stations can fully provide baseline data on the need for the adequate hygienic assessment of the situation.

Methodological approaches for optimization of the monitoring stations placement was approved based on the example of several major cities for different tasks. Thus, the problem of the optimal allocation of minimum sufficient number of sampling stations and the lists of monitored indicators for long-term monitoring over the level of health risk, the forecast of changes in indicators and assessment of the effectiveness of health risk management at the municipal level was posed for the industrial center – the city of Perm. For the cities of Kazan and Sochi, the optimization of monitoring stations was performed for air quality monitoring during mass sporting events (Summer Universiade 2013 and the Winter Olympic Games 2014).

The problem of the stations network optimization for the city of Perm has arisen in connection with high development pressure, elevated levels of morbidity in a number of diseases classes and the need to establish the sources of health risks.

The most complete list of all potentially harmful chemical compounds that can affect humans in the studied area and coming from the air and drinking water (the components of emissions and discharges, chemical compounds and the products of their transformation entering the drinking water and soil were considered) was made at the initial stage. It was found that, about 80 of the 450 contaminants of the full range of chemical factors that pollute the air and drinking water may prove to form the negative effects in the population health status. At that a number of substances (e.g., heavy metals – chrome, manganese, nickel, etc.) can be ingested with the air, drinking water, and soil.

9 clusters with similar properties were obtained for the city of Perm for the set of parameters, which are characterized by homogeneous values of the public health risk. The risk was rated as unacceptable in almost all dedicated parts of the city (individual carcinogenic lifetime risk exceeded; non-carcinogenic risk hazard indexes exceeded 1.0 for some critical organs and systems depending on the exposure specifics). A summarized data on the risk levels in the designated areas are shown in Table 6.2.

Table 6.2

Average parameters for population health risk clusters calculated for the optimization problems of instrumental studies within the SGM in Perm

Number of the station	Health risk value (the worst of the determined ones)		Rank	Recommended monitoring programs
1	Carcinogenic	2E-04	I	The full program in the stationary station mode
	Noncarcinogenic acute	5.8		
	Noncarcinogenic chronic	18.8		
2	Carcinogenic	2E-05	I	The full program in the stationary station mode
	Noncarcinogenic acute	2.3		
	Noncarcinogenic chronic	21.33		
3	Carcinogenic	1E-05	I	The full program in the stationary station mode
	Noncarcinogenic acute	1.43		
	Noncarcinogenic chronic	48.4		
4	Carcinogenic	1E-05	I	The full program in the stationary station mode
	Noncarcinogenic acute	1.37		
	Noncarcinogenic chronic	42.3		
5	Carcinogenic	2E-06	I	The full program in the stationary station mode
	Noncarcinogenic acute	1.03		
	Noncarcinogenic chronic	52.6		
6	Carcinogenic	2E-06	I	The full program in the stationary station mode
	Noncarcinogenic acute	<0.1		
	Noncarcinogenic chronic	30.2		
7	Carcinogenic	1E-04	I	The full program in the stationary station mode
	Noncarcinogenic acute	<1.0		
	Noncarcinogenic chronic	11.2		
8	Carcinogenic	1E-03	II	Monitoring according to the reduced program in the mode of route monitoring station is allowed
	Noncarcinogenic acute	1.37		
	Noncarcinogenic chronic	4.5		
9	Carcinogenic	5E-0.6	II	Monitoring according to the reduced program in the mode of route monitoring station is allowed
	Noncarcinogenic acute	1.73		
	Noncarcinogenic chronic	5.2		

The point of optimal location of the monitoring stations were chosen and chemical impurities contributing to the health risks were identifies for each cluster.

The zoning of city territory with SGM stations placement is shown in Fig. 6.2.

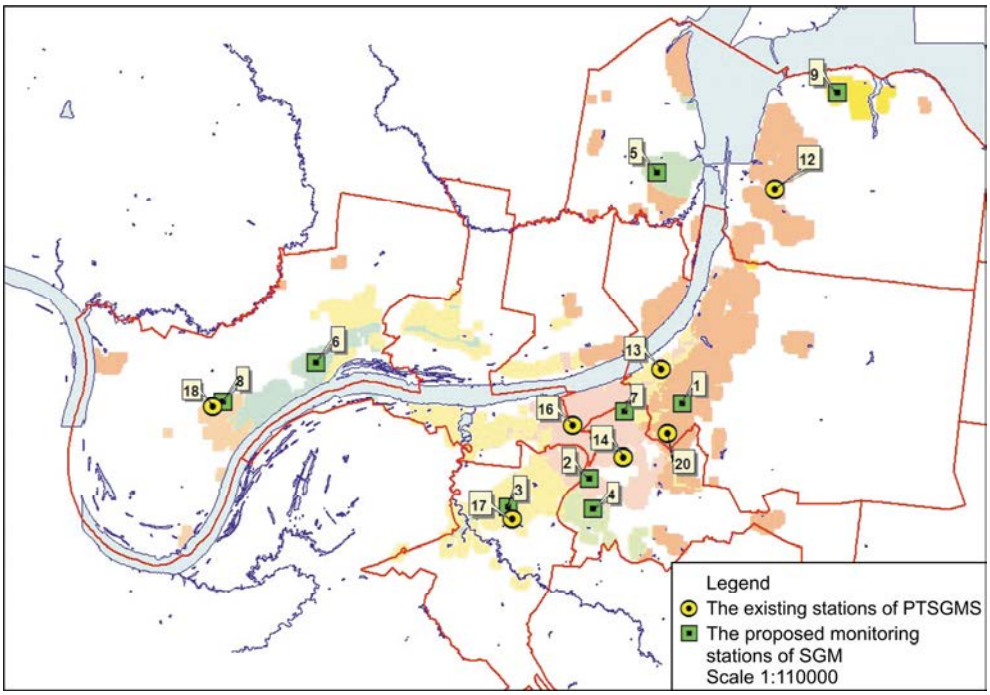


Fig. 6.2. The location of 9 clusters, stations offered for SGM and existing PTSGMS stations

In general, it was revealed that with a significant list of contaminants released into the air of the city with population exceeding one million, more than 80% of health risk form 17 substances that are recommended for inclusion in the monitoring program.

Programs are differentiated according to the structure of risk and the equity contributions of substances to risks.

On the average measurements of 6–9 substances making most contributions to the health risk are recommended at SGM stations. At that, it is required to perform studies on a larger number of chemical impurities – up to 16 (including impurities required for measurement) in the zones where the risk is higher and contamination is more complex and multi-component.

For example, at a stationary post in the zone of the largest multi-discipline industrial hub influence, the mandatory monitoring of benzopyrene and chromium was recommended according to the carcinogenic risk criteria; acrolein, nitrogen dioxide and hydrogen sulfide – according to the criteria of acute non-carcinogenic risk; suspended substances, formaldehyde and benzene – according to the criteria of chronic non-carcinogenic risk.

The obtained risk zones and SGM stations placement points were matched with the location points of the existing Roshydromet stations to avoid the duplication of instrumental studies. Analysis showed that the individual stationary stations of the environmental monitoring are representative for clusters selected according to the criteria of health risk. This indicates that data from stations can and should be used in the SGM system through their supplementation with information about the impurities that are not studied at Roshydromet stations, but form a high population health risk and therefore require the systematic observation.

The analysis showed that a number of Roshydromet stations is located in areas that are attributable to the same cluster, which indicate to the insufficiently high informativity of research systems – data from stations characterize territories close by the level and range of

the contamination. The number of residential areas of the city cannot be characterized by the results of studies of the environmental monitoring system. Thus, SGM should maximize the use of these environmental monitoring systems supplementing and extending it by own sampling points and substances that are significant primarily on the criteria of population health exposure.

Priority risk factors analysis, which allows adjusting the program under the conditions of limited human, financial and other resources was additionally made for the monitoring program at each point.

The whole system of instrumental SGM studies regarding chemical exposure factor was focused on population health risk values being as much flexible and informative as possible.

Similar studies were performed to determine the list of priority chemicals subject to systematic observation and monitoring in ambient air, drinking water and soils during the World Summer University Games (Universiade 2013) in Kazan, and ensuring the making of operational control decisions to minimize risks for the health of athletes and other participants of mass sporting event.

Based on the requirements of the Olympic Charter "... to encourage and support measures to protect the health of athletes" and "... to carry out the games in accordance with environment requirements", the selection of priority chemicals was carried out on the basis of an assessment of compliance with hygienic standards of air, drinking water and soil quality and acute health effects risk assessment. The criteria take into account the recommendations of the international methodology (Environmental Health) and domestic harmonized documents [Guide, 2004] with the following provisions:

– the chemical composition of atmospheric air (outdoor air) determines the chemical composition of the air inside the sports facilities (indoor);

– the breathing rate of an athlete at the maximum load for 20–30 minutes can reach 100–120 m/min. This ventilation increase is provided by increasing breathing frequency and volume, moreover the frequency can be increased up to 60–70 breaths per minute and tidal volume – from 15 to 50% of the lung vital capacity (H. Monod, M. Pottier, 1973);

– the period of Universiade (July 6–17, 2013) is not essential for the formation of chronic effects, and it is appropriate to choose priority chemicals according to the criteria of acute harmful effects on humans;

– adverse weather conditions (surface inversion, no wind conditions, the poor dispersion of industries and motor vehicles emissions) can arise during the sporting events;

– the use of centralized water supply for drinking purposes without the use of special cleaning equipment and agents can take place during the competition;

– Universiade business facilities will operate in normal mode during the Universiade;

– the structure of the used automobile fuels will be unchanged in whole.

The calculation of acute non-carcinogenic risk (expressed through the hazard index HI, the acceptable level of which is equal to 1.0) was performed based on data on the ground-level concentrations of pollutants obtained for the no wind conditions in the summer time. It was determined that a number of sports facilities under the conditions of the low dispersion of emissions from factories and vehicles can form ground-level concentrations capable to cause adverse acute (reflex) responses in athletes and guests of the competition. The example of aggregated data on projected levels of acute risk in location areas of some sports facilities of the Universiade is shown in Table 6.3.

Certain hazard indices for such conditions in respect of the respiratory system (priority affected body system) ranged from 0.26 (sheet shooting complex) to 10–15 ("Vatan" sports complex with a games room and a swimming pool at ul. Bondarenko, 2, "Rubin" stadium and a sports complex at ul. Kopylov).

The most significant factors of acute risk to the health of athletes and guests of the competition are nitrogen oxides, sodium hydroxide, sulfur dioxide, dust, including fine ones.

In this case, the equity contributions of priority contaminants varied depending on the location of the sports facility, but the list of priority pollutants remained unchanged[1]. The example of the assessment of the equity contributions of individual impurities to general acute risk in the event of adverse weather conditions during mass events is shown in Fig. 6.3.

Table 6.3

Summary data on the projected risk of the acute adverse effects of chemicals contaminating air on the respiratory system at the locations of a number of sports facilities of the Universiade 2013 (before the full implementation of measures)

Facility, location	The type of use	Predicted acute risk (hazard index), priority risk factors
Universiade Village	The accommodation of participants and team representatives	*HI*=1.1 – low risk Suspended substances: TSP, PM_{10}, $PM_{2,5}$ (1.1MPC)*
Football stadium for 45,000 seats, ul. Chistopolskaya	The staging of the opening and closing ceremonies of the Universiade. International Press Center. International Broadcast Centre (IPC)	*HI*=1.1 – low risk Nitrogen dioxide
"Miras" Sports Complex ul. J. Faizi, 6	Basketball Competitions by Groups	*HI*=1.4 – low risk Nitrogen dioxide
"Tulpar" Sports Complex ul. R. Gareev, 80	Basketball Competitions by Groups	*HI*<1,0 – acceptable risk
"Triumph" universal sports complex with a games room and a swimming pool, ul. O. Koshevogo, 19	Basketball teams training	*HI*=2.6 – low risk. Suspended substances: TSP, PM_{10}, $PM_{2,5}$
"Forward" Sports Complex, ul. Khimikov, 40.	Basketball teams training	*HI*=1.1 – low risk. Suspended substances: TSP, PM_{10}, $PM_{2,5}$
"St. Petersburg" Volleyball Centre ul. M. Bulatov, 1	Volleyball Competitions by Groups	*HI* = 3,8 – reduced risk. Nitrogen dioxide, carbon monoxide, suspended substances: TSP, PM_{10}, $PM_{2,5}$
"Bustan" Sports Complex prof. Nuzhin passage, 1	Volleyball Competitions by Groups	*HI*=1,5 – low risk. Suspended substances: TSP, PM_{10}, $PM_{2,5}$ (up to 1.5 $MPC_{мр}$)
"Olympiets" Sports Complex, ul. Gorky highway, 160	Volleyball teams training	*HI*<1.0 – acceptable risk
"Rubin" Stadium ul. Kopylov, 2a	Final football competition	*HI*=5.1 – increased risk. Suspended substances: TSP, PM_{10}, $PM_{2,5}$
"Moscow" Sports Complex ul. Moskovskaya, 49	Volleyball teams training	*HI*=2.5 – low risk. Nitrogen dioxide, carbon monoxide

[1] The obtained results were used not only for the development of measures to minimize the risks that have been implemented prior to the competition. A significant improvement in traffic, the implementation of air protection measures in a number of industrial facilities in Kazan (Kazan Aircraft Production Association (KAPO), "Elecon" plant, Kazan Optical and Mechanical Plant, etc.) have resulted in reducing the levels of air pollution and, consequently, human health risks.

The obtained data analyzed in conjunction with existing information from SGM stations in the city allowed forming a network and a program to monitor air quality during the Universiade.

It was assumed that the program will provide an assessment of air quality in the area of all facilities of the Universiade and allow making operational tactical decisions in cases of high risk to the health of athletes and other participants of competition, the visitors of the Universiade and citizens of Kazan.

Population health risk analysis generated by the water ingestion of environmental factors showed that the parameters of non-carcinogenic risk expressed by the coefficients and hazard indexes do not exceed the permissible level. The adjustment of the existing program of drinking water quality control in Kazan was not required. Relative priorities (substances that form the hazard quotient within the acceptable, but higher than other chemical impurities) included copper, magnesium, residual chlorine and fluorides. It has been shown that the placement system of the sample points of drinking water within SGM ensures control completeness within the city. A similar conclusion (on the absence of the need to change the SGM program) was made for soil monitoring.

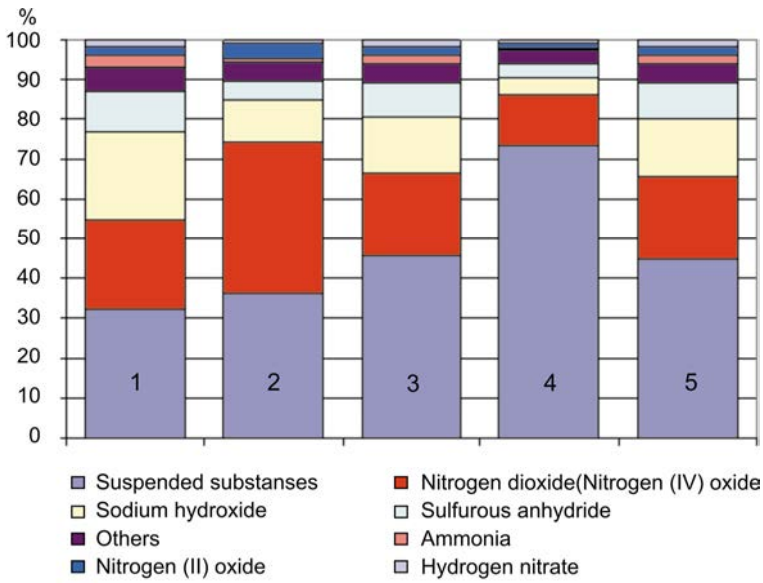


Fig. 6.3. The equity contributions of the individual substances to the hazard index at the location points: 1) "Triumph" universal sports complex (*HI*=6.09); 2) "Saint-Petersburg" volleyball center (*HI*=8.34); 3) Central Stadium (*HI*=10.66); 4) sports complex at ul. Kopylov (*HI*=12.8); 5) stadium at ul. Timiryazev (*HI*=9.74)

415 studies of air samples were conducted during the period of the Universiade in monitoring points recommended by accredited laboratory centers in view of the greatest population health risk. Content of the controlled substances from 07.05.2013 till 10.07.2013: suspended particles PM_{10} and $PM_{2.5}$, soot, carbon monoxide, nitrogen dioxide, formaldehyde, sulfur dioxide, benzene and some other impurities does not exceed single maximum permissible concentrations established for the air of populated areas.

A similar problem was solved for Sochi for the Winter Olympic Games in 2014. Based on the meteorological conditions of the area, the planning of sports and social facilities, the specific design of the road network, the intensity and structure of traffic flows during mass sports activities, and based on an assessment of public health risks (including athletes with increased physical activity), it was recommended to:

– continue the monitoring over the air quality in the stationary automatic Roshydromet stations in Krasnaya Polyana, in the Imereti lowland and Laura Cordone (Table 6.4);

– organize an additional air quality observation station at a point within the Olympic Park territory near the Olympic Village (Fig. 6.4) with coordinates of 43°24'40.77"N latitude, 39°56'31.32"E longitude. Organize the samples selection by contaminants: Carbon monoxide, nitrogen oxide, nitrogen dioxide, sulfur dioxide, the amount of hydrocarbons, benzene, suspended particles: TSP, PM_{10}, $PM_{2,5}$ (Table 6.5). Frequency of observations at the station in the Olympic Village – 4 times a day (full program).

Table 6.4

The coordinates of the locations and the measured impurities at the Roshydromet stations of the automatic control of air quality in places of sporting events

Name	Longitude, °	Latitude, °	Measurable impurities
ACK-A No. 2 Krasnaya Polyana	40.20546	43.68149	Carbon monoxide, nitrogen oxide, nitrogen dioxide, sulfur dioxide, the amount of hydrocarbons, methane, PM_{10}, $PM_{2,5}$
ACK-A No. 3 Imereti lowland	39.98029	43.40243	
ACK-A No. 4 Laura cordon	40.26517	43.69965	

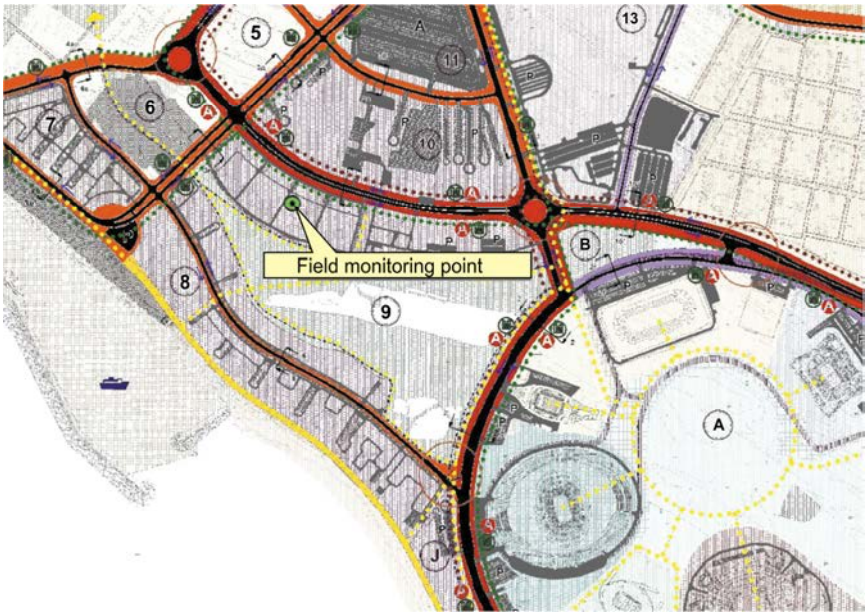


Fig. 6.4. The location of the proposed point of field observations in the Olympic Park

Table 6.5

The coordinates of the proposed station and priority pollutants for air quality control program on the territory of the Olympic Park

Name	Longitude, °	Latitude, °	Priority contaminants
Observation post T-1 on the territory of the Olympic Park	39°56'31.32" eastern longitude	43°24'40.77" northern latitude	Carbon monoxide, nitrogen oxide, nitrogen dioxide, sulfur dioxide, the amount of hydrocarbons, benzene, suspended particles: TSP, PM_{10}, $PM_{2,5}$

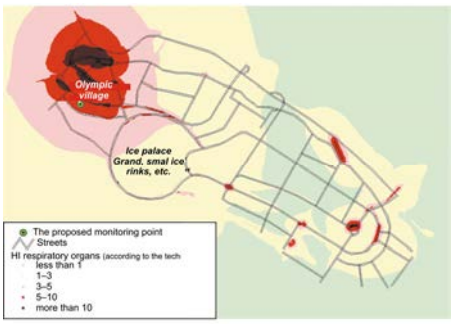
The placing of additional station has been recommended based on the results of health risks assessment when exposed to chemicals, the receipt of which was predicted by the emissions of the cars of guests and participants of the Olympic Games (other sources have not formed significant contributions to health risks). The forecast of intensity and structure of traffic flows during the Olympics was made based on the data of Autonomous Nonprofit Organization "Transport Directorate of the Olympic Games" and taking into account the layout of sports facilities, and it was found that prospective peak traffic density on the territory of the Olympic Park can be up to 3850 cars/h, and could reach 4042 cars/h taking into account the current traffic on the M-27 highway, which runs from the southeast to the northwest of Adler district along the railroad, as well as public and private transport registered in the territory of the Adler district of Sochi, (including: 286 bus/h; 64 microbus/h; 3500 cars/h). Traffic volume in the Olympic village was predicted at the level of up to 370 vehicles per hour.

The simulation modeling of several options of traffic volume and the use of various fuels was performed in the view of these data (Fig. 6.5).

Worst case (maximum traffic density, the use of regular-92 gasoline, unfavorable conditions for dispersion) suggested the presence of the unacceptable acute risk of respiratory disorders.

The simulation of the use of clean fuels and the reduction of the overall traffic density indicated the possibility to achieve the minimization of the risks to an acceptable level.

Taking into account the set of data including the above materials, the organizing committee of the Olympic Games was focused on the restriction and optimal organization of traffic, the priority of public transport, the renewal of rolling stock and the



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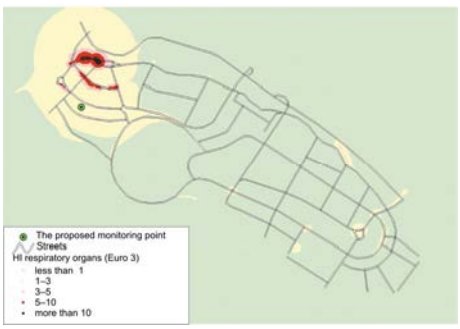

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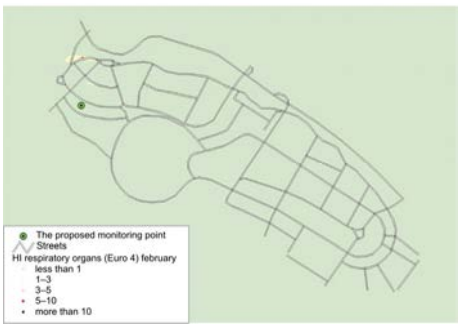

в

Fig. 6.5. The comparative characteristics of the fields of risk from acute respiratory exposure in the territory of the Olympic Park when using different types of fuels (peak traffic load, weather conditions – no wind conditions):
а – fuel according to GOST;
б – fuel of Euro-3 standard;
в – fuel of Euro-4 standard

transfer of public transport to cleaner fuel[1]. In view of the above developments, it was revealed that the study of 1679 air samples during the period of the Olympic Games practically did not record the levels of air pollution, which could lead to the risk of acute health disorders of participants and guests of the Olympics.

Thus, the optimum stations positioning system and instrumental examination program adequate health for risk levels allow receiving highly informative materials suitable for a wide range of decision-making as part of SGM.

However, the use of only instrumentation data monitoring for population health risk assessment within SGM significantly reduces the abilities of the whole system. In this regard, problems of applying the methods of instrumental data interfacing with model calculations are formulated and solved.

6.3. The improvement of the quality of population exposure assessment in the health risks assessment within the social and hygienic monitoring

The improvement of the human environment quality assessment and exposure assessment as a measure of exposure can and should be carried out in different directions: through the refinement of exposure scenarios; through the improvement of the accuracy of methods of quantitative assessment of the factor level; through the assessment of microenvironment, etc.

One way to improve the exposure assessment quality is the matching of direct measurements data and estimated simulation of hazard propagation from its sources. The letter is ubiquitous in the assessment of the inhalation exposures [Bobkova T.E., 2009; Mishina A.L., 2009; Hanna S.R., Kwak B.K., 2010]. In this case, the estimated assessment of the emissions components propagation has a number of benefits: allows building a complete spatial model of the area contamination; allows determining the concentration at any point in the studied area, evaluating the change in concentration depending on the set meteorological conditions, operation modes of stationary sources and/or intensity of traffic flows. The analysis of pollution maps with the location of residential development provides an opportunity to assess the exposure distribution in terms of population number, isolation of contingents with the highest exposure parameters. Possibility to establish a specific air pollution source and, ultimately – a health risk, is also essential. The disadvantage of the estimated method is the dependence of validity of the obtained data on pollutants concentration in the atmosphere on the reliability of the input parameters, the quality of the selected mathematical model and information adequacy for the implementation of this model [Fushimi A. et al., 2005].

To avoid the inaccuracies of the estimated methods, some authors use direct instrumental studies, which provide a more accurate assessment of the environment quality [WHO, 1997; Shaygardanova Ch.H, Khamitova R.J., 2008]. Often such exposure analysis methods are in preference to the calculations results. However, it should be noted that the direct measurement of the environment quality always characterizes the state of the medium at the given moment or a period of time at the particular location area. The reliability level of field studies in the assessment of the spatial differences of points on the territory is low and highly depends on the number of monitoring stations located in the territory. The areas of large industrial centers require a significant number of monitoring stations in order to the spatial contamination pattern of the city was quite correct

[1] The decision of the Board of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare "Results of Sanitary and Epidemiological Surveillance in the preparation and holding of the XXII Olympic Winter Games, XI Paralympic Winter Games in Sochi in 2014" dated May 23, 2014.

[RD 52.04.186-89, 1991]. At that, task of inter- and extrapolation of data from monitoring stations on the adjacent and remote areas remains pressing. The literature describes methods for data interpolation (method of inverse distance, Krige method, Shepard method, triangulation with linear interpolation, etc.) [Davis J. S., 1990; Fushimi A. et al., 2005; Kwak B.K. et al., 2010]. The methodology for pollution levels calculation according to stationary Roshydromet monitoring stations is based on the method of inverse distances, which is currently used most widely in the interpretation of air quality data, including the calculation of background concentrations of impurities (RD 52.04.186-89, 1991). However, all these methods are focused on the transformation either only instrumental, or only estimated data.

In this context, the task of developing a method that combines the positive aspects of the design simulation and instrumental measurements, to adequately assess the air quality in large territory where significant number of population lives under the influence of emission from stationary and mobile pollution sources is relevance and perspective.

The proposed method of population exposure assessment based on the matching of estimated and instrumental data on ambient air quality [Mai I.V. et al., 2013] can be realized through the following successive steps:

– the formation of the actual fullest electronic database of stationary and mobile sources of air pollution in the studied area in relation to the vector map of territory, preferably in GIS;

– the calculations of dispersion on a regular grid with a possible common step on the rectangle, covering the whole studied area;

– the calculation of ground-level concentrations at each point where the instrumental investigations were carried out. Placements of stationary stations of Roshydromet system were considered as such points to approximate the average annual data; all instrumental measurements points were considered as points to approximate data of single pollution levels, including during the route, under plume, or other studies;

– the calculation of the compliance coefficients at the points of instrumental studies in order to match estimted and field concentrations of pollutants (6.2):

$$K_i = \frac{C_i^p}{C_i^y}, \tag{6.2}$$

where i – point (observation station) number;

C_i^r – the estimated concentrations of the pollutant in the i-th observation station;

C_i^p – the actual concentrations of the pollutant in the i-th observation station;

The comparison of the estimated and field data in matching single concentrations is carried out only for uniform meteorological conditions;

– the connection of observation stations points with Delaunay triangulation method by non-crossing segments so that the new segment could not be added without interfering with the existing ones [Skvortsov A.V., 2002] (Fig. 6.6);

– the determining of identification of each points located within a polygon formed by the outer points of instrumental measurements to one of the obtained triangle with the following conditions: point is connected by segments with corners of each triangle; if the area of the triangle is equal to the sum of the areas the three formed triangles $S = S_1 + S_2 + S_3$, it is considered that the point belongs to this triangle $S < S_1 + S_2 + S_3$; if, this point does not belong to this triangle;

– the calculation of the coefficient of conformity at all points inside the polygon. It was assumed that the distribution of compliance coefficient within the polygon formed by the observation stations points is a continuous linear function of two variables, which can be written as follows (6.3):

$$K(x,y) = a_0 + a_1 x + a_2 y, \tag{6.3}$$

where a_0, a_1, a_2 – arbitrary constant coefficients.

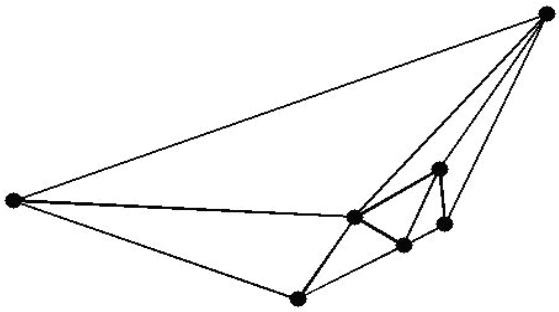

Fig. 6.6. Triangulation of observation station points

The coefficients of concordance at the stations forming a triangle were designated as k_1, k_2, k_3;

– the solution of the system of three linear algebraic equations for the unknown coefficients a_0, a_1, a_2 (6.4):

$$k_i \equiv K(x_i, y_i) = a_0 + a_1 x_i + a_2 y_i, \quad i = \overline{1,3}. \tag{6.4}$$

The solution of the system (6.4) resulted in an unambiguous expression of the function (6.3) through its nodal values and the values of the coefficients in all points lying inside the polygon formed by the points of instrumental measurements stations;

– the extrapolation of the values of the conformity coefficient for points outside the obtained polygon. Coefficient values for these points are equal to the coefficients in the nearest point on the boundary of the polygon formed by the points of instrumental measurements. Approximated values of the compliance coefficient were obtained in all grid points;

– the calculation of pollutants concentrations in each design point in the studied area (6.5):

$$C^r(x,y) = K(x,y)C^p(x,y), \tag{6.5}$$

where C^r – approximated concentration of the pollutant in the design point (x, y);

K – the coefficient of compliance at the design point (x, y);

C^p – total calculated concentrations (from stationary emission sources and vehicles) of the pollutant in the design point (x, y).

The obtained results are the ground-level concentrations of pollutants, including in the points of a regular grid systematically covering the entire study area, where inter- and extrapolation of data from stationary observation stations was adjusted taking into account features of impurities propagation from the real sources of air pollution – industrial plants, highways and etc. Concentration always has true measured value (for the given weather conditions and time period) at the points of instrumental measurements (observation stations), and the change in the content of impurities in the territory is taken into account through the simulation results.

The matching of the approximated data on ambient air quality with the information on the density (number) of the resident population can correctly estimate the number of people living under the conditions of a particular exposure. At that, it is possible to match the estimated and field data to evaluate acute exposure (based on single measurements and calculations of ground-level concentrations for the 20-minute averaging period) and assessment of chronic exposure (based on instrumental measurements of annual average concentrations and calculations of annual average ground-level concentrations).

The testing of the developed approaches was performed based on the example of a number of areas, including the city of Perm – a large industrial center, within which there are more than 11,000 stationary sources of chemicals and a developed street and road network (SRN) with traffic density on alignments of major highways of up to 3.5 cars per hour [Mai I.V. et al., 2013].

The calculations of ground-level concentrations of pollutants from stationary and mobile sources was performed by standardized methods (OND-86) in seven points of stationary Roshydromet stations and in 127 thousand points of a regular grid (estimated rectangle of 5,050×34,800 meters) for different weather conditions and different averaging periods.

At the same time, using the "Highway" software package, the calculation of emissions (g/s, t/year) was performed for the 1,125 sections of the street and road network of the city taking into account the intensity, the structure of traffic flows (the considered areas amounted to 85% of the total length of the SRNof the city), taking into account hourly dynamics of variability of these parameters flows.

Data on the single, average daily and average annual concentrations of chemical inpurities from monitoring stations was received directly from the Perm Center for Hydrometeorology and Environmental Monitoring, Federal State-Funded Healthcare Institution "Center for Hygiene and Epidemiology in the Perm region" and laboratory testing center Federal Budget Institution of Science "Federal Research Center of medical-preventive technologies of population health risk management" in the form of formalized tables or research protocols. All points of instrumental measurements were mapped on the territory map and had a coordinate binding in urban coordinate system.

Data mapping was performed in an environment of geographic information system ARCGIS 9.3 c using vector area map. To assess exposure, the contour lines of pollution levels crossed with thematic layers characterizing the placement of children's educational institutions, residential areas, recreational areas, etc.

Spatial analysis using the technique of "inverse distances" (RD 52.04.186-89) was performed for comparative assessment of the proposed approaches, and instrumental measurements were performed to verify the methodology at 14 locations in the city not included in the calculations, and compared the forecast data with the results of field measurements at the selected points.

The obtained results were ground-level concentrations of pollutants in the points of a regular grid systematically covering the entire study area, where inter- and extrapolation of data from stationary observation stations was adjusted taking into account features of impurities propagation from the real sources of air pollution – industrial plants, highways and etc. Concentration always had true measured value (for the given weather conditions) at the points of instrumental measurements (observation stations), and the change in the content of impurities in the territory was taken into account through the simulation results.

The comparison of the predicted concentrations of nitrogen dioxide with ones measured at 14 locations showed that the dispersion calculations give systematically lowered results. Actual concentrations were not obtained in any of the points at or below the values calculated based on the consolidated database on the sources. The absolute error of the predicted levels ranged from 0.11 to 1.5 $MPC_{мр}$, which generally does not allow the use of data for reliable estimates of the risk to population health. The average absolute errors of the method of inverse distances when using only the data from stationary stations, and the method of matching the field and calculated data were lower and amounted to 0.465 and 0.255 $MPC_{мр}$ in absolute value respectively at the error ranges from (-0.680) to 1.0 and from (-0.240) to 0,410, respectively. In this case, the mean square deviation, which characterizes the scattering of an ordered series, was almost twice lower than in the application of the developed method. The patterns of deviations between the calculated data from the measured values between the results obtained by different methods have been established. Similar data were obtained by

comparing the predicted and instrumental data on sulfur dioxide, phenol, and benzene. In general, the obtained results showed that the proposed methodological approaches could improve the accuracy of assessment of the contaminants content in the air.

Since the exposure is a measure of the hazard contact with a person, spatial analysis of the air quality of the city and the evaluation of population living under the influence is very important from the standpoint of the proposed method.

Fig. 6.7 shows the results of the spatial analysis of ground-level concentrations of nitrogen dioxide with the approximation of data using the proposed method and without it.

The obtained results suggest the appropriateness of the proposed approaches, because they can significantly change the perception of risk levels in an area, facilities, located in areas of unacceptable risks, and the population resident under a particular exposure (Fig. 6.8).

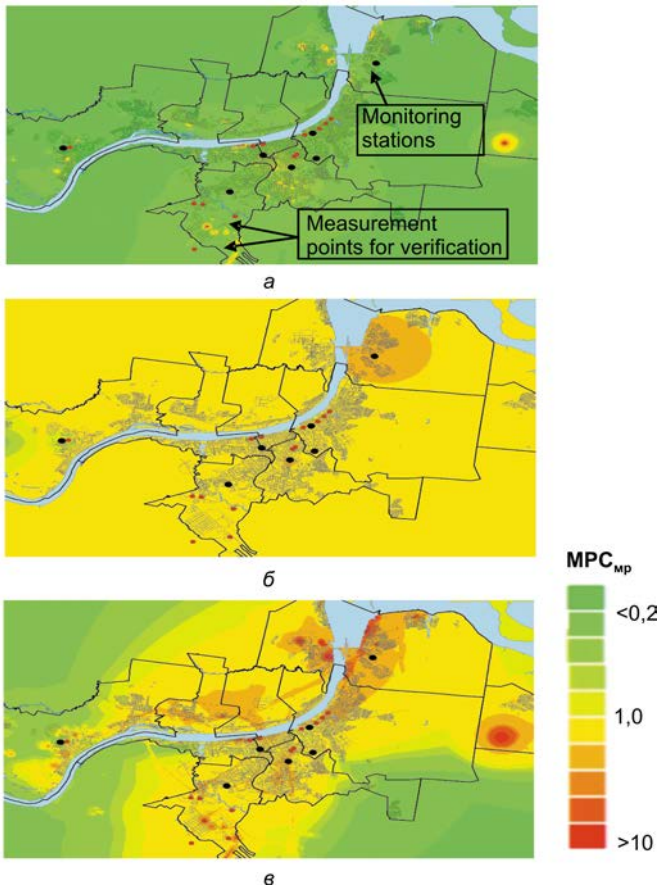

Fig. 6.7. The spatial distribution of air pollution with nitrogen dioxide (summer 2012, no wind conditions, temp. 25–26 °C) in the city of Perm: *а* – according to the dispersion calculations; *б* – taking into account the approximation of the data from monitoring stations by inverse distances method; *в* – taking into account the data approximation with a Delaunay triangulation method

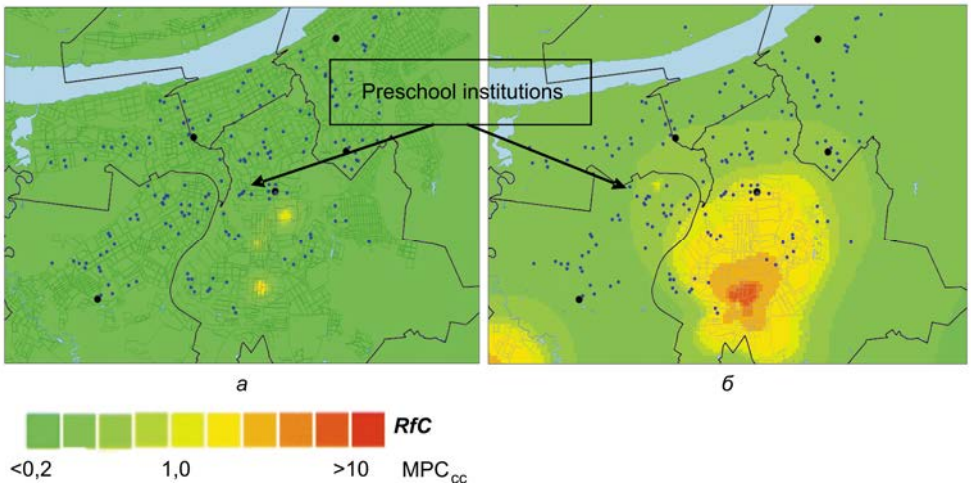

Fig. 6.8. Zoning of the city area in terms of the average annual concentration of phenol in ambient air and location in different areas of exposure of the preschool institutions: *а* – according to the dispersion calculations; *б* – taking into account approximation of data using the proposed method

Similar approaches can be used in the assessment of human exposure to other hazards – noise, electromagnetic fields, etc.

Thus, improving the approaches to the system of instrumental measurements, matching of field and calculated data provide a significant increase in correct assessment of population exposure, and hence the reliability of hygiene assessments, including aspects of the health risks assessment.

6.4. The hygienic assessment of environmental factors and public health using the methodology of risk assessment

At the moment, such commonly used methods as statistical analysis of the parameters of living environment quality (according to the criteria of hygienic standards) and comparative analysis of population health status values [Baydaulet I.O. et al., 2013; Sokolova N.V. et al., 2013; Nehoroshev A.S. et al., 2013; Zhukov A.A., 2012] are gradually supplemented and verified by assessments based on the risk methodology in the hygienic assessment of the situation. This is due to the fact that only the cross-spectrum analysis of data on environment and human health makes it possible to identify the causes of poor health and demographic situation, to assess the contribution of individual factors in the increased mortality and morbidity of the population and to make appropriate decisions to manage the situation. The task of cross-spectrum analysis is set by the need to manage the health of the nation as the main resource of the state.

That is why the WHO guidelines «Linkage Methods for Environment and Health Analysis» (1996) from the perspective of materials preparation for decision makers considers the following methods of data processing:

– epidemiological analysis;
– environmental analysis;
– the method of time series;
– the method of spatial geographical analysis;
– the method of risk (hazard) analysis.

Health Risk Assessment has a special place in a series of methods for the sanitary-epidemiological situation analysis.

First, risk assessment is based on the relevant scientific data on the qualitative characteristics and quantitative parameters of relationships between environmental factors and health problems. This allows the use of universally recognized science-intensive data and criteria for hygienic assessment of tasks in any territory.

Second, the risk assessment can use both design and instrumentally obtained data on exposure levels.

Third, the risk assessment method allows simulating a virtually unlimited number of situations, assessing the impact of risk factors in any combination and assessing the equity contributions of individual factors to the total risk.

As part of the SGM, it is supposed to implement all stages of risk assessment: hazard identification, harmful factor exposure determination, establishment of "exposure – response" dependence and risk characterization for the health of the exposed population.

The measurement and evaluation of a significant list of indicators that characterize the quality of the environment and living conditions of the population, as well as historical data about the negative effects that can be formed under the influence of these factors as part of SGM allow you to identify risks and determine priorities in hygiene assessments at different levels.

The consideration of data of FIF SHM in terms of from hazard identification (accounted for more than 100 indicators) allowed establishing the following factors most important (according to the priority of potential impact on the health of the population) for the Russian Federation at the level of the Russian Federation as a whole in the preparation of national reports on the sanitary and epidemiological welfare of the population [State Report, 2014]:

– chemical, biological, and physical environmental factors with an estimated number of exposed population, 103.77 million people (72.9% of the population);

– social factors, with an estimated number of exposed population – 83.14 million people (58.4% of the population);

– lifestyle factors, with an estimated number of exposed population – 78.75 million people (55.3% of the population) (Table 6.6).

The priority specific hazard environment factors that adversely affect the health of the population include a air pollution with suspended substances, nitrogen dioxide, benzopyrene, aromatic hydrocarbons (benzene, toluene, xylene), phenol, formaldehyde (Table 6.7).

Table 6.6

Environmental factors forming the health of the population of the Russian Federation

The main groups of living environment factors	Indicators included in the groups of environmental factors	The number of subjects of the federation and the number of population exposed to the factors
Chemical, biological, and physical environmental factors	The contamination of food, drinking water, air, and soil. Physical factors. The terms of education and raising of children and adolescents in organized groups. Working conditions and production factors at the industrial enterprises	51 subject, 103.77 million people
Social factors	Industrial and economic development of the area. Social unrest in the territories. The level of social welfare of the population	49 subject, 83.14 million people
Live style factors	The volume of sales of alcoholic beverages. The cost of tobacco products purchasing. Deviations from the recommended standards of food consumption	43 subject, 78.75 million people

Table 6.7

Priority environmental factors forming the medical and demographic losses of the Russian Federation in 2013

Priority environmental factors	The main types of health disorders associated with hazard factor
Air pollution with chemical components (suspended substances, nitrogen oxides, benzopyrene, aromatic hydrocarbons, fluorine and its compounds, phenol, formaldehyde, and heavy metals) – 76 regions of the Russian Federation	Mortality due to the diseases of the respiratory, circulatory organs, and neoplasms
	The morbidity of respiratory organs, eyes, endocrine system, blood, hemopoietic organs and certain disorders involving the immune mechanism, neoplasms, certain conditions originating in the perinatal period
The contamination of drinking water with chemical components (chlorine, aluminum, lead, arsenic, sulfate, organochlorine compounds) and microbiological agents – 80 regions of the Russian Federation	Mortality caused by infectious diseases, the diseases of the digestive system, the diseases of the circulatory system
	The morbidity of digestive system, circulatory system, skin and subcutaneous tissue, musculoskeletal system, blood, haematopoietic organs and certain disorders involving the immune mechanism, urogenital system, endocrine system, nutritional and metabolic disorders, infectious and parasitic diseases
Physical environmental factors (noise, electromagnetic radiation, ionizing radiation, illumination, vibration) – 79 regions of the Russian Federation	Mortality caused by external causes
	The morbidity of eyes, musculoskeletal system, consequences of external causes
Soil contamination with heavy metals (cadmium, mercury, lead), microbiological and parasitic contamination – 81 regions of the Russian Federation	Mortality caused by neoplasms, respiratory and circulatory system diseases
	The morbidity with certain infectious and parasitic diseases, respiratory diseases
Social factors (population with income below the subsistence minimum; the specific weight of the total area not equipped with water supply and sanitation; the average monthly nominal accrued wage; total living area on average per capita; the specific weight of the total area not equipped with central heating; expected life expectancy at birth) – 83 regions	The mortality of the population caused by infectious and parasitic diseases, circulatory, respiratory system, digestive organs diseases. Mortality caused by the external causes, malignant neoplasms, infant mortality
	The incidence of diseases of the circulatory system, digestive system, skin and subcutaneous tissue, blood, haematopoietic organs and certain disorders involving the immune mechanism, diseases of the urogenital system, endocrine system, nervous system and sensory organs, nutritional and metabolic disorders, infectious and parasitic diseases, neoplasms

The threats of excess mortality and increased morbidity in almost all types of diseases are formed at the same time. The presence of organic and inorganic impurities in air of urban and rural areas, including ones with carcinogenic effect, creates a risk of disorders of respiratory, cardiovascular system, blood system, hematopoietic, immune and endocrine systems, etc.

The increased levels of water hardness, iron, manganese, aluminum, chlorine, and organochlorine compounds, as well the presence of a number of microbial agents are the causes of the formation of diseases of the digestive, circulatory, skin and subcutaneous tissue, musculoskeletal system, blood, haematopoietic organs and certain disorders involving the immune mechanism, infectious diseases, including ones of flash character.

The priority hazard factors may also include the microbial contamination of soils and the presence of heavy metals (cadmium, mercury, lead and its inorganic compounds) in soils. Hazards associated with the threats of the occurrence of mortality and morbidity from neoplasms, infectious diseases, disorders of the circulatory system, respiratory system, etc.

Risk factors associated with a complex of health problems are certain levels of socio-economic indicators, namely: a high proportion of the population with incomes below the subsistence minimum; insufficient total area of living rooms on average per inhabitant; a high percentage of residential areas not equipped with water supply and sanitation; lowest average monthly nominal accrued wage; high cost of the consumer basket relative to the average wage.

The comparative analysis of risk factors on the subjects of the Federation has shown that in some cases the regions are significantly different from each other in terms of performance, in some cases they are similar. This allowed performing the classification of the subjects of federation on aggregate indicators characterizing the sanitary-epidemiological situation in the regions, and gives some generalized hygienic evaluation for future management decisions within the SGM results processing.

One way to classify regions is clusterization (absolute rankings), which suggests a definition of indicators distribution features (problem areas) for each type; the allocation of "frontier" areas (areas with similar characteristics of several types) and the determination of the conditions of the transition from one type to another (Adinets et al., 2011).

The results of social and hygienic monitoring for 2010–2013 allowed the identification of regions of the Russian Federation with the similar complex and severity of socio-economic and sanitary-hygienic risk factors that largely determine the level of sanitary and epidemiological welfare of the population (Fig. 6.9).

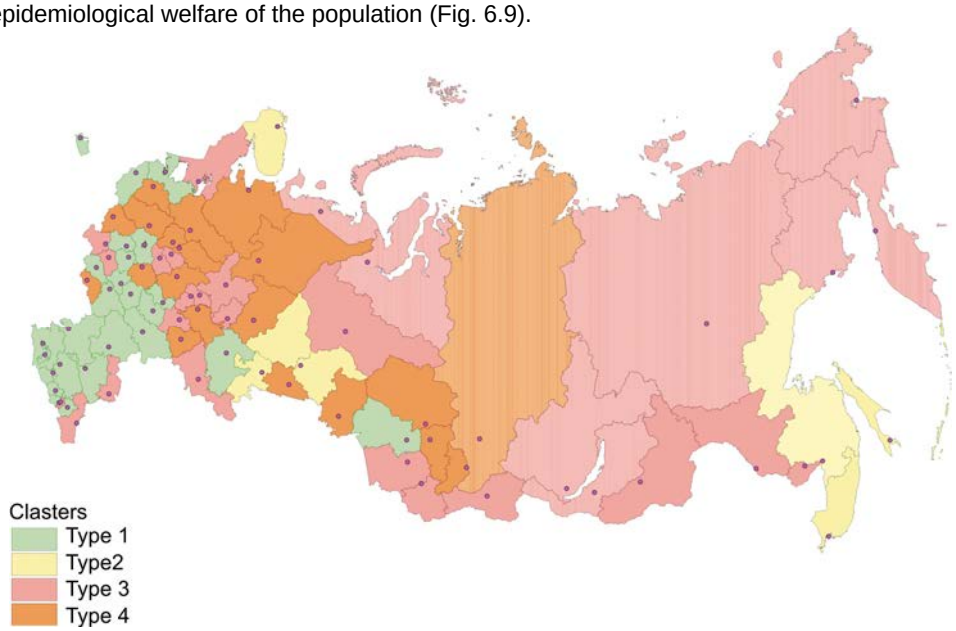

Fig. 6.9. The types of the territories of the Russian Federation in terms of sanitary and epidemiological welfare of the population [State report, 2014]

According to the State report "On the state sanitary and epidemiological welfare of the population in the Russian Federation in 2013", the subjects of the Russian Federation with the most favorable indicators of the sanitary-epidemiological situation and average level of socio-economic indicators (type 1) include: Kabardino-Balkaria, Karachay-Cherkess Republic, Stavropol Territory, the Republic of North Ossetia –Alania, Krasnodar region, Voronezh region, Republic of Kalmykia, Leningrad, Volgograd, Moscow Region, Republic of Adygea, Tambov, Kursk, Penza, Rostov, Pskov, Lipetsk, Novosibirsk, Saratov, Kaliningrad, Kaluga, Tula region, the Republic of Bashkortostan, Mordovia.

The lowest frequency of theexceedance of the hygienic standards of ambient air quality – 1.12% (in addition there is a positive trend to the reduction in this indicator compared to

2012); the moderate frequency of drinking water hygienic quality nonconformities with hygienic standards for sanitary-chemical indicators; the lowest proportion of soil samples exceeding hygienic standards for sanitary-chemical and microbiological parameters – 3.86% (a decrease compared to 2012), and 5.58%, respectively; the average ratio of per capita income for the consumer basket – 3.12 (pronounced growth); the lowest proportion of old and dilapidated housing – 2.18% were identified.

The subjects of the Russian Federation of this type are characterized by the lowest values of mortality and morbidity ratios associated with sanitary and hygiene factors (at the level of 0.22 incidence/1,000 people and 24.8 incidence/1,000 people respectively) and moderate values of mortality and morbidity ratios associated with socio-economic factors (0.92 incidence/1,000 people and 36.6 incidence/1000 people, respectively).

The typical sanitary and hygienic problem of the subjects of the Russian Federation of this type is the poor quality of water supplies and drinking water supplied to the population. On average in 2013, drinking water samples portion with the exceedance of the hygienic standards by the type amounted to 22.7% for the sanitary and chemical indicators and 5.88% for microbiological ones.

The subjects of the second type include the regions of the Russian Federation with more severe sanitary-hygienic problems and the highest rates of socio-economic development: the city of Moscow, the city of St. Petersburg, Tyumen region, Sakhalin region, Krasnoyarsk region, etc. This group also includes the Murmansk region. The value of the ratio of the average wage to the minimum consumer basket is the highest in the regions of this type in the country – 2.42; the range of values – 1,7–3,64, the average share of old and dilapidated housing – 3.1 (0,3–9,3%), the highest in the country GRP per capita 462.444 thousand rub/person. (185.68–987.4170).

As part of the health and demographic indicators, this cluster is characterized by the higher mortality rate (the average value for a cluster is of 10.47 incidence/1000 people; value range 7.42÷14.42), the level of the primary morbidity (754.67 incidence/1000 people; min = 717.23 max = 890.59), the increased frequency of air quality hygienic standards exceedance (0.88%, the range of 0.12÷5.26%). The region is characterized by an increased frequency of discrepancies on sanitary and chemical quality of drinking water (45.1%, the range of 19.17÷58.3%). The higher portion of non-standard soil samples is observed in the regions of the cluster both for the sanitary-chemical and microbiological parameters (mean values for a cluster is of 14 and 11%, respectively).

In the regions of this type, there are the lowest levels of the risk of death associated with the studied social and economic factors in the Russian Federation. Priority threats remain sharp and associated with sanitary-hygienic problems identified by the problems of large- and medium-sized cities (Moscow, St. Petersburg, Krasnoyarsk, Bratsk, Yuzhno-Sakhalinsk, etc.). As a result, mortality and morbidity ratios associated with sanitary and epidemiological factors are above the the average Russian ones (0.81 incidence/1,000 people and 72.8 incidence/1000 people, respectively).

The regions of type 2 require a strong focus on reducing air, drinking water, and soil pollution in the places of the permanent residence and organization of public health risk factors monitoring. It should be noted that the improvement of socio-economic indicators will also positively affect the health and demographic indicators in the region.

The subjects of the Russian Federation with a relatively more pronounced sanitary and epidemiological problems and the national average socio-economic indicators (type 3) include Belgorod region, the Republic of Tatarstan, Tomsk region, Omsk region, Kostroma region, Ryazan region, the Republic of Komi, Perm territory, Nizhny Novgorod region, Smolensk region, Samara region, Kurgan region, Yaroslavl region, Tver region, Kemerovo region, Republic of Khakassia, Novgorod region, Vologda region, and Arkhangelsk region.

On socio-economic indicators, the subjects of the Russian Federation of the third type are inferior to the subjects of the Russian Federation of the second type for GRP per capita, the availability of living space per capita, the level of housing provision with water supply, sanitation and other indicators.

Contaminants in the air and drinking water contamination can be health risk factors. High specific weight of drinking water samples exceeding hygienic standards for sanitary-chemical (42.1%) and microbiological (9.5%) indicators is observed on the territory of the third type. The proportion of soil samples exceeding hygienic standards is 8.9% for the sanitary-chemical and 7.9% for microbiological parameters.

In general, sanitary environmental factors in the subjects of the Russian Federation of the third type additionally form 0.72 of death incidence and about 66.3 of disease incidence per 1000 population; socio-economic factors - about 0.92 of death incidence and 80.7 of disease incidence per 1000 population. Thus, socio-economic factors make a slightly larger contribution to the loss of population health compared with sanitary-hygienic ones.

The subjects with a complex of sanitary-epidemiological and socio-economic issues, which form the highest levels associated with the negative impact of environmental factors of health disorders (4th type) include: Astrakhan region, Orenburg region, Kamchatka territory, Amur region, the Republic of Mariy El, Altai territory, Republic of Altai, the Republic of Buryatia, Bryansk region, the Republic of Dagestan, Ulyanovsk region, the Udmurt Republic, Irkutsk region, Republic of Karelia, the Chuvash Republic, the Republic of Sakha (Yakutia), the Jewish Autonomous Region, Kirov region, Magadan region, Ivanovo region, the Trans-Baikal territory, Vladimir region, the Republic of Ingushetia, the Khanty-Mansi Autonomous Okrug, the Republic of Tyva, Nenets region, Yamal-Nenets region, Chukotka Autonomous Okrug.

This group forms the high risks of excess population deaths probability associated with the negative impact of environmental factors. These factors determine about 92.4 disease incidences per 1000 population; socio-economic factors of the living environment form about 1.21 death incidences and 80.7 disease incidences per 1000 population.

The pollution of air and drinking water, as well as the factors of socio-economic nature are identified hazards. This group of regions recorded high levels of air pollution (up to 4.4% of samples), a high proportion of drinking water samples exceeding hygienic standards for sanitary-chemical (21.1%) and microbiological (8.6%) indices. These subjects of the federation are characterized by the most adverse socio-economic indicators: the lowest level of gross regional product per capita; the highest proportion of old and dilapidated housing; the lowest value of the ratio of average wages to the consumer basket.

The poor quality of drinking water throughout the country produces about 14.1 thousand of death incidences and 3,151.9 thousand cases of disability (disease cases and care for a sick family member) of the employed population.

The cumulative impact on public health of priorities physical factors – noise, vibration, electromagnetic (non-ionizing) radiation, and low light at the objects of public utilities is associated with 6.7 thousand of additional mortality of the employed population and the population morbidity of diseases of the nervous system and sense organs, and diseases related to external reasons, about 2,837.8 thousand cases.

Indicators obtained with the use of risk assessment methodology, including the above ones can and should be used in strategic planning, be the subject of the discussion by the authorities of regions and municipalities. It is also necessary to communicate the results of SGM hygienic assessment to the representatives of business, which is the source and cause of many hazards and, simultaneously, the party interested in the preservation and growth of the human potential of the country, especially of labor potential.

Thus, the data of public health monitoring allow the identification and prioritization of hazards, highlighting areas with different sets and levels of these hazards, performing hygiene assessment forecasting potential public health risks generated by the identified hazards.

The hygienic assessment of the public health risk at the level of settlements is of great demand. Thus, for example, the assessment of the multimedia population health risk in Perm revealed that 17 pollutants of 450 impurities that are released into the air of the city form health risks (Table 6.8).

Almost none of 50 chemicals that pollute the drinking water generate unacceptable risks (Table 6.9). The arsenic hazard coefficient somewhat exceeds 1, however, this excess is extremely small and fits within the error measurement limits of the impurities in drinking water.

Table 6.8

The parameters of population health risk from exposure to airborne chemical environmental factors in Perm (2006–2010)

No.	Substance	HQ_{ac_i}	HQ_{cr_i}
1	Nickel oxide	0.003–**1.046**	**1.550–206.050**
2	Copper sulphate	0.000003–0.001	**1.550–206.050**
3	Cupric oxide	0.0004–0.158	
4	Suspended substances	0.095–**74.958**	0.248–**51.941**
5	Benzpyrene		0.000–**33.000**
6	Formaldehyde	0.292–**37.68**	0.082–**37.392**
7	Acrolein	0.815–**50.699**	0.143–**36.141**
8	Hydrogen chloride	0.020–**2.056**	0.046–**17.857**
9	Chromium (3+; 6+)		0.090–**11.840**
10	Manganese and its compounds		0.120–**5.440**
11	Benzene	0.194–**11.801**	0.005–**5.114**
12	Phenol	0.0003–0.070	0.087–**4.587**
13	Sulfuretted hydrogen	0.014–0.773	0.175–**2.958**
14	Nitrogen dioxide	0.088–**4.961**	0.080–**2.636**
15	Xylene	0.020–**1.153**	0.002–**2.208**
16	Acetaldehyde	0.014–**1.181**	0.006–**2.156**
17	Ammonia	0.005–0.531	0.048–**1.348**
18	Nitrogen oxide	0.004–0.091	0.071–**1.014**
19	Carbon monoxide	0.045–**12.982**	0.102–1.000
20	Lead and its compounds		0.010–0.832
21	Gaseous fluorides	0.009–**7.170**	0.055–0.792
22	Maleic anhydride	0.0008–0.121	0.006–0.467
23	Iron oxide		0.005–0.428
24	Toluene	0.019–**1.606**	0.0004–0.408
25	Chlorine	0.003–**4.798**	0.0003–0.228
26	Sulfur dioxide	0.025–0.308	0.015–0.121
27	Other impurities (maximum 20)	The maximum value in the residential area does not exceed 0,1*HQ*	

Table 6.9

The parameters of population health risk from exposure to water oral environmental factor in Perm (2005–2010)

Substance	$HQ_{cr_{wo}}$ – Children	$HQ_{cr_{wo}}$ – Adults
Chloroform	0.696–1.845	0.30–0.79
Residual chlorine	0–0.932	0.00–0.40
Arsenic	1.065	0.00–0.46
Fluorides	0.021–0.816	0.01–0.35
Strontium	0–0.463	0.00–0.20
Dichloromethane	0.001–0.327	0.00–0.14
Calcium	0.087–0.287	0.04–0.12
Common chromium	0–0.256	0.00–0.11
Other impurities	The maximum level does not exceed 0,01*HQ*	

Thus, the air quality in the regional center forms a potentially much higher health risks than the quality of drinking water.

The implementation of the environmental risk factors for the entire population of the city may potentiate about 19 thousand of the additional cases of respiratory diseases including more than 10 thousand cases for children and adolescents.

The analysis of the risk assessment results from the perspective of the possible types of health disorders showed that the greatest risks are formed in relation to respiratory diseases, hematopoietic and immune systems diseases, eyes and nervous system diseases. Priority contribution is the impurities contaminating the air (Fig.10).

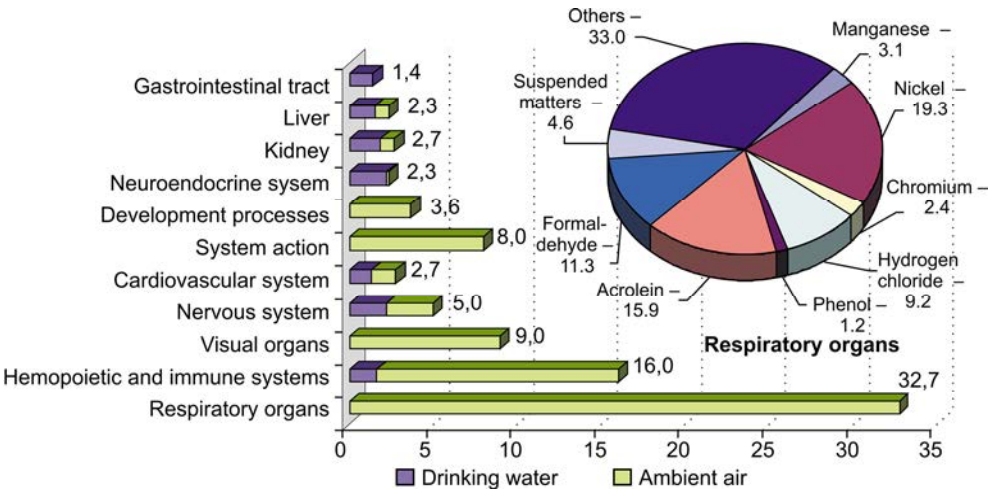

Fig. 6.10. The average values of the hazards of the combined multimedia risk of individual organs/target systems and the contributions of environmental factors (%)

It was determined that virtually the entire population of the city (1013.88 thousand people) is subject to the risk of respiratory, hematopoietic and immune systems diseases formation. About 400 thousand people including more than 150 000 children are at risk of damage to the nervous system and visual organs. The obtained data on the unacceptable levels of population environmental risk in Perm are consistent with those of long-term statistics on health and demographic indicators.

Settlements zoning by health risk criteria revealed areas with the highest levels of risk, which is the basis for the formation of targeted health and preventive measures (Fig. 6.11).

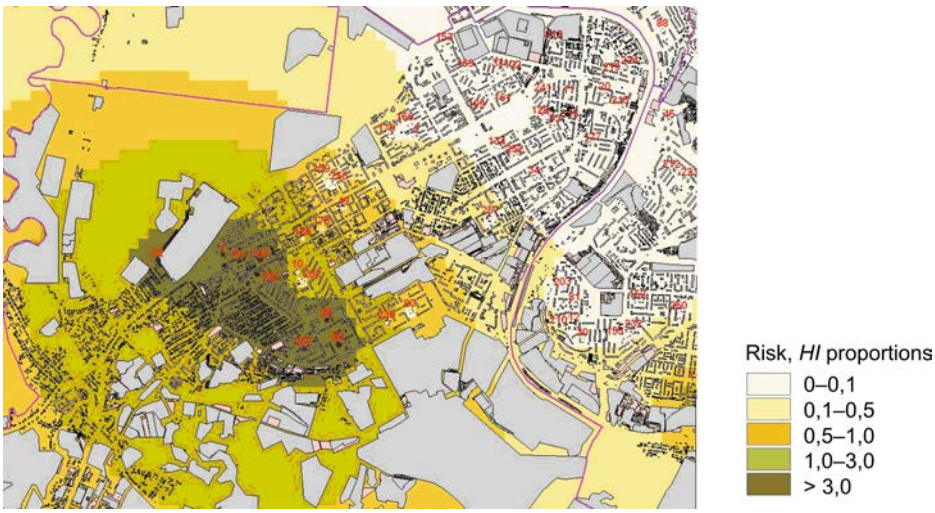

Fig. 6.11. The zoning of the city area according to the health risk criteria
(index of chronic non-carcinogenic risk of hematopoietic and immune system disorders)

Thus, the hygienic assessment of environmental and population health factors in Perm executed based on the data of socio-hygienic monitoring using risk assessment methodology allowed quantitative assessment of the probability of adverse effects on human health, determining the zones (areas) with different health risk levels, the justification of the program of medical and preventive measures that are included in a comprehensive program to ensure the environmental safety of the population of the city.

However, it should be noted that the socio-hygienic monitoring also allows setting a number of new dependencies at different levels of generalization derived from the SGM information, which is essential in a virtually unlimited combination of hazards and conditions for these dangers and threats implementation.

6.5. The determination of cause-and-effect relationships between the state of public health and the influence of environmental factors

The process of cause-and-effect relationships establishment between the indicators of the living environment and responses in the form of health disorders – the most important component of the SGM. Identification and parameterization of new "exposure – response" dependencies makes it possible to predict, calculate and characterize health risks.

The general algorithm of cause-and-effect relationships establishment between population health condition and the impact of environmental factors on the SGM database is shown in Fig. 6.11. The algorithm consists of several stages, each of which uses special methodological approaches adequate to the set tasks.

The pretreatment of initial data and the preparation of data sets, the analysis of the completeness and correctness of the initial data, the detection and elimination of gross and systematic errors in the original data, the procedures of data aggregation to the necessary extent, indices and integral indicators calculation and the interfacing of heterogeneous arrays for complex calculations is performed when collecting background information. Indicators are reduced to a single scale of measurement appropriate to the analysis level: for the federal level – it is the scale of the Federation, for regional level – municipal formations. It should be noted, that if the prepared and officially published data that do not require additional transformations are most often used for the health indicators assessment, the results of instrumental studies of environmental facilities quality require reduction to the scale of the territory (the subject or municipality), for example, using weighted averaging method (6.6) when, information on the number of people living in an area characterized by monitoring point is used as a weighting factor:

$$\overline{x} = \frac{\sum_i x_i N_i}{\sum_i N_i}, \qquad (6.6)$$

where x_i – the value of i-th indicator change;

N_i – the number of people living in the area of the i-th indicator measurement.

The assessment of information completeness is carried out on the basis of data integration in the context of individual areas and the assessment of the occurrence frequency, that ensures the formation of a priority list of indicators, which are used to carry out the analysis of the cause-and-effect relationships and evaluation of the sanitary-epidemiological situation. The main output of the first stage is a single systematic coordinated database containing the values of the state of public health, the environment, population lifestyle and the activity of authorities and organizations of the Rospotrebnadzor.

To account for and eliminate the correlations between the factors in order to avoid getting incorrect models, as well as for combination of factors in a group and getting some

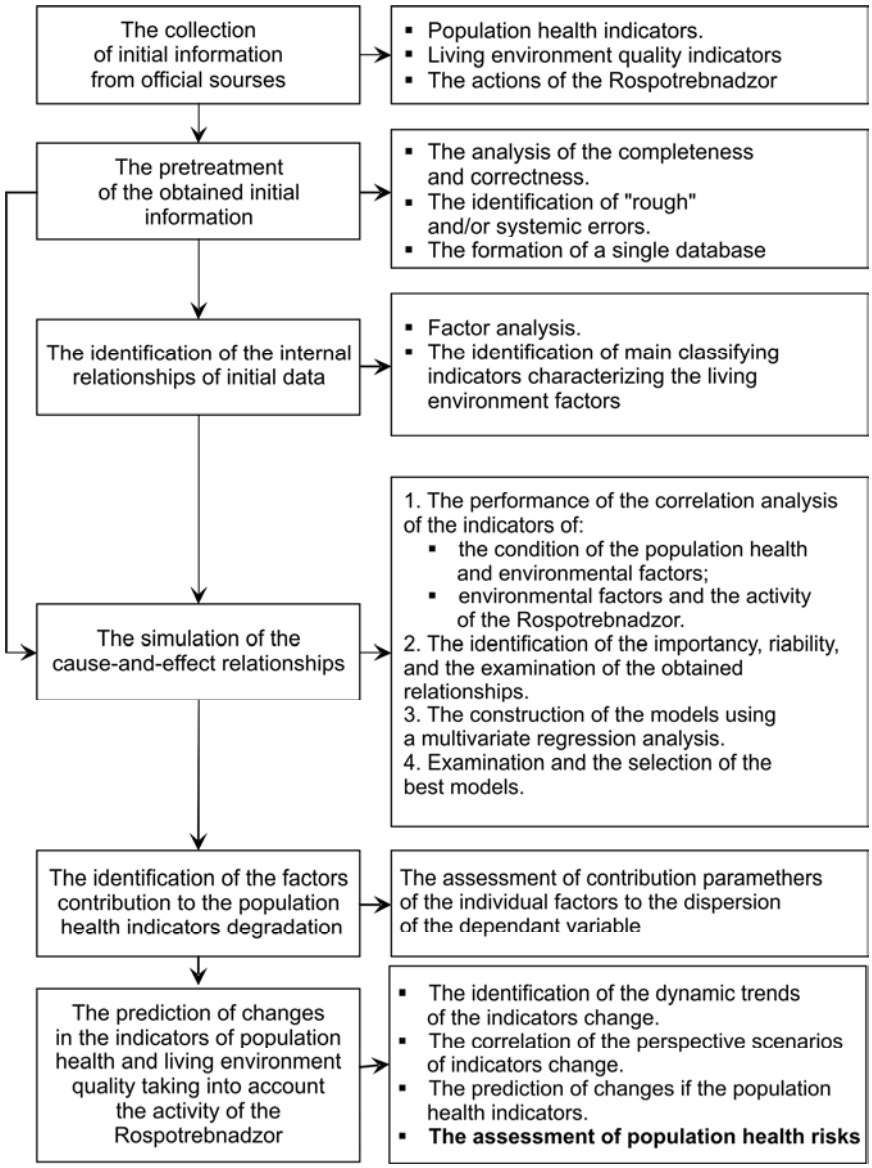

Fig. 6.11. The general algorithm of establishing cause-and-effect relationships in the "Environment – Health" system

"marker" indicators that would characterize a group of interrelated factors, it is appropriate to use the method of factor analysis. The method allows formation of groups of related factors and provision of basic classification indicators by reducing the dimension of the initial data array and preparing data for subsequent analysis. The assessment of internal relationships system is recommended to be perform using the method of principal components factor analysis by transforming the original system of variables with correlation relationships into the system of orthogonal (not related to each other) common factors. Common factors are linear combinations of the incoming variables and have no physical and biological sense, therefore, they are used only as classifying variables.

Since the territories of the country have significant differences in the structure of the environmental pollutants, which leads to the availability of the large number of missing values in the original data array, it is appropriate to use a correlation matrix between the variables as input data for factor analysis. The construction of the correlation matrix can be performed using the same software. If a variable in the input data set has less than 5 numeric values (the rest are missing), it must be excluded from consideration. Criterion to limit the number of common factors (reduction of dimensionality of the original system of variables) is the contribution of the common factors to the total dispersion of less than 5%. The inclusion of this criterion is achieved by entering the parameter, rejecting the factors with "eigen values" of less than 1. It is optimal to perform factor analysis with the "rotation" procedure using Varimax method. The "matrix of factor loadings" containing the coefficients of correlation between the input variables and common factors, is an output array of factor analysis.

The classification of indicators system is performed based on the analysis of the "matrix of factor loadings". Indicators are considered to be closely related to each other (having systemic relationships) if they have the maximum factor load in absolute value with the same common factor. Unidirectional and oppositely directed indicators should be allocated among interconnected ones. Unidirectional indicators are characterized by the same sign of factor loadings, oppositely directed indicators – by different signs.

The classification of indicators by factor analysis method allows identification of a number of indicators (by the number of common factors), minimally sufficiently representing the whole system of indicators. Maximum modulus of factor load for each common factor is selection criterion. It is necessary to consider the composition of indicators classes and the direction of relationships in the further simulation of the effect of environmental factors and lifestyle on the population health status based on the selected indicators.

In the analysis of the relationships between the factors, the procedure of factor analysis is performed separately for socio-economic factors, lifestyle factors, and sanitary-hygienic indicators for the living environment facilities, etc.

The use of special software that implements the methods of statistical analysis (such as software packages Statistika, PASW, SAS, etc.) is optimal to perform factor analysis.

The most knowledge-intensive and difficult stage of SGM – the simulation of cause-and-effect relationships between the environmental factors, socio-economic indicators, lifestyle factors and population health indicators - generates the most important and required results. This is also actually derived relationships models and values of medical and demographic losses, which can be calculated from the simulation results. At this stage, the social and hygienic monitoring generates data that may be an information-analytical base for optimization of control and surveillance activities, as well as tool to assess the effectiveness of this activity.

The establishment of cause-and-effect relationships is claimed within social-hygienic monitoring at different levels of territoriality. To establish the dependencies at the level of the Russian Federation, the subjects of the Russian Federation act as the unit of observation.

The method of simulation is the step-by-step regression analysis modified by the sorting of line, square and exponential functions for the independent variables. The models are characterized by:

– dependence formula, containing the values of all coefficients;

– reliability parameters;

– the values of the indicators that reflect the quality of the model.

Indicators that are defined based on the results of the factor analysis as the marker ones and are included in the simulation in order to establish cause-and-effect relationships.

A general view of the model of health indicators dependency on the risk factors is presented by the following relation

$$y = a_0 + a_1 f_1(\Phi CO_1) + a_2 f_2((\Phi CO_2) + \ldots, \quad (6.7)$$

where y – dependent variable (population mortality, disability, morbidity, incidence/100,000);

LEF_1, LEF_2, … – independent variables – environmental factors;

a_0 – the free term of the model that characterizes the controllability limit of the health indicator due to the changes in factor;

a_i – model parameters characterizing the effect of the *i*-th indicator of living environment quality on health indicator;

f_i (LEF_i) – the function of the independent variable at which the quality of the model (coefficient of determination) is maximum.

To perform the calculations of additional cases of health problems, only models meeting the corresponding criteria of reliability and adequacy are used.

The calculation is performed in the context of individual subjects (cases), followed by summation. The availability of data on dependent and all independent variables it is necessary to include regions in the calculation.

The coefficient of determination (R^2) resulting as model parameters describes the proportion of variance of the dependent variable explained by the resulting dependence model, i.e. allows assessing the degree of health indicators association with hazards.

The relative number of the additional cases of health problems (morbidity, disability, mortality) for each observation (region) is calculated as the difference between the estimates of the model with the actual levels of the independent variables and the minimum observed (target) ones in all regions involved in the calculation:

$$\Delta y_k = a_1 f_1 (LEF_{1k}) + a_2 f_2 (LEF_{2k}) + \ldots, \quad (6.8)$$

where Δy_k – public health disorders (mortality, disability, morbidity rates) associated with the studied factors in the *k*-th observation (region);

LEF_{1k}, LEF_{2k}, …. – the values of the independent variables for the *k*-th observation (region).

The resulting relative indicators are reduced to an absolute form (using the number of population), and the average proportion of cases is determined due to the influence of factors such as the ratio of the total number of additional cases to the total number of actual (observed) cases in all regions taken into account. Calculations are performed for each year under consideration.

The absolute number of the additional cases of health disorders (deceased, disabled, diseases) is determined under the relations (6.9)

$$\Delta Y_k = \Delta y_k ЧН_k / 100000, \quad (6.9)$$

where ΔY_k – is an absolute number of prevented cases of health disorders (death, disability, diseases) associated with environmental factors in the *k*-th observation (region);

$ЧН_k$ – is a number of population in the *k*-th region.

The proportion of the additional cases of health disorders due to the deviation of the living environment quality of the norm for the Russian Federation is calculated using equation (6.10):

$$\delta y = \Sigma(\Delta Y_k) / \Sigma(Y_k), \quad (6.10)$$

where δy – the proportion of additional cases of health disorders associated with environmental factors;

where ΔY_k – is an absolute number of prevented cases of health disorders (death, disability, diseases) associated with environmental factors in the *k*-th observation (region);

The calculation of the absolute number of cases for the Russian Federation is determined as the factum of cumulative number of cases in the Russian Federation by the calculated average share of additional cases associated with the living environment factors (6.11):

$$\Delta Y = Y_{РФ} \delta y, \quad (6.11)$$

where ΔY – is an absolute number of cases of health disorders for population (death – ЧУ; disablement – ЧИ; diseases – СВН) associated with environmental factors.

The regions with a proportion of more than 95% of the actual level of the dependent variable are rejected from consideration when performing the calculations.

In general, each of the results is: a complex of the internal relationships of risk factors; the set of the models of cause-and-effect relationships between health indicators

and risk factors; the priority groups of risk factors and population health indicators associated with their negative impact; the equity contributions of individual risk factors in an adverse change in population health indicators - can be used individually or in the system for a wide range of administrative decisions.

Processing using the proposed algorithm of multidimensional data of the Federal Information Fund of Social and Hygienic Monitoring 2009–2012 allowed establishing about 40 significant relationships between health risk factors and actually generated indicators of health status at the level of the Russian Federation. Table 6.10 shows the number of paired and multiple dependencies that confirm the reality of the posed threats to the population of the country [State Report, 2014; Zaitseva N.V. et al., 2014].

Table 6.10

The examples of bouble and multiple models of the relation of the risk factors of living environment and population mortality

Dependent variable	Independent variable	Model parameters		
		free term	parameter value	determination coefficient
Population mortality from respiratory diseases (adult population of retirement age)	The percentage of studied air samples exceeding MPC in nitrogen dioxide content in settlements (a)	143.203	1.026	0.2488
Population mortality from respiratory diseases (child population (0–17 years)	The percentage of tested air samples with the exceedance of nitrogen dioxide content	3.791	0.586	0.233
	The percentage of tested air samples with the exceedance of MPC of aromatic hydrocarbons content		0.008	
The standardized coefficients of mortality from malignant neoplasms (total population)	The percentage of studied air samples with the exceedance of MPC for benzopyrene content in urban and rural settlements	168.175	0.299	0.111
	The percentage of the studied soil samples in residential areas that do not meet hygienic standards for cadmium		1.572	
Certain conditions originating in the perinatal period (children population)	The percentage of studied air samples with the exceedance of MPC for benzopyrene in urban and rural settlements	2870.35	0.86578	0.1215
Blood, hemopoietic organ diseases and certain disorders involving the immune mechanism (children population)	The percentage of drinking water samples exceeding hygienic standards for residual chlorine	1562.17	33.04	0.1176
Population mortality from viral hepatitis (adults of working age)	The number of doctors of all specialties	–0.499	0.323	0.062
The diseases of the osteomuscular system and connective tissue (children population)	The percentage of drinking water samples exceeding hygienic standards for aluminum	3982.07	23.26	0.134
Population mortality from tuberculosis (adult population of working age)	The percentage of apartments without running water	45.561	0.172	0.457

End of Table 6.10

Dependent variable	Independent variable	Model parameters		
		free term	parameter value	determination coefficient
Population mortality from intestinal infections (adult population upward the working age)	The percentage of persons with incomes below the subsistence minimum	1.794	0.057	0.141
	The number of living space per 1 person		–0.087	
Standardized mortality coefficients from certain infectious and parasitic diseases (total population)	The percentage of persons with incomes below the subsistence minimum	33.782	0.666	0.188
	The number of living space per 1 person		–0.974	
Endocrine system diseases, eating disorders and metabolism disorders (children population)	The percentage of apartments without running water	1392.513	11.881	0.036
The diseases of the circulatory system (child population)	Health care costs	954.1748	–0.01	0.037

The resulting models depending on the level of a particular factor (the concentration of the pollutant in the ambient air, drinking water, soil, socio-economic parameter) registered by the SGM system in a particular region and in the Russian Federation allow assessing the excess deaths or diseases of the population associated with this factor, and the proportion of these cases in the total mortality or morbidity. An example of such an assessment is provided in Table 6.11.

Table 6.11

Mortality from cardiovascular diseases associated with air pollution with suspended substances and soil contamination with heavy metals, according to the simulation results based on socio-hygienic monitoring (total population, incidence/100,000 people) [State report, 2014]

Region	2010	2011	2012	Mortality portion 2012, %
Altai region	14.38	17.93	16.71	2.91
Amur region	–	20.13	9.12	1.17
Belgorod region	7.26	12.13	6.69	0.99
Bryansk region	13.00	5.20	3.34	0.47
Volgograd region	4.66	3.58	1.06	0.19
Vologda region	51.12	12.38	10.49	1.54
Voronezh region	2.75	5.11	4.70	0.83
The city of Moscow	14.03	0.83	0.62	0.16
The city of Saint-Petersburg	1.28	3.36	3.98	0.78
Jewish Autonomous Region	–	19.88	5.36	0.64
Ivanovo region	25.62	1.33	23.35	4.94
Irkutsk region	5.30	4.60	3.08	0.44
The Republic of Kabardino-Balkaria	8.99	0.00	0.00	0.00
Kaliningrad region	2.22	3.59	1.62	0.28
Kaluga region	26.53	11.95	3.21	0.48
Kamchatka Territory	0.00	0.11	0.75	0.10
Kemerovo region	11.04	9.44	7.47	1.26

End of Table 6.11

Region	2010	2011	2012	Mortality portion 2012, %
Kirov region	9.81	1.26	24.75	3.77
Kostroma region	0.00	0.15	0.00	0.00
Krasnodar region	1.59	1.30	3.27	0.61
Krasnoyarsk territory	2.75	7.88	13.61	2.34
Kurgan region	20.33	4.23	7.30	1.32
Leningrad region	3.76	0.28	1.23	0.20
Lipetsk region	36.36	15.14	28.92	4.76
Moscow region	5.60	1.92	1.01	0.15
Murmansk region	39.81	66.65	37.27	5.18
Nizhny Novgorod region	13.39	0.25	0.34	0.05
Novgorod region	1.08	2.74	2.55	0.34
Novosibirsk region	5.55	21.63	16.59	2.72
Orenburg region	3.80	5.43	6.04	0.92
Oryol region	3.47	0.41	5.46	0.79
Penza region	0.99	2.07	10.65	1.62
Perm Region	19.42	1.62	1.97	0.30
Primorsky Territory	8.18	232.70	29.34	4.19
The Republic of Adygea	22.83	5.94	9.36	1.51
The Republic of Bashkortostan	1.36	2.62	2.26	0.43
The Republic of Buryatia	11.15	48.70	66.66	10.09
The Republic of Dagestan	44.74	68.77	9.40	2.46
The Republic of Kalmykia	0.00	0.00	0.00	0.00
The Republic of Karelia	2.89	0.64	0.00	0.00
The Republic of Komi	0.00	0.00	0.00	0.00
The Republic of Mariy El	4.67	0.86	0.00	0.00
The Republic of Mordovia	0.62	0.00	0.00	0.00
The Republic of Sakha (Yakutia)	10.47	21.97	3.18	0.49
The Republic of Tatarstan	9.24	7.48	6.61	1.25
The Republic of Khakassia	0.00	0.00	0.93	0.15
Rostov region	20.23	9.90	12.46	1.96
Ryazan region	20.14	20.13	5.62	0.95
Samara region	5.14	9.04	9.16	1.69
Saratov region	15.81	6.45	6.77	1.29
Sakhalin Region	15.17	10.86	0.00	0.00
Sverdlovsk region	52.87	45.28	10.98	1.85
Smolensk region	20.02	11.05	4.10	0.66
Stavropol region	3.67	3.95	3.54	0.62
Tambov Region	7.91	0.00	0.00	0.00
Tver region	4.82	0.00	0.00	0.00
Tomsk region	0.82	1.41	1.54	0.31
Tula region	5.61	2.13	10.38	1.61
Tyumen region	3.41	14.61	22.00	3.75
The Udmurt Republic	1.23	2.12	3.15	0.53
Ulyanovsk region	4.75	0.65	14.91	2.32
Khanty–Mansi Autonomous Okrug – Yugra	34.54	33.22	29.21	5.17
Chelyabinsk region	6.10	9.54	6.04	1.00
The Chuvash Republic	0.40	0.00	0.40	0.08
Yamal-Nenets Autonomous Okrug	6.43	0.25	0.00	0.00
Yaroslavl region	0.00	1.56	0.00	0.00
Total in the Russian Federation	6.59	5.96	5.47	0.42

Thus, air pollution with suspended substances in conjunction with the presence of heavy metals in soils in concentrations exceeding hygienic standards, probabilistically associated with excess mortality of the population from diseases of the cardiovascular system (from 0.0 to 140.0 cases per 100 000 population). On average in Russia, in recent years, this value amounted from 6.63 to 5.5 incidences/100 000 population or about 7.8 thousand of additional deaths in the whole country (0.42% of total population mortality). This hygienic assessment is possible in the context of the whole complex of the risk factors observed in the SGM and responses to their effects.

In 2013, social and environmental factors observed within SGM stipulated more than 144.1 thousand of death which corresponds to the risk of $7{,}95 \cdot 10^{-4}$ in the country as the whole. Risk levels according to the generally accepted classification exceed the level acceptable to the population (equity contribution of the social factors to the increased mortality amounted to about 76%, contribution of the environmental factors – about 24%).

In addition, socio-economic factors determine the probability of about 2.1 million diseases of different classes, sanitary-hygienic factors – about 5.5 million diseases (Fig. 6.12).

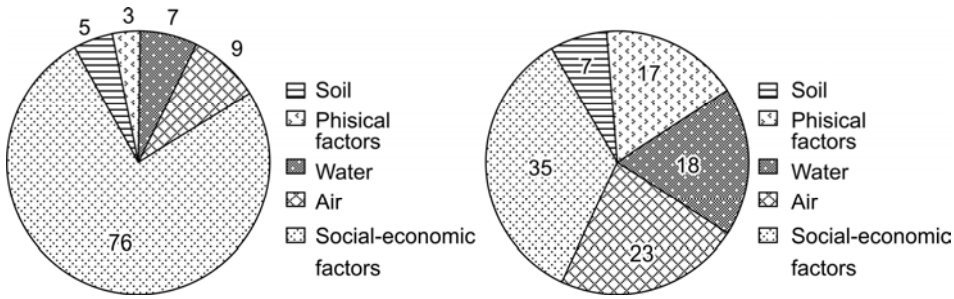

Fig. 6.12. The structure of the mortality (a) and morbidity (b) of the population (%) associated with negative environmental factors

The solution of the equations system allows also evaluating health and demographic losses in a particular region. An example of such a solution (in terms of sanitary-hygienic indicators of the living environment and additional population mortality) for one of the subjects of the Federation is given in Table 6.12.

Table 6.12

The number of death incidences in terms of class reasons associated with the quality of the environment in the *N*-th region of the Russian Federation

Age group	The class of death causes	The number of absolute incidences		
		2010	2011	2012
The adult population of pension age;	The diseases of the respiratory system	1	1	1
	The diseases of the digestive system	173	175	157
	Other reasons	138	76	212
The adult population of working age;	Circulatory diseases	322	123	147
	Other reasons	502	264	742
Children population (0–17 years old)	The diseases of the respiratory system	1	1	1
	Circulatory diseases	4	4	3
	Other reasons	8	2	19
Total		1149	646	1282

In recent years, the following was recorded in the region:

– the proportion of drinking water supply sources of centralized water supply that does not meet sanitary norms and rules at the level of 6.2–9.4%;

– the proportion of the studied air samples exceeding the MPC for nitrogen dioxide content at the level of 0.9–1.2% in urban and rural settlements;

– the proportion of tested samples exceeding MPC in drinking water for the content of aluminum – from 31.1 to 38.4%;

– the proportion of the studied air samples exceeding the MPC for benzpyrene content in urban and rural settlements – from 3.1 to 3.4 %;

– the proportion of the studied soil samples from residential areas that do not meet hygienic standards for the content of heavy metals – from 9.3 to 10.5%;

– the proportion of tested samples exceeding MPC in drinking water for the content of chlorine – from 8.8 to 21.5 %;

Using these data as independent variables in mathematical models led to the conclusion that the presence of the above risk factors determines the probability of about 1,000 deaths each year including the population under the age of retirement, i.e. these deaths could not have happened during the year in a hygienically safe level of air and soil pollution. With the region's population of about 2 million people, the risk of death due to pollution of the living environment can be estimated as $5 \cdot 10^{-4}$, that is considered as an unacceptable risk according to the the common classification.

In addition to excess mortality, environmental hazards are associated with additional cases of diseases of varying severity. The probability of formation of cancer under the influence of environmental factors is of about $2.8 \cdot 10^{-3}$, for the studied region, which is unacceptable to the population.

The algorithm is universal in general. In this case, the output information obtained upon the implementation of each stage is the independent result and can be used by researchers, depending on the set tasks.

It should be noted, that the paired and multiple models of factors relationship with different types of health disorders received at this stage can serve as a basis for modeling of the risk evolution after a careful analysis, which is very important for solving the problems of accumulation of mathematical models bank and their subsequent verification.

The identified cause-and-effect relationships also allowed performing the forecast of the sanitary and hygienic situation in the future.

This requires the development of prospective scenarios of indicators change caused by the activities of authorities and organizations of the Rospotrebnadzor. The development of future scenarios uses the models of cause-and-effect relationships between indicators, target levels of socio-economic and sanitary-hygienic indicators or values of these indicators calculated on the basis of the dynamic trends (6.12):

$$x_i^{\text{Персп}} = x_{it} \overline{T}_i', \tag{6.12}$$

where $x_i^{\text{Персп}}$ – the prospective value of the *i*-th factor;

x_{it} – the value of *i*-th factor in the *t*-th year;

$\overline{T}_i'$ – average annual growth rate of the *i*-th factor.

In the preparation of future scenarios, it is assumed that the current trends persist for the future years. Retention of these trends allows predicting the change in the health status of the population on the basis of risk assessment.

In general, the obtained quantitative and qualitative assessment of individual indicators of sanitary-epidemiological welfare are analytical and information base for quantitative assessments of current and future risks and, as a result, the basis for making different types of decisions and inform a wide range of persons concerned.

6.6. The hazard assessment of large-scale noninfectious morbidity associated with environmental factors

Hazard identification allows establishing the causes and identifying conditions for the occurrence and spread of mass non-communicable diseases. At the initial stage, it is suitable to assess the hazards of these diseases according to the data of social-hygienic monitoring. The result of this assessment is the identification of areas characterized by this hazard, and supervision objects stipulating it.

The term "mass noninfectious diseases (poisonings)" in the Federal Law No. 52-ФЗ dated 30.03.1999, (rev. dated 11.25.2013) "On the sanitary-epidemiological welfare of the population" (Article 1. Basic concepts) is characterized as a human diseases, the occurrence of which is caused by the exposure to physical and (or) chemical and (or) social environmental factors.

The methodological recommendations "The identification of thresholds of mass noninfectious morbidity and their use in planning of supervisory activities" [MR 5.11.0081-13] clarified that "mass noninfectious diseases" - is the presence of an unusual amount or groups of cases, clinically characterized nosological form of the disease, the occurrence of which is stipulated by the the impact of physical and (or) chemical and (or) social environmental factors, confirmed by the results of clinical, sanitary-hygienic and epidemiological studies.

It should be noted that the mass noninfectious diseases can arise as a result of emergencies, such as emergency emission, effluents, food poisoning, the extreme pollution of the working environment, etc. This situation requires focusing on the supervision facilities hazards. In this case, their classification according to the probability criteria of sanitary legislation violation, the possible severity and extent of health disorders is justified.

In relation to this cases, the instruction for filling the form of federal statistical monitoring No. 18 "Information on the sanitary status of a subject of the Russian Federation" [Instruction approved by the Order of the Federal State Statistics Service No. 287 dated 10.12.2009] explained that the noninfectious diseases should be considered as mass ones starting with 20 cases or more. However, clarification on the extent (organization, municipality, region, etc.) and the period of the registration of such number of cases is not provided in this document.

In the context of long-term or recurring violations of sanitary legislation within regions, municipalities, populations and subpopulations, mass noninfectious diseases can be registered with unspecified persons. In this case, it is advisable to consider the concept of mass noninfectious diseases as an abnormally high level of morbidity due to the failure to comply with hygiene standards. It is reasonable to perform hazard assessment as a first step to establish the causes and conditions of mass noninfectious diseases.

Based on the definition of hazard and mass noninfectious diseases, the term "the risk of mass noninfectious diseases associated with environmental factors" can be defined as the ability of physical and (or) chemical and (or) social environmental factors in the violation of hygienic standards to cause unusually high levels of morbidity on individual classes and nosologic forms of diseases.

In this regard, it is necessary to propose the criteria of abnormally high morbidity. Statistically validated criteria of this type may be thresholds of mass noninfectious diseases that evidence the abnormally high levels of this indicator in the assessment similar to the epidemic thresholds. As part of mass noninfectious diseases hazard assessment related to the environmental factors, it is necessary to establish the territories with the hazard of its occurrence and the facilities that make up this danger.

Guidelines "Determination of thresholds of mass noninfectious diseases and their use in planning of oversight activities" [MR 5.11.0081-13] are developed for methodological support for the establishment of the causes and the identification of conditions for the occurrence and the spread of mass non-communicable diseases. This paper proposed a series of actions that allow calculating the criteria for mass noninfectious diseases, establishing its possible connection with the violation of hygienic standards of the environment pollution.

The purpose of the identification of the thresholds of mass noninfectious diseases is to identify the priority areas and facilities for the actions of authorities of the Rospotrebnadzor on

the identification of the causes of mass noninfectious diseases and for planning of oversight activities, as this is part of the Rospotrebnadzor functions[1]. According to this method, the morbidity in the territory for the individual classes of diseases and nosological forms above the set threshold is defined as the mass one. The allocation of territories to establish the causes, identify conditions for the occurrence and spread of mass noninfectious diseases is carried by comparing the hazard of exposure to environmental factors with mass morbidity in these areas. The hazard of exposure to the environmental factors is determined on the basis of information on the violations of sanitary legislation, such as the exceedance of the established hygienic standards of environmental quality and pollution of the individual environmental objects, for example, the volume of pollutants released into the air, and hazard indicators calculated on their basis.

The determination of priority objects in the planning of supervisory action is based on an assessment of the health hazard of environmental pollution sources in the selected areas.

The following actions consistently implemented to determine the thresholds of mass noninfectious morbidity and their use in planning of oversight activities of authorities and organizations of the Rospotrebnadzor:

– the preparation of initial information;

– the calculation of the thresholds of mass noninfectious morbidity for the classes of diseases and nosologic forms;

– the identification of areas with mass noninfectious morbidity;

– the hazard assessment of environmental factors effect on the formation of classes of diseases and nosologic forms with the allocation of areas with the greatest hazard;

– the comparison of the hazard of environmental factors exposure with mass morbidity in the territories;

– the allocation of areas with hazard of mass noninfectious morbidity associated with violations of hygienic standards of environment contamination for planning of priority supervisory actions;

– the identification of the priority components of pollution and the objects of supervision forming the hazard of mass noninfectious morbidity.

In order to establish the hazard of mass noninfectious diseases, one of the most important steps is the presence of baseline data. The sources of baseline data may be the results of socio-hygienic monitoring – the results of the annual statistical observations of noncommunicable morbidity rates on the territories of the subject of the Russian Federation[2]. Data on the quality of the environment, including the individual indicators and population health status is enough to identify areas with hazard of mass noninfectious morbidity using the technique on "Identification of thresholds of mass noninfectious diseases and their use in planning of surveillance activities" in the existing forms of reporting. The proposed methodological approaches allow authorities and organizations of the Rospotrebnadzor to identify areas with mass noninfectious diseases under the hazard of its formation under the negative influence of the environment, set the priority risk factors and surveillance facilities.

For the calculations, it is necessary to have the data of social and hygienic monitoring in the information database – the results of annual statistical observations of noninfectious diseases rate in the territories of the subject of the Russian Federation; the data of the mandatory health insurance fund (if necessary to calculate morbidity rates according to different age groups).

In order to calculate the threshold of mass noninfectious morbidity, in the first stage, it is necessary to select nosological form or class of diseases according to socio-hygienic monitoring data, which are formed by statistical reporting[3] forms, and prepare initial data as

[1] See p. 5.4 "Provision on the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance".

[2] Form No.12 "Data on the number of patients living in the area of the medical preventive institutions activity", Information about the sanitary condition of the subject of the Russian Federation" (Form 18), etc.

[3] Form No.12 "Data on the number of patients living in the area of the medical preventive institutions activity"

an array of "Morbidity rates (MR) for the selected nosological form or class of diseases for the age group (C, T, A) four years prior the estimated period.

Calculate the arithmetic mean selective ($\overline{П3}$) and average selective standard deviation (S) on the basis of the resulting array:

In order to identify areas with the abnormally high values of morbidity, it is necessary to assign selection markers (R) to the territories according to the rule:

if $П3_i^j \le \overline{П3} + 2S$, than $R_i^j = 0$, (6.13)

if $П3_i^j > \overline{П3} + 2S$, than $R_i^j = 1$. (6.14)

The further calculation of the threshold of mass noninfectious morbidity requires to exclude the value of the morbidity rate with selection marker "1", count k_0 – the number of areas 4 years prior the estimated year with the selection markers equal to "0".

The second step of mass noninfectious morbidity thresholds determination is to calculate threshold indicators of mass noninfectious morbidity to determine the territory of the subject of the Russian Federation with mass noninfectious morbidity. In this case, the arithmetic mean selective ($\overline{П3_0}$) and average selective standard deviation (S_0) are calculated only for areas with selection markers equal to "0".

The threshold of mass noninfectious morbidity (P) for each class of diseases and nosologic forms is the value

$$P = \overline{П3}_0 + 2S_0. \quad (6.10)$$

If the morbidity on the territory is below the threshold of mass noninfectious morbidity ($П3_i^G \le P$), the mass noninfectious morbidity of the studied type on the territory in the in the estimated year is not registered, and it is assigned a selection marker "0", otherwise the mass noninfectious morbidity in the estimated year is recorded on this territory, and it is assigned a selection marker "1".

For territories with a selection marker equal to "1", it is necessary to establish relationships of morbidity of this class of diseases or nosologic form with environmental risk factors and the monitoring facilities, which are the probable sources of adverse effect on human health.

The third step of the method is to identify areas with mass noninfectious morbidity of the population and maximum hazard of environmental pollution.

To evaluate the possible relation of mass noninfectious morbidity with negative environmental factors caused by the supervision facilities, at the first step it is necessary to carry out a comparison of areas characterized by mass noninfectious morbidity, with hazardous indicators of this class of diseases or nosologic form.

The same algorithm is applied to determine the risk of the violations of sanitary legislation, which may stipulate the possibility of negative influence of the environment facilities. The marking of territories is carried out in accordance with the formulas

if $O_i^j \le \overline{O} + 2S$, than $RO_i^j = 0$, (6.15)

if $O_i^j > \overline{O} + 2S$, than $RO_i^j = 1$, (6.16)

and the hazard criterion is calculated according to the formula

$$P = \overline{O}_0 + 2S_0. \quad (6.17)$$

The indicators characterizing the proportion of the samples of the environmental object (air, drinking water, soil, etc.) that do not meet hygienic standards for sanitary-chemical indicators are used in this case (Fig. 6.13).

In addition, the index of relative carcinogenic hazard (HRI_{opr}) is used to evaluate the possible relationship of mass noninfectious morbidity (except neoplasms) with the negative factors of air pollution [R 2.1.10.1920-04].

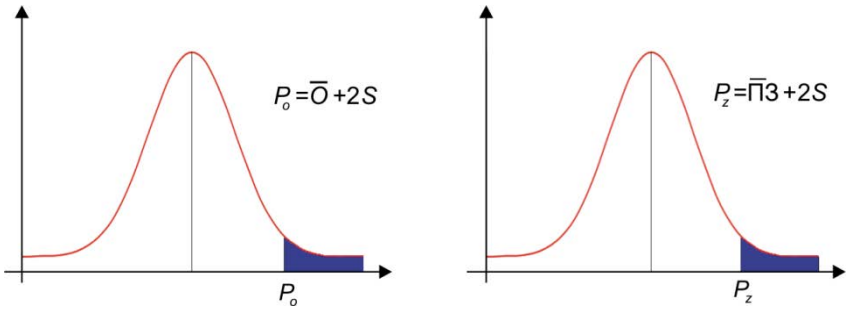

Fig. 6.13. The calculation of mass noninfectious morbidity (P_z) thresholds and hazard criteria of environmental objects (P_o)

The indices of the relative non-carcinogenic hazard of developing the certain types of responses ($HRI_{орг}^{терр}$) in the territory are the sum of indices values of the relative non-carcinogenic hazard of compounds adversely affecting the same critical system or organ

$$HRI_{орг}^{терр} = \sum_{l,t} HRI_{l,t}\ , \qquad (6.18)$$

where $HRI_{l,t}$ – the index of the relative non-carcinogenic hazards of certain chemicals from separate sources potentially hazardous for the development of the pathology of critical organs and systems;

l – chemical substance $(l = \overline{1,L})$;

t – the object of supervision $(t = \overline{1,T})$.

To identify the priority classes of diseases according to the ICD-10, it is necessary to summarize the indexes of relative non-carcinogenic hazards of certain critical systems and organs. It is advisable to choose critical organs and systems in accordance with R 2.1.10.1920-04. Determination of compliance of the critical organs and systems with classes and nosological forms of disease should be based on the primary disorder of a particularsystem or organ in the clinical signs of the disease.

To select territories characterized with the hazard of certain diseases classes, the total index of relative hazard for subjects of the Russian Federation is calculated by the following formula

$$HRI_{орг}^{субъекта} = \sum_{терр} HRI_{орг}^{терр}\ , \qquad (6.19)$$

where $HRI_{орг}^{терр}$ – the index of the relative non-carcinogenic hazard of the impact on organs and systems for individual territories.

Territories with the highest hazard, which cause at least 95% of the total index of relative hazard ($HRI_{орг}^{субъекта}$) in the subject of the Federation, i.e., in an amount equal to not less than than ($0{,}95 \cdot HRI_{орг}^{субъекта}$) are further defined. For this contribution of each territory to the total index of relative hazard ($HRI_{орг}^{субъекта}$) in the subject of the Federation is calculated as a percentage, and then the territories are sorted according to of the index of relative noncarcinogenic hazard of exposure on organs and systems ($HRI_{орг}^{терр}$). Territories with the highest index of relative noncarcinogenic hazard for the organs and systems, the contribution amount of which is equal to 95% are defined. The selection marker is assigned to such territories $RO_i^G = 1$, the rest of the territories are assigned with selection marker $RO_i^G = 0$.

Territory, which simultaneously marked by the selection marker $R_i^G = 1$ according to the criterion of mass noninfectious diseases and the selection marker $RO_i^G = 1$ according to the hazard criteria of the development of this disease, are identified as areas with hazard of formation of mass noninfectious morbidity. These territories have a territory selection marker $U_i^G = 1$ in all other cases $U_i^G = 0$.

The final step in setting the thresholds of mass noninfectious morbidity is to identify priority pollution components and objects of supervision forming the hazard of mass noninfectious morbidity.

At this stage, the index of relative hazard for each object of supervision forming this indicator on the territory is used in the priority areas for the establishment of supervision objects, which are the sources of environmental pollution.

$$HRI_{\text{орг}}^{t} = \sum_{l} HRI_{l}\ , \tag{6.20}$$

where t – the object of supervision $(t = \overline{1,T})$;

l – chemical substance $(l = \overline{1,L})$.

Supervision objects with the maximum hazard are defined just as when selecting territories with a maximum hazard of certain diseases classes development. These supervision objects stipulates at least 95% of the total index of the relative hazard on the territory, that is, they are equal to not less than ($0,95HRI_{\text{орг}}^{\text{терр}}$) in an amount.

Thus, the proposed methodological approaches allow authorities and organizations of the Rospotrebnadzor to determine the threshold of mass noninfectious morbidity, to allocate the territories of thesubjects of the Russian Federation with the exceedance of the threshold of mass noninfectious morbidity, the sources of the substances intake in the environment, identify the areas with the highest risk of the environment contamination, identify areas with the highest hazard of certain diseases classes development (nosological forms), and to identify priority pollution components (risk factors), the objects of supervision, forming the risk of mass noninfectious morbidity.

Due to the necessity of processing large amounts of data, this technique is supported by the respective software product (Fig. 6.14).

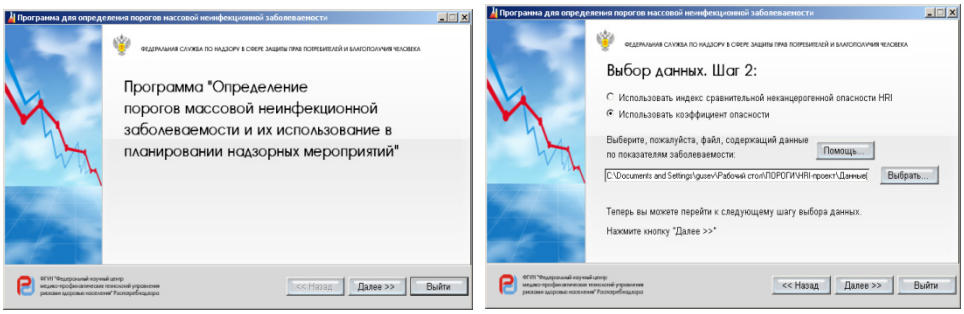

Fig. 6.14. Screenshots of the software "Determination of thresholds of mass noninfectious diseases and their use in planning of oversight activities"

The analysis of mass noninfectious morbidity hazard was performed using the proposed methodological approaches and software due to the harmful effects of environmental factors in the context of the subjects of the Russian Federation. The classes of diseases and nosological forms, the development of which was stipulated by the human living environment were selected in view of the critical organs and systems:

– to assess the impact of non-compliance with hygienic standards for air pollution on the health of adults – disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; diseases of the nervous system; respiratory diseases; diseases of the circulatory system; neoplasms;

– to assess the impact of non-compliance with hygienic standards for air pollution on the health of children – disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; diseases of the nervous system; respiratory diseases; diseases of the circulatory system; neoplasms;

– to assess the impact of non-compliance with hygienic standards for drinking water contamination on the health of adults – the disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; the diseases of the genitourinary system; the diseases of the nervous system; the diseases of the digestive system; the diseases of the circulatory system; endocrine systems diseases, nutritional and metabolic disorders;

– to assess the impact of non-compliance with hygienic standards for drinking water contamination on the health of children – the disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; the diseases of the genitourinary system; the diseases of the nervous system; the diseases of the digestive system; the diseases of the circulatory system; endocrine systems diseases, nutritional and metabolic disorders;

– to assess the impact of non-compliance with hygienic standards for soil contamination on the health of adults – diseases of the skin and subcutaneous tissue; disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; diseases of the nervous system; diseases of the digestive system; endocrine systems diseases, nutritional and metabolic disorders;

– to assess the impact of non-compliance with hygienic standards for soil contamination on the health of children – the diseases of the skin and subcutaneous tissue; the disease of the blood, hemopoietic organs and certain disorders involving the immune mechanism; the diseases of the nervous system; the diseases of the digestive system; endocrine systems diseases, nutritional and metabolic disorders.

Mass noninfectious diseases thresholds were defined and territories with the exceedance of the mass noninfectious diseases threshold were allocated for these classes of morbidity – by diseases classes and nosology in accordance with the International Classification of Diseases of the 10th Revision (ICD-10).

The examples of mass noninfectious morbidity thresholds associated with air, drinking water, and soil pollution are presented in Table 6.13–6.15.

Table 6.13

The thresholds of the mass noninfectious morbidity of the population of the Russian Federation related to air pollution, ‰

Disease code according to ICD-10	Disease name according to ICD-10	2012	
		Adult population	Child population
L00-L99	Diseases of the skin and subcutaneous tissue	58.54	147.3
D50-D89	Blood, hemopoietic organ diseases and certain disorders involving the immune mechanism	4.45	30.58
N00-N99	Diseases of the genitourinary system	80.51	46.48
G00-G99	Nervous system disorders	19.83	69.02
J00-J98	Diseases of the respiratory system	218.98	425.98
I00-I99	Circulatory diseases	45.65	16.08
H65-H75	Diseases of the ear and mastoid process	33.22	83.15
E00-E35	Endocrine system diseases, eating disorders and metabolism disorders	14.21	29.47
C00-D48	Neoplasms	18.21	8.1
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	5.97	60.67

Table 6.14

The thresholds of themass noninfectious morbidity of the population of the Russian Federation related to drinking water pollution, ‰

Disease code according to ICD-10	Disease name according to ICD-10	2012	
		Adult population	Child population
L00-L99	The diseases of the skin and subcutaneous tissue	78.75	147.3
D50-D89	Blood, hemopoietic organ diseases and certain disorders involving the immune mechanism	5.74	30.58
N00-N99	The diseases of the genitourinary system	115.14	46.48
G00-G99	Nervous system disorders	33.7	69.02
I00-I99	Circulatory diseases	56.1	16.08
E00-E35	Endocrine system diseases, eating disorders and metabolism disorders	20.96	29.47
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	8.23	61.48
K00-K93	The diseases of the digestive system	71.92	132.87

Table 6.15

The thresholds of the mass noninfectious morbidity of the population of the Russian Federation related to soil pollution, ‰

Disease code according to ICD-10	Disease name according to ICD-10	2012	
		Adult population	Child population
L00-L99	The diseases of the skin and subcutaneous tissue	77.28	147.41
D50-D89	Blood, hemopoietic organ diseases and certain disorders involving the immune mechanism	5.48	32.49
G00-G99	Nervous system disorders	26.01	69.35
I00-I99	Circulatory diseases	–	–
E00-E35	Endocrine system diseases, eating disorders and metabolism disorders	19.42	29.58
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	7.55	61.65
K00-K93	The diseases of the digestive system	61.94	132.9

The following values are established for hazard indicators in 2012: for air 0.75% of samples that do not meet hygienic standards, for drinking water – 16.39% thereof.

The cross-spectrum analysis of the monitoring results of air quality and population morbidity showed that the risk of mass noninfectious children morbidity associated with the violation of air pollution regulations for various types of diseases was found in 52 regions of the Russian Federation in 2012. At the same time, the hazard of mass noninfectious children morbidity on 3 classes of diseases and more was marked on 6 territories: Arkhangelsk region, Murmansk region, Ulyanovsk region, Trans-Baikal Territory, the Krasnoyarsk Territory, the Republic of Sakha (Yakutia).

According to the SGM data, the hazard of mass noninfectious morbidity was identified on the class of respiratory diseases, for example, in 2012, in 52 subjects of the Russian Federation: 10 subjects of the Central Federal District; 4 subjects of the Southern Federal District; 5 subjects of the North-West Federal District; 7 subjects of the Far Eastern Federal District; 10 subjects of the Siberian Federal District; 5 subjects of the Urals Federal District; 8 subjects of the Volga Federal District; 3 subjects of the North Caucasian Federal District. The following diseases are highlighted as main nosological forms of diseases for which the hazard is formed: allergic rhinitis (hay fever), chronic disease of tonsils and adenoids. This hazard is primarily concerned with the exceedance of air MPC for ammonia, suspended substances, formaldehyde, nitrogen oxides.

The class of circulatory system diseases is on the second place by the prevalence of the hazard of mass noninfectious diseases (6 subjects: Belgorod region, Arkhangelsk region, the Republic of Tatarstan, Ulyanovsk region, the Trans-Baikal and Krasnoyarsk Territory); this class is mainly represented by diseases characterized by high blood pressure and cardiomyopathy. This hazard is related to the exceedance of MPC for suspended substances and carbon monoxide content in ambient air.

The hazard of mass noninfectious morbidity by the class of neoplasms is extended to five regions (Arkhangelsk region, Kaliningrad region, Murmansk region, the Trans-Baikal Territory, the Republic of Sakha (Yakutia)). This hazard is related to the exceedance of MPC for formaldehyde.

The hazard of mass noninfectious morbidity on the class of blood, hemopoietic organs diseases and certain disorders involving the immune mechanism has been established in three areas of the country – in the Republic of Ingushetia and Bashkortostan, the Trans-Baikal Territory, that is associated with the probability of exceedance of MPC for nitrogen oxides, formaldehyde, and carbon monoxide. Among nosological forms, this class is represented mainly by anemia.

The hazard of the development of mass noninfectious morbidity of the nervous system diseases was recorded in 4 subjects – Nizhny Novgorod and Ulyanovsk regions, the Trans-Baikal Territory, the Republic of Sakha (Yakutia), which is due to exceedance of MPC for carbon monoxide.

The analysis of the adult population morbidity and the results of air quality monitoring showed that the risk of mass noninfectious morbidity associated with the violation of air pollution regulations for various types of diseases was found in 9 regions of the Russian Federation in 2012. At the same time, the hazard of mass noninfectious morbidity of adult population on 3 classes of diseases and more was marked on 3 territories: The Republic of Ingushetia, Altai and Trans-Baikal Territory.

The hazard of mass noninfectious morbidity on the class of cardiovascular diseases was formed in 2012 in 5 subjects of the Russian Federation (Belgorod region, the Republic of Ingushetia, Altai and Trans-Baikal Territory, Omsk region). The following diseases are determined as main nosological forms in relation to which the hazard was formed: diseases characterized by high blood pressure; ischemic heart disease (acute and chronic); stenocardia. This is related to the exceedance of air MPC for suspended substanses and carbon dioxide.

The hazard of mass noninfectious morbidity of the adult population in the class of diseases of blood, hemopoietic organs and certain disorders involving the immune mechanism, was defined in three areas (the Republic of Ingushetia, Altai and Trans-Baikal Territory), which is presented by anemia and associated with the exceedance of air pollution standards for nitrogen oxides formaldehyde, and carbon monoxide.

The territories of the occurrence hazard of mass noninfectious morbidity on the class of diseases of the nervous system include three subjects (the Republic of Ingushetia, the Trans-Baikal Territory, Republic of Sakha (Yakutia)), that is caused by the exceedance of carbon monoxide MPC in ambient air.

The occurrence hazard of mass noninfectious morbidity on the class of neoplasms is identified for four subjects (Samara Region, Ulyanovsk region, Altai and Trans-Baikal Territory). This hazard is related to the exceedance of MPC for formaldehyde in ambient air.

The occurrence hazard of mass noninfectious morbidity of respiratory diseases is set for 1 area (Trans-Baikal Territory). This class of diseases is mainly represented by nosoforms: bronchitis; chronic disease of tonsils and adenoids; asthma, asthmatic status; allergic rhinitis (hay fever); acute laryngitis and tracheitis.

In 2012, the hazard of mass noninfectious diseases is defined in the territories, which were recorded in 2011: for the class of diseases of the blood, hemopoietic organs and certain disorders involving the immune mechanism – in the Trans-Baikal Territory; for the class of diseases of the nervous system – in the Trans-Baikal Territory, the Republic of Sakha (Yakutia); for the class of respiratory diseases – in the Trans-Baikal Territory; for the class of diseases of the circulatory system – in the Omsk region and Trans-Baikal Territory;

for the class of neoplasms – in Samara and Ulyanovsk regions, Altai and Trans-Baikal Territories.

The risk of hazard of mass noninfectious morbidity of adults associated with air pollution is recorded in the Trans-Baikal Territory for most classes of diseases (diseases of the blood, hemopoietic organs and certain disorders involving the immune mechanism; diseases of nervous system; respiratory diseases; circulatory system diseases; neoplasms).

The hazard assessment of mass noninfectious morbidity of the adult population associated with the poor quality of drinking water of centralized drinking water supply has shown that the hazard of mass noninfectious morbidity by the class of circulatory system diseases was formed in 2012 in 9 subjects of the Russian Federation (Belgorod region, Tambov region, Arkhangelsk region, the Republic of Kalmykia, the Republic of Mordovia, the Republic of Tatarstan, Ulyanovsk region, the Trans-Baikal and Krasnoyarsk Territories). The main nosological forms representing this class are primary hypertension and cardiomyopathy.

Second place (7 subjects) with the hazard of mass noninfectious morbidity occurance takes a class of diseases of the digestive system (Bryansk region, Arkhangelsk region, Ulyanovsk region, the Republic of Kalmykia, the Republic of Mordovia, the Republic of Tatarstan, Trans-Baikal and Krasnoyarsk Territories) presented by the main nosoforms – disease of the liver, pancreas; noninfectious enteritis and colitis.

The six territories of the hazard of mass noninfectious morbidity occurrence is established for each of the following classes: the diseases of the nervous system (the Udmurt Republic, the Chuvash Republic and the Nizhny Novgorod Republic, Ulyanovsk region, Trans-Baikal Territory, the Republic of Sakha (Yakutia)), the diseases of the genitourinary system (The Republic of Komi, Arkhangelsk region and Samara region, the Chuvash Republic, Trans-Baikal and the Primorsky Territories).

Increase in the number of areas with the hazard of mass noninfectious morbidity is identified for 5 classes of diseases compared to 2011: diseases of the blood, hemopoietic organs and certain disorders involving the immune mechanism – 5 territories (in 2011 – 4); diseases of the nervous system – 6 (in 2011 – 4); diseases of the genitourinary system – 6 (in 2011 – 3); diseases of the digestive system – 7 (in 2011 – 4); circulatory system diseases – 9 (in 2011 – 8). The changes in the number of areas with hazard on of mass noninfectious morbidity for the class of diseases of the endocrine system, nutritional and metabolic were not registered.

In 2012, the hazard of mass noninfectious diseases is defined in the territories, which were recorded in 2011: for the class of blood, hemopoietic organs diseases and certain disorders involving the immune mechanism – in the Trans-Baikal Territory; for the class of diseases of the genitourinary system – in the Republic of Komi, Arkhangelsk and Samara regions, the Trans-Baikal Territory; for the class of diseases of the nervous system – in the Udmurt Republic, Trans-Baikal Territory, the Republic of Sakha (Yakutia); for the class of diseases of the digestive system – in Bryansk, Samara and Omsk regions, the Trans-Baikal Territory; for the class of diseases of the circulatory system – in the Arkhangelsk region, the Republic of Tatarstan, the Trans-Baikal Territory, etc.

An algorithm of sanitary and epidemiological investigation shown in Fig. 6.15, which was approved by the example of several areas was proposed in order to identify the causes and conditions of occurrence and propagation of mass noninfectious diseases.

The proposed methodological approaches have been also tested at the level of individual territories of the Russian Federation.

For example, water quality did not meet the established standards in the K. city: 66.1% of samples did not meet hygienic standards for microbiological indicators, 30.8% – for sanitary and chemical indicators. The value of the share of the specific combined water pollution index was 3.10 that allow attributing the water of the surface water source to the quality class "3Б" (very polluted). The high level of microbiological contamination stipulates the necessity of the intensive water sterilization.

The sanitary-chemical parameters of water quality from utility and drinking water system networks are not satisfactory (20.3% of non-standard samples). According to the results of socio-hygienic monitoring, products of hyperchlorination (residual free chlorine –

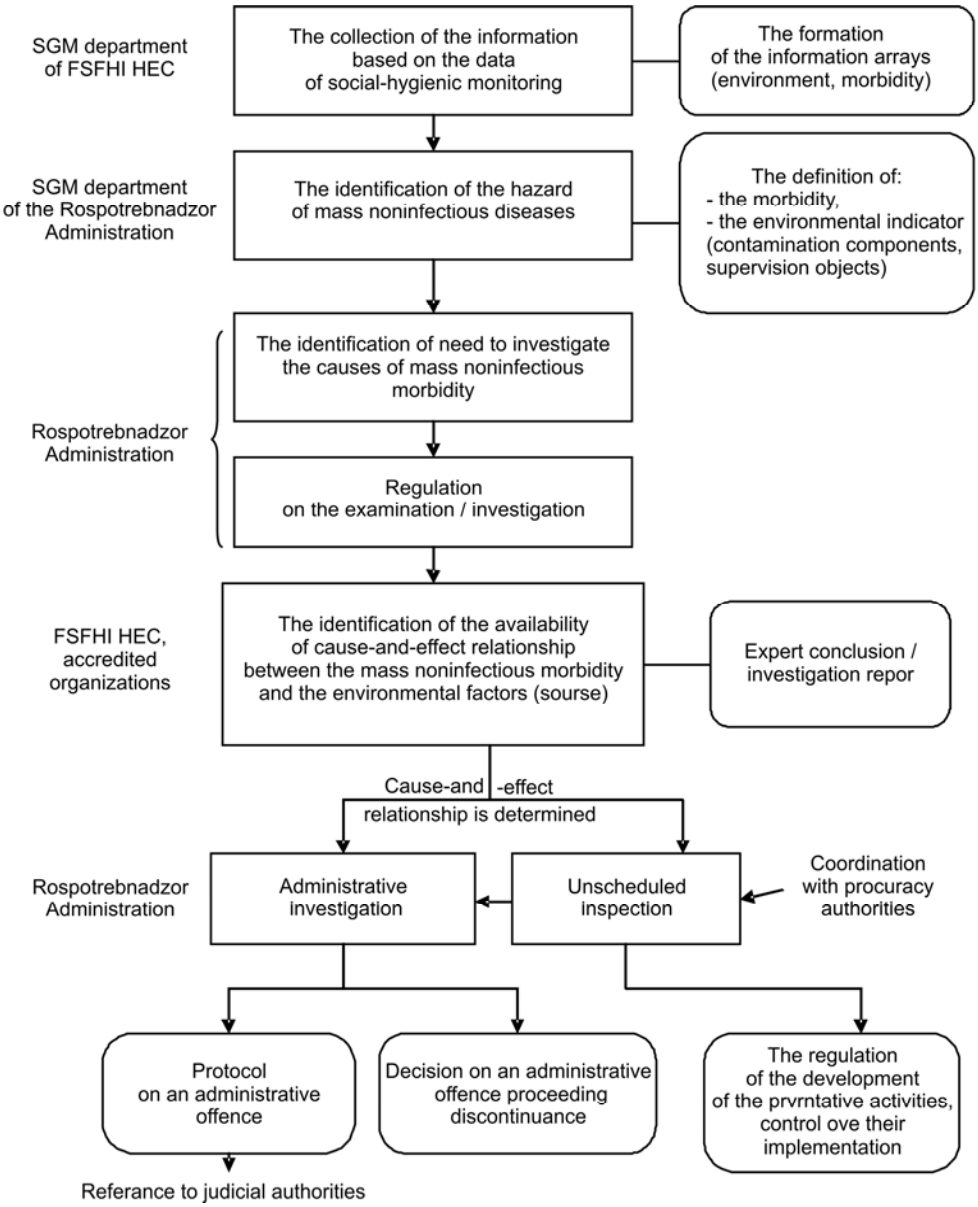

Fig. 6.15. The algorithm of the sanitary and epidemiological investigation of the causes and the identification of the conditions for the occurrence and propagation of mass noninfectious diseases established by the Federal Service for Supervision of Consumer Rights Protection and Human Welfare

62.5% of samples above the MPC, residual bound chlorine – 12.5% of samples above MPC) are the main components of drinking water contamination. Compounds formed during chlorination – chloroform, carbon tetrachloride, dichloroethane, and dihlorbrommetan dibromochloromethane – were found in drinking water as the results of the studies. Assessment on the criterion of the amount of the detected concentrations relations to the

value of the MPC (summation effect) in accordance with SanPin 2.1.4.1074-01 showed that this figure exceeds the permissible level in up to 2.5 times.

The level of mass noninfectious disease in the territory of the K. city for noninfectious enteritis and colitis amounted to 5.25 ‰ at a threshold of 5.16 ‰, the diseases of the pancreas – 16.14 ‰ (threshold level of 13.04 ‰), other diseases of the genitourinary system – 15.43 ‰ (threshold level of 13.57 ‰).

The analysis of morbidity in the K. city on the health-care seeking confirms the presence of the mass noninfectious morbidity hazard for the digestive organs (pancreas). The application of children population for medical assistance due to gallstones, gallbladder diseases, biliary tract and pancreas diseases is 4.64 times higher than that in the territory of the comparison.

Thus, the presence of the hazard of mass infectious morbidity for the digestive organs and urinary tract system associated with poor quality of drinking water from the centralized water supply system is identified for the population of the K. city.

The hazard of mass noninfectious diseases of the blood, hemopoietic organs and certain disorders involving the immune mechanism associated with the negative impact of air pollution was identified in the P. city for the child population. It was determined, that the concentrations of nitrogen dioxide in the air was up to 5.75 MPC_{cc}, benzene – up to 1.9 MPC_{cc} (critical organs and systems – the blood system, the immune system). The threshold of mass noninfectious morbidity (90.76 ‰) was significantly exceeded. The morbidity level of diseases of the blood, hemopoietic organs and certain disorders involving the immune mechanism amounted to 1260.1 ‰. Refinery enterprises and highways have been identified as objects causing the danger of mass noninfectious morbidity.

6.7. The preparation of proposals for the adoption of the necessary measures to eliminate the identified harmful effects of environmental factors by the federal executive bodies, executive bodies of the subjects of the Russian Federation, and local government authorities

The results of social and hygienic monitoring in the form of hygiene assessments with the identification of hazard factors, the definition of health risk contingents, the priority risk areas, etc. can and should be the basis for making managerial decisions of different levels.

Chapter 4 outlines the basic principles of risk communications and defines the requirements to the information that is most adequately perceived by decision-makers. Chapter 3 provides the methods of risk management.

According to the government reports on the sanitary-epidemiological welfare of recent years, about 2–3 thousand projects of managerial decisions are justified annually in the country based on the results of social-hygienic monitoring and risk assessment, about 70% of them are implemented (Table 6.16).

Table 6.16

The number of administrative decisions based on the results for SGM and risk assessment in the Russian Federation

Indicator	Year			The rate of growth in 2011, %
	2011	2012	2013	
The number of the proposed projects of management decisions based on the results of SGM introduction and risk assessment, total	2679	2955	3634	18.7
The number of the accepted projects of management decisions based on the results of SGM introduction and risk assessment, total	1958	2166	2512	13.8

The greatest number of managerial decisions based on the results of SGM and risk assessment is made in the Sverdlovsk region, Smolensk region, Tambov region, Moscow region, Voronezh region, Kaliningrad region, Irkutsk region, Perm region and Krasnodar Territory.

In 2013, 1058 (29.1%) of the total number of the managerial decisions made are the decisions within the regional target programs for the prevention of mass noninfectious diseases due to exposure to the exposure to the environmental factors, 217 (8.6%) – the decision of the Chief State Sanitary Doctor for the subjects of the Russian Federation on the prevention of mass noninfectious diseases, 111 (4.4%) – the results of work performed by accredited authorities on risk assessment (Table 6.17).

Table 6.17

The number of made administrative decisions based on the results for SGM and risk assessment in the Russian Federation for 2013

Measure	Number, absolute	Specific weight, %
The number of made management decisions, total	2,512	100
within the framework of regional programs for the prevention of mass non-communicable diseases	1,058	42.1
within the regulations of the Chief State Sanitary Doctor on the prevention of mass non-communicable diseases	217	8.6
within the work performed by accredited bodies on risk assessment	111	4.4
other	1,126	44.8

The largest number of regional target programs for the prevention of mass noninfectious diseases and works on the assessment for public health risks was conducted in the Ural and Central Federal Districts; the largest number of decrees of the Chief State Sanitary Doctor on the prevention of mass noninfectious diseases are issued in the Central, North-West and North Caucasian Federal Districts.

The results of social and hygienic monitoring formed the basis of the investment programs aimed at improving the water supply of populated areas in Belgorod, Irkutsk, Lipetsk, Moscow, and Smolensk regions. Measures of targeted "Clean Water" programs are implemented in Krasnoyarsk and Kamchatka Territories, Chelyabinsk, Tula, Samara, Kaluga and Vladimir regions, the Republic of Dagestan, Komi, Mordovia, Kabardino-Balkaria, and the city of St. Petersburg. The reconstruction of water-supply and sewage treatment plants was performed in the Krasnoyarsk Territory, the Komi Republic, Tula and Chelyabinsk regions. The reconstruction of networks of centralized water supply, sewerage and wastewater treatment was performed in the Kamchatka Territory, Kaluga and Vladimir regions, the Republic of Kabardino-Balkaria, the Republic of Mordovia.

In 2013, a long-term comprehensive programs aimed to ensure safe drinking water supply were adopted in a number of subjects of the Russian Federation: "The development of water supply systems of administrative units of the Komi Permian District for 2010–2015", "Drinking water supply for 2011–2017" in the Komi Republic, "The development of the water-economic complex in the Smolensk region for 2012–2014", "Development of the water-economic complex of the Stavropol Territory for 2013–2020", "The use and protection of water bodies in the Kamchatka region for 2013–2020" "The development of the water-economic complex of the Tambov region in 2013–2020", "Development of the water-economic complex of the Samara region for 2013–2020" "On approval of long-term program of the Moscow region "Clean water of the near Moscow for 2013–2020 years".

In order to reduce air pollution, the Law "On the regulation of restrictions on the movement of vehicles in the settlements, places of recreation and tourism, in protected areas in order to reduce emissions of harmful substances (pollutants) into the air", the decision of city administration of Orenburg "On approval of the municipal program "Environmental Protection in the city of Orenburg for 2014–2016", a long-term regional target program "Reduction of air pollution in the Kamchatka region for 2012–2014" departmental

target program "Organization of system for accounting and monitoring of major air pollutants on the territory of the Smolensk region for 2012–2014" was adopted in the Lipetsk region.

A number of managerial decisions aimed to improve the education and raising of children, prevention of students morbidity in secondary education schools were adopted and implemented in recent years.

The Government Decision on the implementation of the regional state target program on the "Development of a network of preschool educational institutions in the Sverdlovsk region for 2010–2014" and on the implementation of the regional target program on the "Development of Education in the Sverdlovsk region ("Our New School") for 2011 2015" were adopted in the Sverdlovsk region; these programs included repairs of country medical and health institutions, activities for prevention of children diseases and the organization of rational nutrition of children.

The resolution of the Government of the Oryol region approved a long-term regional target program on the "Construction of warm sanitary-hygienic facilities in educational institutions of the Oryol region for 2012–2014".

Regional target program "Children's school meals for 2010–2014" approved by the Decree of the Government of the Udmurt Republic aimed to provide students of 1–5 classes with fortified milk and confectionery was implemented in the Udmurt Republic.

The resolution of the Government of the Leningrad Region "On Amendments to the Resolution of the Government of Leningrad Region No. 295 dated 24.10.2006 "On the approval of the procedure of free food provision for students in the educational institutions and students studied according to the programs of elementary vocational education in educational institutions implementing these programs located in the Leningrad Region" was accepted.

Programs on "School meals in the Republic of Khakassia for 2011–2015"; "Ensuring the availability of pre-school education in the Republic of Khakassia (2011–2015)"; "Development of Vocational Education in the Republic of Khakassia" are implemented in the Republic of Khakassia within the framework of the long-term target program "Development of Education in the Republic of Khakassia (2011–2015)".

Major and routine repairs are conducted, school canteens are equipped with technological equipment for two hot meals, students from low-income families are provided with free hot meals within the framework of the republican target program "The improvement of school meal organization in the Altai Republic for 2012–2015".

The improvement of the quality of health risks assessment within the public health monitoring will inevitably lead to increased interest of the state and local authorities in this information and the growth of its demand at various levels.

The optimization of the system of own observations and processing methods can contribute primarily to improve the quality of health risk assessment.

In general, the introduction of risk assessment methodology into the system of social and hygienic monitoring provides the latest with a new impetus to the development, improvement and practical use. It is the risk assessment that allows the minimization of the cost of SGM, receiving the most informative results suitable to validate managerial decisions at various levels. This development is actually a process of system optimization that is achieved by:

– the identification of strategic, tactical, and local priorities of different levels – from federal one to the object level that allows the development of action plans and programs with a focus on factors that could form the largest medical and demographic losses;

– the possibility to allocate problem blocks identical to a number of regions that can be the basis for the formation of the federal and inter-regional target programs aimed at the minimization of the hazard factors;

– the ability of the population risks to identify the economic damages associated with mortality, disability, and morbidity of the population, including the working population, creating gross domestic product based on the assessment results, which is extremely important for the tasks of strategic planning and goal setting;

– the definition of health risks contingents, and critical periods of chronic exposure to hazards at the use of the risk evolution models, that allows creation of programs of targeted preventive medical care for the population, taking into account the urgency of measures;

– the possibility of situational simulation and forecasting of health and demographic implications of any changes in the living environment quality, the level of socio-economic indicators or life style;

– decrease in the total number of instrumental studies due to the reduction in the portion of non-informative measurements and integration of the estimated data with the field ones, the use of high technologies of spatial analysis, as well as correct (science-based) location of minimally sufficient number of stations (points) of observations in the areas of the greatest risk for the health and measurement only of the priority factors.

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7. METHODOLOGY, METHODS AND PRACTICE TO EVIDENCE THE HARM TO HEALTH CAUSED BY THE NEGATIVE IMPACT OF RISK FACTORS

7.1. Legal foundations for risk assessment in the system of health harm evidence

In some cases, risk being the probabilistic value cannot be considered as an argument for decision-making. Judicial proceeding can be the special case of such situation when it is required to proof the harm, but not only the existence of danger, threat or the risk of its occurrence. The current Russian Legislation uses the term "harm to health" in more than 20 federal laws, which also declare the obligation of its compensation by the party, which caused the harm[1]. The Act No. 52-FZ (Federal Law) "Concerning the Sanitary and Epidemiological Welfare of the Population" defines the sanitary and epidemiological welfare as the health status of population and living environment at which there is no harmful impact of habitat factors on the human, i.e there is no harm to the health. The term "harm to health" is used by a number of sanitary norms and regulations, standards and other normative documents. The term "health risk" is used much less frequently. In that context, matching the concepts of "health risk" and "harm to health" and the availability of methodological base to evidence the risks realization is absolutely essential.

In general, the establishment and assignment of the "risk" and "harm" concepts relation will allow extending the field of the application of risk assessment methodology and giving the legal importance to works on risk assessments.

According to the Resolution of the Russian Federation Government dated August 17, 2007 No. 522 "On adoption of the Guidelines to determine the severity level of harm caused to human health", the harm caused to human health is defined as the violation of anatomical integrity and physiological function of human organs and tissues in the result of impact of physical, chemical, biological, and psychogenic environmental factors. Articles 11.5 and 12.2 of the Code of Administrative Offences of the Russian Federation, Articles 111–113 of the Criminal Code of the Russian Federation and the Order of the Ministry of Health and Social Development No. 194n dated April 24, 2008 establish the medical criteria for determining the heavy, medium and light harm to health, classify injuries, poisonings, and other health problems, as well as the degree of loss of capacity for work in the result of disease. The list of health problems is open and can be supplemented. The numerous studies established that the described and qualified signs of harm to health are registered

[1] Art. 1064 "General grounds of liability for harm" of the Civil Code of the Russian Federation (Part Two) No. 14-FZ dated January 26, 1996; Art. 14 "Property responsibility for the harm caused due to the defects in goods (works, services)" Federal Law No. 2-FZ dated January 9, 1996 "On Protection of Consumers' rights"; Art. 79 "Compensation for harm caused to health and property of citizens as a result of violation of legislation in the field of environmental protection" of the Federal Law No. 7-FZ dated January 10, 2002. "On Protection of Environment" and others.

and are the basis for risk assessment and establishment of safety criteria under the impact of risk factors of external environment. These signs include: disorder of vital functions of the human body [Vlasov V.N., 2006; Zaitseva N.V., 2005, 2011; Onishchenko G.G., 2006], acute heart and (or) vascular failure, cerebrovascular disease [Kadyrmaeva D.R., 2004], severe acute respiratory failure; acute poisoning by chemical and biological substances, including toxic metals or gases, food poisoning, temporary dysfunction of organs and (or) systems, etc. [Ananjev V.Y., 2011; Kuzmin S.V., Gurvich V.B. et al., 2009; Protasova V.V., 2011; Sadovnikova Y.M., 2011 et al.].

It is important that the establishment of the facts of harm to the health is an integral element of control and supervisory activity of Federal service in the sphere of the Consumer Rights Protection and Human Welfare. Thus, the assessment of the harmful effects of living environment factors on the human is required in identifying the causes and conditions of occurrence and dissemination of infectious diseases and mass non-communicable diseases (poisoning) (Art. 42 of the Federal Law No. 52-FZ), in the validation of unscheduled inspections (par. 2, Art. 10 of the Federal Law No. 294-FZ) as well as at applying the number of administrative measures in accordance with the Code of Administrative Offences under Articles 6.17; 14.43; 14.44; 14.46, which provide increasing of the liability in the event of harm to human health.

The Article 42 of Federal law No. 122-FZ dated August 22, 2004 provides the implementation of sanitary and epidemiological expertises, investigations, inspections, researches, tests, toxicological, hygienic and other types of assessments which are the basis for the sanitary and epidemiological conclusions including ones concerning the existence of harm to health and reasons which caused it. These conclusions are made by the Chief State Sanitary Physicians in the established order[1].

The assessment of harm to health is demanded within the Criminal Code of the Russian Federation in the validation of the measures of criminal liability. Thus, according to Art. 238: "Production, storage or transportation ... execution of works or rendering of services which do not meet the safety requirements for life or health of consumers ... if they: caused the infliction of heavy harm to health due to the negligence ... are fined at the rate of ... up to five hundred thousand rubles ... or by imprisoned for up to six years ... ".

The terms "harm to health" and "threat of harm" are closely related in legislative and legal acts (the Code of Administrative Offences of the Russian Federation, the Criminal Code of the Russian Federation, Federal Laws No. 52-FZ dated March 30,1999; No. 96-FZ dated May 04, 1999; No. 184-FZ dated December 27, 2002 and many others). Thus the term "threat of harm to health" is poorly concertized and has no expressed qualitative or quantitative assessment criteria. The term "health risk" can have quantitative expression and qualitative characteristics, and the high unacceptable risk can be considered as the risk of harm to health. In this regard the approximation of terms "threat" and "risk" and the extension of the use of the term "health risk" in health legislation is reasonable, including at the proof of harm to health.

7.2. General methodological scheme to proof the harm to health in the negative impact of environmental factors and the place of risk assessment in it

The complexity of problem solving on identification and proof of cause and effect relationships between contamination of living environment and the harm to health is recognized by many researchers [Rosenberg D., 1998; Vorobyov V.A., 2008; Brunekreef B., 2008; Mai I.V. et al., 2010]. The basic principles of evidence-based medicine and

[1] The Order of the Russian Federal Consumer Rights Protection and Human Health Control Service No. 359 dated April 30, 2009 "On the sanitary and epidemiological expertises, inspections, researches, tests and toxicological, hygienic and other types of assessments".

environmental epidemiology, which should be the basis for the formation of evidence base of harm to health of population due to the negative impact of living environment factors are identified [WHO, 2002; Fletcher, R., 2004]:

– exposure precedes the effect;
– exposure effect is expressed and observed in several (various) exposed persons;
– effect depends on the degree of exposure;
– effect is stable and reproducible;
– the biological plausibility of the "exposure – effect" relation is established;
– there are no other explanations for the occurrence of this effect.

A general algorithm of the formation of the evidence base of harm to health based on the example of chemical substances' exposure is shown in Fig. 7.1.

As it is seen from the presented data, the algorithm includes a number of successive stages including the central stage – the health risk assessment.

The data collection and analysis is performed; and the preliminary hygiene, town-planning and another assessment of situation or the analog of hazard identification and preparation of program of further action or rejection of it is conducted on the first two stages.

Health risk assessment in the system of evidence formation of harm allows solving the several problems at once: to establish the risk factors (stage of hazard identification), to obtain the data on the level and duration of human contact with hazardous agent (exposure assessment), to set the types of potential adverse effects (assessment of "exposure – response" dependencies and their intensity), to obtain the quantitative values of health risks concerning critical organs and systems.

The scientific evidence about the different types of health problems that can be formed in the conditions of exposure are studied and summarized, and the possibility of acute or chronic effects is surveyed at the stage of risk assessment. Presence of unacceptable health risk revealed by standardized methods is one of signs of harm included in the evidence base.

It is recommended to perform the assessment of exposure for each point, characterizing the place of permanent residence of human for which the study of exposure markers and response markers is performed. As a result the individual exposure level is set in respect to the specific chemical substance or acting factor for each exposed person taking into account the values, frequencies, durations, and the ways (routes) of influence.

The type of estimated risk (carcinogenic, acute, or chronic non-carcinogenic) is defined by objectives of the study (investigation, expertise). Thus, it should be noted that the further in-depth studies should be considered inexpedient in the conditions when the health risk is recognized acceptable on the basis of conjugate analysis of calculated and field data on the quality of living environment, and/or when there is no data on the proven effects for health under the conditions of known exposure. If the risk is evaluated as unacceptable, it is the reason for the deployment of medical and biological programs.

In general the stage of risk assessment is intended to justify the adequate exposures of diagnostic complexes and the programs of functional, instrumental, and clinical examinations, which will be used in subsequent stages. Thus, the programs of in-depth medical and biological inspections are oriented on identification and the assessment of those effects and diseases in relation to which the risk was established as unacceptable or close to unacceptable. This allows determining the minimum sufficient volume of laboratory studies (often expensive and/ or time-consuming), forming the team of doctors including highly specialized doctors that will be optimal on composition for conducting medical examinations, and the complex of diagnostically important instrumental and functional researches.

As a consequence, the result of stage is the definition of: the parameters of health risk; risk factors with the allocation of priority substances and the ways of their receipt by the population; the priority gender and age or territorial population groups; critical organs and systems, probable types of health problems and marker indices typical for established impact (exposure).

Thus, the stage of risk assessment is systemically important determining, on the one hand, the factor hazard level, and on the other hand - allowing selecting the cohort of risk,

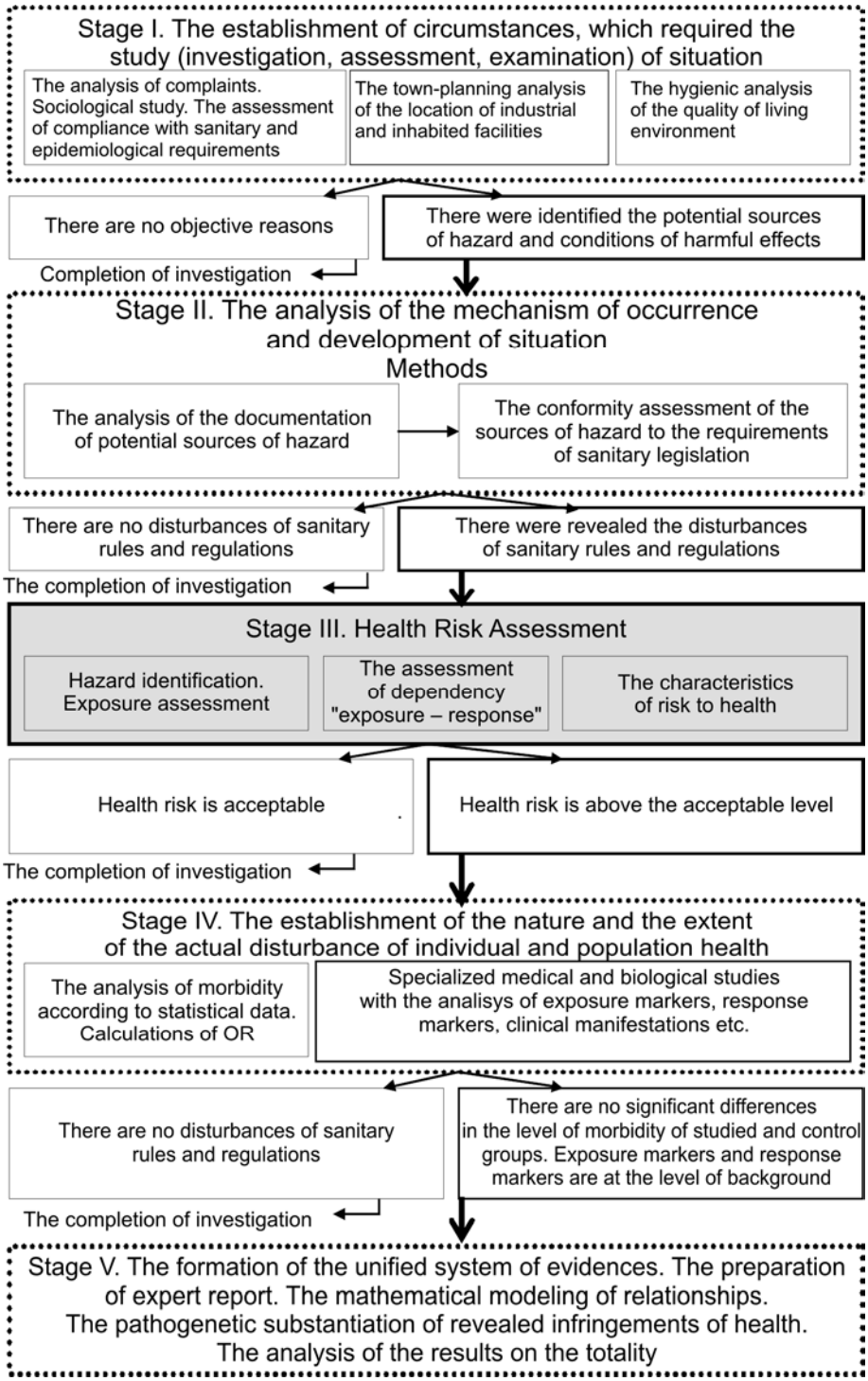

Fig. 7.1. General algorithm to form the evidence base of harm to health of population by the negative impact of living environment factors

predicting the probable negative effects on the part of health of the exposed population (group) and forming the programs of in-depth inspections that acquire the clear directionality and specificity by the result of risk assessment.

The confirmation or negation of the fact (s) of risk implementation – the occurrence of the predicted types of health deterioration adequate to the exposure – is carried out on the next stage "The identification of a nature and a degree of the actual disorder of individual and population health" in the course of medical examinations, followed by laboratory, functional, and instrumental studies.

Health assessment and the diagnostics of disorders is performed by the physician having an idea of the type and intensity of exposure of the patient, and of the risk levels of development of critical organs and systems disruption, as well as possessing data on the group and individual levels of exposure markers and response markers set in the course of the study.

The evidences of harm to health associated with the harmful influence of factors are the following:

– the registration of the biological evidences of human contact with dangerous factor (exposure markers);

– the establishment of clinical signs and the data of laboratory, instrumental and functional tests on the basis of systemic analysis in the group of exposed persons with identical diagnoses and having reliable biologically justified connections with exposure (effect markers);

– the registration of functional disorders of critical organs and systems, for which the risk was assessed as unacceptable. Thus, the frequency of these disorders significantly exceeds those in the comparison group;

– scientific data on the similar diseases occurring in the conditions of similar exposure.

The aspects of exposure and response markers selection are examined more detailed in Section 7.3.

The important elements of the existence evidence of harm associated with the harmful effects of the factor is the existence of unidirectional repeated changes of indicators at the surveyed exposed persons reflecting the impact of chemical substance; the identification of significant correlation between the indicator and the exposure level or the exposure marker; the presence of the homogeneous (similar) complexes of health indicators disorders at several persons in the group, with the assumption that there are scientific data on the biological plausibility of indicator or the complex of indicators at the given level of exposure.

The collection and analysis of data on individual and mean group lifestyle differences as well as production, genetic and other factors is carried out with a view to prove that other factors that could cause the similar health disorders are known and eliminated. This element of harm assessment and its relation to the factors of living environment is extremely important, and its implementation should be carried out especially carefully.

The stage of the system processing of total information on the types of effects, exposure criteria and the available models of the description of the cause-and-effect relationships of "exposure – effect" is carried out with a view of the conjugate processing of the whole information complex that completes with the formation of a single evidence base of presence or absence of harm to health caused by exposure of living environment factors. All elements of evidence base range into the system, and the availability of reliable connections between the individual elements is analyzed using mathematical operations with logical variables.

The establishment of harm as a consequence of the negative impact of the factors of living environment at the level of a specific person requires, as a rule, the presence of proven population dependencies. The absence of the last significantly reduces the arbitration value of personal results. Thus, even at the establishment of the high level of contaminant in the patient's body (blood, urine, hair), conclusions on the presence of significant correlation between the exposure level and the exposure marker, as well as, for example, between exposure markers and deviations of the number of tests from physiological norms can be done only when there is data at the level of the whole group. Signs and criteria for the formation of evidence base at the level of individual and the groups of individuals are shown in Table 7.1.

Table 7.1

The signs of harm to health in connection with the negative impact of living environment factors

Sign	I. Criterion (group level)	II. Criterion (individual level)
1. The presence of negative impact source	1. There is a source of harmful impact	1. There is a source of harmful impact
2. The accommodation (residence) of person under the conditions of exposure	2. The group of inspected persons was under the conditions of known exposure* to chemical substance(s)	2. Patient was under the conditions of known exposure* to chemical substance(s)
3. Risk level for the health of individual or the group of individuals	3. Risk level for health is evaluated as unacceptable	3. Risk level for health is evaluated as unacceptable
4. The content of chemical substance in the organism	4.1. Scientific data confirmed the possibility of the presence of substance(s) from the living environment or sustainable metabolite in biological media under the conditions of the known exposure (WHO and EPA data, normative and methodological documents of the Russian Federation)	4.1. Scientific data confirmed the possibility of the presence of substance(s) from the living environment or sustainable metabolite in biological media under the conditions of the known exposure (WHO and EPA data, normative and methodological documents of the Russian Federation)
	4.2. The mean group indicator *(M ± m)* of the content of chemical substance in the biosubstrate of exposure marker is reasonably higher than the comparison value *(Mk ± mk) (p≤0.05)*	4.2. The level of chemical substance (exposure marker) in the organism of patient is higher than the upper permissible limit of comparison vakue (*Mi> M ± m*)
	4.3. For the studied group of exposed persons, the content of chemical substances in biosubstrate is in reliable correlation with the exposure level (*p*≤0.05)	4.3. There are data on the existence of the significant relations of the content of chemical substances in biosubstrate with the exposure level at the group level.
5. The level of laboratory parameter, functional tests (assays), and the results of instrumental studies	5.1. A number of the patients of group have unidirectional changes in laboratory parameters, reflecting the impact of chemical substance *(nP>Pk ± pk; n>5%)*	5.1. The level of laboratory parameter adequate for chemical load is above (below) the upper (lower) limit of physiological norm *(P>Pk ± pk)*
	5.2. For the studied group of exposed persons, the parameter is in reliable correlation with the level of exposure or exposure marker *(p≤0.05)*	5.2. There are data on the existence of the reliable biologically justified dependence of parameter change on the exposure level or exposure marker at the group level
	5.3. Several patients in the group have homogeneous (similar) complexes of laboratory parameters violations indicating the presence of functional disorders *(n>5%)*	5.3. The complex of laboratory parameters having deviations from physiological norm indicates the presence of functional disturbance of a certain organ (system) in the patient
	5.4. Sample indicator that is average for a group of patients and adequately reflecting the effect of chemical substance, is above (below) the physiological norm *(p≤0.05)*	5.4. The level of functional test, biologically adequately reflecting the effect of chemical substance, is above (below) the physiological norm

The end of Table 7.1

Sign	I. Criterion (group level)	II. Criterion (individual level)
	5.5. Several patients in the group have unidirectional changes of parameter to the level above (below) the physiological norm *(nP>Pk ± pk; n>5%)*	5.5. There are data on existence of correlation between functional impairment and exposure (exposure marker) at the group level
	5.6. There are scientific data on the biological plausibility (pathogenetic relation) of parameter or the complex of parameters at the given level of exposure (exposure marker) (WHO and EPA data, normative and methodological documents of the Russian Federation)	5.6. There are scientific data on biological plausibility (pathogenetic relation) of a parameter or a complex of parameters at the given level of exposure (exposure marker) (WHO and EPA data, normative and methodological documents of the Russian Federation)
6. "Dose – effect" Relation	6.1. The parameter (the system of parameters) is in reliable correlation with the exposure level or exposure marker *(p≤0.05)* in the studied group	6.1. Patient is included into the group in which the parameter (the system of parameters) is in reliable correlation with the level of exposure or the exposure marker ($p \leq 0.05$); there are scientific data on existence of stable reliable "exposure – response marker" relations
	6.2. There are data on biological plausibility (pathogenetic relation) of parameter or the complex of parameters at the given level of exposure (exposure marker) (WHO and EPA data, normative and methodological documents of the Russian Federation)	6.2. There are data on biological plausibility (pathogenetic relation) of parameter or the complex of parameters at the given level of exposure (exposure marker) (WHO and EPA data, normative and methodological documents of the Russian Federation)
7. Disease	7.1. Several patients in the group have the same diagnosis associated with the system of laboratory parameters and functional tests having reliable biologically justified connections with the exposure (the exposure markers) *(n> 5%)* in addition to the clinical signs	7.1. Patient have diagnosis associated with the system of laboratory parameters, functional tests and clinical parameters having reliable biologically justified connections with the exposure (the exposure markers) in addition to the clinical signs
	7.2. The frequency of the revealed (par. 6.1) diagnosis significantly exceeds that in the comparison group ($p \leq 0.05$)	7.2. The revealed diagnosis refers to the critical organs and systems in the respect of which the risk was assessed as unacceptable. There are scientific data on the similar diseases occurring in the conditions of similar exposure
	7.3. Diagnosis met with greater frequency than in the comparison group, refers to critical organs and systems in the respect of which the risk was assessed as unacceptable. There are scientific data on the similar diseases occurring in the conditions of similar exposure.	
8. The presence of other negative influencing factors	8. Other factors that could cause the similar health disorders are known and eliminated	8. Other factors that could cause the similar health disorders are known and eliminated

Each stage of the formation of the evidence base of harm to health has its own methodological features that need to be considered to obtain correct results. At that, the completeness and reliability of evidence base should be sufficient as in the case of determining the existence of harm to health associated with factors of living environment, and in the case of negation of such harm.

The "case control" method is preferred at the stage of medical and biologic researches for identification and assessment of harm to health. Sample size for study at the population level is established according to the principle of sufficiency to ensure the statistical significance of the study and is calculated based on the necessary condition of existence of dependence between the compared signs, namely the reliability of the determination coefficient with the specified significance level:

$$N \geq 2 + t_{\alpha}^{2}(\frac{1}{R^{2}} - 1), \qquad 7.1$$

where N – sample size for the research;

t – Student's coefficient;

R^2 – determination coefficient;

α – significance level, α=0.05.

At the significance level αequal to 0.05, the quantile of Student's distribution tends to the value of 1.96.

Setting the specific value of the determination coefficient, the minimum sample size allowing evaluating the relationship between the analyzed indicators is determined using the ration (7.1) The total sample size should include not less than 40 observations for the assessment of dependencies of low degree of manifestation (R^2~0.05).

The selection of population groups for medical and biologic researches is carried out considering the expected adverse effects the data on which are received at the stage of risk assessment. The large number of effects on the impact (susceptibility, the condition of immunity, etc.) depends on the age and number of social and economic conditions. This defines the requirements for the conducting of studies which lies in the fact that the group should be homogeneous age category according to gradations accepted by the practice with the inclusion of persons of both sexes (for example, 0–4 years, 5–9 years, 10–14 years; 15–19 years; 20–24 years; 25–29 years; 30–34 years; 35–39 years; 40–44 years; 45–49 years; 50–54 years; 55–59 years; 60–64, etc.). The surveyed persons should have no acute infectious diseases at least for 2 weeks prior to beginning of the study, and the chronic diseases should be in decompensation stage (4th group of health); a group should be homogeneous in social, welfare and economic living conditions; lifestyle factors, the factors of production and other activities which may significantly affect the results of medical and biologic researches, must be studied and taken into account when processing the results.

The correct choice of exposure markers and response markers, which are the link between the level of risk factors and health disorders is extremely important for the formation of evidence base.

7.3. Exposure markers and the markers of the response to the impact under the conditions of unacceptable health risks and the evaluation of their relationship

Health risk assessment allows orienting the researcher on the priority danger factors and the probable negative responses on the part of health. However, the parameter confirming the measure of contact of agent and the person is required from the position of harm conclusiveness.

According to the WHO definition, the biological marker is an indicator or system of indicators characterizing the interaction of organism with the potentially dangerous agents of

different nature[1]. Biological marker detected and measured in the laboratory can provide the conclusion about the direct actual effect and thus it is significantly reduce the uncertainty in estimates of health risks [Cerna M., Spevackova V. et al., 1997; Brooks A., 2001; Berman T., 2012 et al.].

The universally recognized evidence of human contact with chemical risk factor is the identification in various biosubstrates of the organism (tissues, excreta, biological liquids, and exhaled air, etc.) of chemical impurities which are present in the living environment or their resistant metabolites. Exposure markers are the immutable exogenous impurities or their proven metabolites which are widely used when proving the impact within several decades [Christensen H.M., 1995; WHO, 2000]

Currently, the methodical and hardware base of Russian scientific and practical organization allows identifying up to several hundreds of inorganic and organic compounds in the blood, urine, breast milk, bile, hair, teeth, etc. The most modern methods of combined gas chromatography mass-spectrometry, atomic absorption spectrometry, including those in the mode of flame atomization as well as gas and high performance liquid chromatography allow qualitatively and quantitatively determining the chemical impurities in very small concentrations. This offers an opportunity to confirm the fact of human contact with chemical agent, even in the conditions of low and/or short-term exposures [Dmitriev M.T., 1998; Revich B.A., 2004; Skalniy A.V., 2003; Onishchenko G.G., Zaitseva N.V., 2011].

In this case, the diagnostic informativeness of different biological media with regard to chemical components is not identical. This fact must be considered when choosing the object of research (the example of the informativeness of the determination of a number of metals in the blood, urine and hair are given in Table 7.2). In general, evidentiary importance of the method is very high. Impurity which is correctly selected for the identification can be considered as exposure marker clearly indicating the presence of contact of a person and the influencing factor. This provision is recognized by scientists of the whole world. Ken Sexton et al. (2004) called the measurement of chemical impurities in biological media as "gold standard"

Table 7.2

The informativeness of identification of a number of chemical compounds in the blood, urine, and hair [Skalniy A.V., 2003]

Element	Blood	Urine	Hair
As	+	+	+
Al	–	–	+
Ba	–	–	+
Bi	+	–	–
B	–	–	+
Cd	+	+	+
Ca	+	+	+
Cr	+	+	–
Co	+	–	–
Cu	+	+	+
Fe	–	–	+
Pb	+	–	+
Mg	–	–	+
Hg	+	+	–
P	–	–	+
Se	+	–	–
Ag	+	–	–
Sr	–	–	+
Tl	+	–	–
Zn	+	–	+

[1] http://www.tsalliance.org/documents/UnlockBiomarkersDescription.pdf.

of exposure assessment in conditions of living environment pollution. As a consequence, the methods of qualitative and quantitative identification of chemical impurities in biological media and criteria of their evaluation are developing and introducing into the practice quite intensively [Barr D.B., 2008, Elflein L. et al., 2003, Orlov O.I., 2010, etc.].

It should be noted that the establishment of the criteria of comparison is extremely important in identification of exposure markers. The average statistical levels justified by the results of large-scale studies can be used as such criteria [Clinical Guide, 2003].

However, in some cases, especially for some regions where the levels of chemical impurities in biological environments are different from the average statistical they are determined by the feature of geochemical composition of soils, natural (and, accordingly, drinking) waters as well as the number of genetic characteristics of population and it is appropriate to use the regional ("background") values as criteria for levels of exposure markers.

The task of the determination of background levels is put and solved on the basis of several assumptions:

– the calculation of background levels is performed according to the data of measurements of toxic substances in biological media of persons not exposed to contamination, i.e. living on the relatively unpolluted areas away from the large emission sources, main highways, etc. Groups of persons gathered for the study of biological media from such regions are defined as the control groups (comparison group);

– the concentration of substance (value of indicator) in biological substrate of the human is a random variable. It is assumed that the distribution of this random variable corresponds to the normal law of distribution;

– the value of average indicator in comparison group is also a random variable. Thus, the law of distribution of such random variable is generally unknown.

The directional study (complex of chemical and analytical procedures) and the check of results from the perspective of assessment of nature of indicator's distribution is carried out for the calculation of value of background regional level. The "drop out" values are allocated from all the sample if necessary. The order of the formation of correct samples for calculation of background concentration is described in project by S.Y. Balashova and D.A. Kirjanova (2010).

When the number of values satisfies all the tests conducted, the calculation of directly regional background levels is performed taking into account the following conditions:

- the background levels of specific substance in vivo is defined by some interval having the lower and the upper bound;
- the lower bound of the interval can't be less than zero.

Background interval is calculated on the basis of interval estimations of mathematical expectation defined by values of indicator in the control group with significance level equal to α0.05. As the indicator values are normally distributed according to the axiom, we can use the following statistical relation (7.2):

$$\frac{M - M^{\Phi}}{S}\sqrt{n} \to t_{n-1}, \tag{7.2}$$

which is distributed according to Student's distribution law with n–1 degrees of freedom. In this case, the lower and the upper confidence intervals for mathematical expectation (M) are respectively equal to (7.3–7.4)

$$M_{\text{н}}^{\Phi} = M - t_{n-1,1-\alpha/2} S / \sqrt{n}, \tag{7.3}$$

$$M_{\text{в}}^{\Phi} = M + t_{n-1,1-\alpha/2} S / \sqrt{n}, \tag{7.4}$$

where $t_{n-1,1-\alpha/2}$ – the quantile of Student's distribution with n–1 the degrees of freedom and significance level α.

In the case, when the lower confidence limit is less than zero, it is necessary to accept: $M_{\text{н}}^{\Phi} = 0$.

The value of indicator *M* is considered as the point estimation of background value and can be used as the criterion of comparison.

The examples of the background regional levels of the content of metals in biological media that are used as comparison criteria in the Perm Territory, are shown in Table 7.3.

Table 7.3

The background regional levels of the content of some metals in biological mediums of child population of the Perm Territory

Chemical contaminant	Concentration, mg/dm^3	
	in the blood	in the urine
Cadmium	0.00±0.00	0.018537±0.0029
Cobalt	0.52±0.05654	0.101±0.0096
Magnesium	33.25±2.8656	35.75±15.082
Manganese	0.0194±0.0015	0.0163±0.003
Copper	1.059±0.0332	0.038±0.0027
Arsenic	0.00±0.00	Not established
Nickel	0.2299±0.0200	0.1604±0.0127
Plumbum	0.1326±0.0072	0.1098±0.0143
Strontium	0.00±0.00	Not established
Chrome	0.0163±0.0016	0.01302±0.0017
Zinc	4.5208±0.1337	0.4415±0.0378

It should be noted that in some cases the criterial values of indicators for different regions are close. So, according to the data of Ufa researchers listed in methodological guidelines 2.1.10.2809-10 "Usage of biological markers for assessment of contamination of living environment by metals in the system of social-hygienic monitoring" (2010) the following values were accepted as the background levels of chemical elements content in the whole blood of residents of some regions of Republic of Bashkortostan:

– for copper – from 1.0±0.1 mg/dm^3;

– for manganese – from 0.022±0.003 mg/dm^3;

– for zinc – from 4.5±0,4 mg/dm^3;

The background levels can be significantly different for some elements. Thus, in Bashkortostan the background content of lead amounts to 0.078±0.0076 mg/dm^3, that is less than the lower confidence bound of background value established for the Perm territory. With regard to cadmium, on the contrary, the background levels in Bashkortostan are significantly higher than in the Kama region (0.036±0.006 and 0.000±0.000 mg/dm^3 respectively).

The represented data evidences the extremely important role of the comparison criteria in the formation of evidence base of harm to health associated with environmental factors.

Table 7.4 shows the background regional levels for a number of organic impurities contaminating the living environment of the population of Perm Territory.

Table 7.4

The background regional levels of the content of organic impurities in biological mediums of child population of Perm Territory

Chemical contaminant	Concentration, mg/dm^3	
	in the blood	in the urine
Acetaldehyde	0.0778±0.0086	0.068±0.008
Acetone	0.45±0.148	0.056 ±0.010
Benzpyrene	0.00±0.00	0.00±0.00
Benzene	0.00±0.00	0.00±0.00
Butyl alcohol *	0.00±0.00	0.00±0.00
Dibromochloromethane	0.00±0.00	0.00±0.00

The end of Table 7.4

Chemical contaminant	Concentration, mg/dm^3	
	in the blood	in the urine
Dichlorbrommetan	0.00±0.00	0.00±0.00
Isobutyl alcohol	0.00±0.00	0.00±0.00
Isobutyraldehyde	0.00±0.00	0.08768±0.0433
Isopropyl alcohol	0.61±0.07	1.09±0.16
Butyl aldehyde	0.00±0.00	0.00±0.00
Methyl alcohol	0.369±0.117	1.25±0.29
M-cresol	0.00±0.00	0.00±0.00
O-cresol	0.00±0.00	0.00±0.00
O-xylene	0.00±0.00	0.00±0.00
P-, m-xylene	0.00±0.00	0.00±0.00
Propyl alcohol	0.00±0.00	0.00±0.00
Toluene	0.00±0.00	0.00±0.00
Phenol	0.01±0.001	0.00±0.00
Formaldehyde	0.005±0.001	0.004±0.0009
Chlorobenzene	0.00±0.00	0.00±0.00
Chloroform	0.00±0.00	0.00±0.00
Carbon tetrachloride	0.00086±0.0002	0.00007±0.00001
Ethylbenzene	0.00±0.00	0.00±0.00
Ethyl alcohol	0.606±0.103	0.00±0.00

The identification and quantitative assessment of exposure markers is the extremely important element of evidence base, but the exposure marker reflects the contact of organism with hazardous agent, but not the consequences of this contact. It makes relevant the identification of response (effect) markers – the indicators which quantitatively characterize the biochemical, physiological, behavioral, or other modification in vivo, according to the degree of severity of which the actual or potential health problems are determined.

The significant amount of data on the proven effects, at the influence of living environment factors, on critical organs and systems, exposed by chemical substances presented in external environment and on mathematical models, describing the relationship of the level of living environment factors and health problems is accumulated for today. Harmful effects of chemical factors that are reflected in databases of Agency for Toxic Substances and Disease Registry (ATSDR), National Center for Biotechnological Information (NCBI), Integrated system of information on risks (IRIS), World Health Organization (WHO), World Trade Organization (WTO) as well as the Commission of Codex Alimentarius are most fully described. Domestic database is formed within the framework of Russian register of potentially hazardous chemical and biological substances.

Data on a number of chemical substances and laboratory parameters, biologically plausibly reflecting the specific and non-specific effects of these substances on the organism, and which are received at the analysis of international scientific materials tested and refined in conditions of epidemiological studies on the territory of the Russian Federation, are presented in Table 7.5.

The deviations from the norms of laboratory parameters (biochemical, immunological, immunogenetic, etc.) are most commonly used as the response markers. In the recent years, the scientific studies on justification of biochemical, cytogenetic, immunological, and molecular and genetic criteria for assessment of impact of technogenic chemical factors are carrying out very widely [Zhurkov V.S., Revazova Y.A et al., 2000].

The use of specific effect markers of indicators which directly indicate on biological effect at the influence of various harmful factors is optimal for the formation of evidence base. Thus, specific markers of specific exposure are the certain types of immunoglobulins: IgE to nickel, manganese, formaldehyde, specific IgG to Benzpyrene, vanadium, strontium, phenol, lead, chloroform [Guidelines, 2009], specific marker is the increase of the content of coproporphyrin in the urine at increased content of lead in vivo, increasing of level of carboxyhemoglobin in the blood at increased content of carbon dioxide in inspired air etc.

Table 7.5

Laboratory effect markers, for which the significant connections with markers of chemical exposure and the specific types of diseases are established

Chemical factor	The route of exposure	Critical bodily organs and systems	The concentration of exposure marker		Laboratory parameter - the effect marker	Disease according to ICD-10
			in living environment	in biosubstrates		
1	2	3	4	5	6	7
Chrome	Inhalative	Respiratory organs	0.00001–0.0001 mg/m^3 (0.1–1 RFC_{cr}) Acceptable risk *(HQ = 0.1–1.0)*	0.0007–0.018 mg/dm^3* (blood) (0.1–0.6 from the reference level in the blood –0.0007–0.028 mg / dm^3*)		
			0.00011–0.00026 mg/m^3 (0.07–0.2 TLV_{ce} (Threshold Level Value continuous exposure) Unacceptable risk *(HQ = 1.1–3)*	0.0181–0.032 mg/dm^3* (blood) (0.61–1.2 from the reference level in the blood)	• IgE general, IgE specific to chrome in blood serum. • Eosinophilic–lymphocyte index in the blood	X. The diseases of respiratory system, including: J30.4 – allergic rhinitis, unspecified; J31 – chronic rhinitis, nasopharyngitis and pharyngitis; J35 – chronic diseases of tonsils and adenoids, including: J35.1 – hypertrophy of tonsils, J35.2 – hypertrophy of adenoids; J37.1 – chronic laryngotracheitis; J38.9 – disease of the upper respiratory tract, unspecified; J44.8 – other specified chronic obstructive pulmonary disease; J45.0 – bronchial asthma with the predominance of allergic component
			0.000261–0.00087 mg/m^3 (0.21–0.6 TLV_{ce} (Threshold Level Value continuous exposure)) Unacceptable risk (*HQ* = 3.1–9.0)	0.0321–0.052 mg/dm^3* (blood) (1.21–2.0 from the reference level in the blood)		
			More than 0.00087 mg/m^3 (more than 0.6 TLV_{ce} (Threshold Level Value continuous exposure)) Unacceptable risk (*HQ*>9)	More than 0.052 mg/dm^3* (blood) (more than 2 from the reference level in the blood)	• IgE general, IgE specific to chrome in blood serum. • Eosinophilic-lymphocyte index, white blood cell differential, ESR in the blood	

Table 7.5 Continued

1	2	3	4	5	6	7
Manganese	Inhalative	Respiratory organs	0.000004–0.00005 mg/m^3 (0.1–1.0 RfC_{cr}) Acceptable risk *(HQ = 0.1–1.0)*	0.011–0.015 mg/dm^3* (blood) (1.0–1.3 from the reference level in the blood – 0,0109±0,0006 mg / dm^3*)	• Eosinophils (absolute number) in the blood.. • IgE general, IgE specific to manganese in blood serum. • Eosinophilic-lymphocyte index	X. The diseases of respiratory system, including: J30.4 – allergic rhinitis, unspecified; J31 – chronic rhinitis, nasopharyngitis and pharyngitis; J35 – chronic diseases of tonsils and adenoids, including: J37.1 – chronic laryngotracheitis; J38.9 – disease of the upper respiratory tract, unspecified; J44.8 – other specified chronic obstructive pulmonary disease; J45.0 – bronchial asthma with predominance of allergic component
			0.000055–0.0002 mg/m^3, Unacceptable risk (*HQ*=1.1–4.0)	0.0151–0.030 mg/dm^3* (blood) (1.31–2.7 from the reference level in the blood)		
			0.00021–0.0005 mg/m^3 (0.21–0.5 TLV_{ce} (Threshold Level Value continuous exposure))	0.030–0.045 mg/dm^3* (blood) (2.71–4.0 from the reference level in the blood)		
			More than 0.0005 mg/m^3, Unacceptable risk (*HQ*>10)	More than 0.045 mg/dm^3* (blood) (in the blood) (more than 4 from the reference level in the blood)		
		Endocrine system		More than 9.37±0.88 µg in 100 mg ** (blood)	• Total protein, albumin in the blood serum. • Glucose in the blood serum. • Cholesterol, HDL and LDL lipoproteins, triglycerides in the blood serum. • Dehydroepiandrosterone in the blood serum, 17-KS in urine. • TSH, $T4_{free}$ in the blood serum. • Chondrotropic hormone in the blood serum.	IV. The diseases of the endocrine system, including: E46.0 – protein-energy malnutrition; E67.8 – excess of body weight; E34.3 – dwarfism; E34.4 – tallness; E01 – disorders of thyroid gland related to the iodine deficiency, E02 – subclinical hypothyroidism affected by iodine deficiency; E03 – other forms of hypothyroidism; E04.9 – nontoxic goiter, unspecified

1	2	3	4	5	6	7
Manganese	Oral	CNS		0.028–0.03 mg% ** (brain) 1–16 mg% ** (blood)	• Dopamine, norepine-phrine and acetylcholine in the blood serum. • GABA, glutamate in the blood serum, potassium / sodium ratio	VI. The diseases of the nervous system, including: R45.0 – asthenoneurotic syndrome; R53 – malaise and fatigue; G62.2 – polyneuropathy affected by other toxic substances; G62.9 –polyneuropathy, unspecified G93.8 – neurosis-like syndrome; G92 – toxic encephalopathy
Tetra-chloromethane	Inhalative	CNS	6 mg/m^3 (in atmospheric air)		• Cortisol and adrenaline in the blood serum	VI. The diseases of the nervous system, including: R45.0 – asthenoneurotic syndrome; R53 – malaise and fatigue; G62.2 – polyneuropathy affected by other toxic substances; G62.9 –polyneuropathy, unspecified G92 – toxic encephalopathy G93.8 – neurosis-like syndrome;
Ethyl benzene	Inhalative	Blood system and hematopoietic system	30–60 mg/m^3, Exposure for 7 years		• Hemoglobin, erythrocytes, hematocrit, and reticulocytes in the blood. • Average content of hemo-globin and mean cor-puscular volume. • Ferrum, total and incom-plete iron binding potency of blood serum • Ferritin and transferrin in the blood serum. • Coproporphyrin and delta-aminolevulinic acid in the urine	III. The diseases of blood and blood-forming organs, including: D50.8 – other iron-deficiency anemia; D50.9 – other iron-deficiency anemia, unspecified; D61.2 – aplastic anemia caused by other external agents; D64.8 – other specified anemia; D64.9 – anemia, unspecified

The end of Table 7.5

1	2	3	4	5	6	7
Styrene	Oral	Liver		More than 0.55 mg/l ** (venous blood)	• Albumin, α-, β-, γ-globulins and C-reactive protein in the blood serum. • Cholesterol, HDL and LDL lipoproteins and triglycerides in the blood serum. • GPT, GOT, LDH-3, γ-glutamyl transferase and alkaline phosphatase in the blood serum. • Malondialdehyde, hydroperoxide lipid and alfafetoprotein in the blood serum. • Total AOA, superoxidedismutase and glutathione-peroxidase	XI. The diseases of digestive system, including: K71 – toxic liver damage with cholestasis; K72 – hepatic impairment; K73 – chronic hepatitis; K74 – fibrosis and cirrhosis of liver; K75 – other inflammatory diseases of liver; K76 – other diseases of liver

Notes: * – children population; ** – adult population.

Response markers on the impact of organic compounds and heavy metals providing modified and adjuvant effect on pathogenetic mechanisms of formation of infringements of biochemical, immunological, neurohormonal, apoptotic and mediator regulation of homeostasis are considered. Thus, it was established that immunogenetic markers of negative effect at the exposure of heavy metals (chromium and manganese) in the presence of phenol and formaldehyde are the following: indicators of apoptotic regulation (CD25 +, CD95 +, CD4 + CD25 + 127-, p53, TNFRI, bcl-2, Annexin V-FITC + 7AAD-, Annexin V-FITC + 7AAD +), sensitization effect markers: T-lymphocytes (CD4+, CD16+/56+, CD25+, Treg); cytokines IL1-β, IL-6, IL-8, IFN-γ, α-TNF; common IgE, IgE specific to formaldehyde, chromium, manganese; leukotrienes LTC4/D4/E4.

All more in-depth studies allow detecting the genetic indicators of the assessment of immune disturbances and modified metabolism at the exposure of technogenic chemical factors of living environment that are the genes of enzymes of system of xenobiotics' detoxification; genes participating in pathogenesis of technogenic disturbances in target organs; genes of susceptibility to cancer-proliferative states; genes of condition of components of immune response: CYP1A1, MTHFR, APO-E, TNF, MMP9, MMP12, CPOX, VEGF, NO-synthase, p53, BRCA1, BRCA2, ESR1, SULT1A1. [Zaitseva N.V., Dolgikh O.V. et al., 2010–2014]. Approved markers characterizing the morphological and functional condition of organism (somatometry, physiometry, cardiovascular, respiratory and nervous system).

Methodical approaches are developed and the data on the markers of the impact of physical factors are accumulated.

Certainly, the nonspecific effect markers indicating on the overall response of organism on the impact of various harmful factors are less informative, but in the proof system they may and must be used in full. Thus, for example, the increased content of malonic dialdehyde in the blood plasma reflects the development of oxidative stress as at exposure of a number of heavy metals, and at exposure of aromatic hydrocarbons. However, the marker may indicate the negative impact of the specific substance in conjunction with the study of contamination of biological media.

An obligatory element of inclusion of response marker in the evidence base of harm to health is the biological plausibility of responses established in several large-scale studies, the inclusion of those responses in toxicological profiles of chemical substances and recognition of databases on the global level, etc.

The correct choice of exposure markers and effect markers significantly improves the quality of the evidence base of harm to health.

The simulation of dependencies in the "living environment – the health of population" system is the process of the identification of the parameters of mathematical models reflecting the influence of chemical factors of living environment on indicators of health status on the basis of selective epidemiological studies.

The procedure of simulation in the "living environment - health of population" system is held in two stages, each of which assumes the construction of appropriate models.

The dependence between the exposure of chemical factors of living environment and the content of substances in the biological media of organism (exposure marker) is determined on the first stage. The models of dependencies between the content of chemical substances in biological medium (exposure marker) and the deviation of clinical, clinical and laboratory or functional parameters (response markers) from physiological norm are built on the second stage.

The concentration of substances in the objects of environment or the dose at single-environmental or multi-environmental routes of exposure could be used as the exposure parameter to build the model of dependence between chemical factors of living environment and the content of substances in the biological media of organism (exposure marker).

The use of linear dependencies is permissible under the conditions of low-dose (or low level) of chronic exposure of contaminants in concentrations in limits of 0.1–0.5 TLVce (Threshold Level Value continuous exposure). Mathematical model describing the analyzed dependence have the form of linear equation of the next type

$$x = b_1 D + b_0, \tag{7.5}$$

where D – is the average daily dose, averaged on the chronic exposure of chemical substance mg/ (kg per day);

x – is the concentration of chemical substance in biological media, mg/dm^3;

b_0 and b_1 – are the parameters of model, characterizing the initial level of concentration of substance in biological media and the rate of absorption.

In the case of the concentration of contaminants in the objects of environment more than 0.5 MAC the mathematical model is defined by *S*-shaped curve and is described by equation

$$C = \frac{k}{1 + e^{b_0 + b_1 D}}, \tag{7.6}$$

where C – is the concentration of substance in biological medium;

D – is the daily dose taking into account the routes of admission of substance;

k, b_0 and b_1 – are the parameters of the model.

The feature of the research of dependences between the dose and the content of substances in the body (biological media) is the fact that the level of concentration in biological medium of the majority of substances has the values of the same magnitude with the sensitivity of techniques according to their determination. In this regard, the approach, based on analysis of data at significant dispersion of initial values is used to build the model of "dose of externally-environmental exposure – concentration of substance in the blood" dependence. The more detailed description of the method to determine the dependence parameters of organs and system dysfunction risk caused by the exposure of the factors of living environment is described in Chapter 2 (Section 2.2).

Cause-and effect relationships in "exposure – exposure marker – effect marker" system are considered proved if:

1) the presence of the adequate exposures of contaminants in the organism in concentrations exceeding the specified levels of comparison (background, physiological, reference, etc.) is revealed in persons living in conditions of exposure. Besides, chemical substances in biological media of persons living outside the exposure are absent (set at the level or below of thresholds of determination methods) or are within the normal limits (reference, background and other levels);

2) it was revealed that the examined contingent have the responses in the form of negative deviations of laboratory, functional, clinical, epidemiological and other indicators, as well as adequate chemical contaminations;

c) significant (p<0.05) relationships are established between the exposure level and the level of the content of chemical substances *in vivo*;

d) the presence of significant connections between the content of chemical substances in vivo and the response of organism (laboratory, functional, clinical, epidemiological, and etc.) is established;

d) all revealed communications have the pathogenetic basis described in scientific literature.

The obtained data are an integral part of the overall evidence base of harm to health.

7.4. Medical examinations and functional studies in the harm proof system. The formation of general conclusion about the harm to health associated with hazard factor

Physical examinations are organized in order to identify the clinical manifestations of health disorders probably associated with the risk factors in the investigated territory (in the study group), with the level of chemical substances in biological media – exposure markers and with the level of the deviation of laboratory parameters from physiological standards.

The execution of functional studies which are proved by the data of literature on the potential adverse effects of functional disorders at the exposure of chemical substances is expedient at the conduction of inspections.

When carrying out inspections, the doctors register the presence (absence) of those disorders which can be formed at the marked level of exposure and which can be pathogenetically associated with the last. The disorders of critical organs and systems in the respect of which the risk was defined as unacceptable should be considered.

The results of medical examinations are:

– diagnoses for each patient (main and concomitant) are established taking into account the complex of laboratory parameters and the results of functional studies;

– the results of objective examination described for each patient;

– the results of functional studies described for each patient;

The statistical processing of the data of physical examinations and functional investigations is performed taking into account the scale of the measurement of indicators and the distribution pattern of quantitative indicators. For this purpose the test on the normalicy of distribution with the use of Pearson's test is performed.

The following indicators are calculated in the course of statistical data processing:

– the absolute and relative frequencies of the values of nominal indicators (including revealed diagnoses and parameters of objective status) in the groups;

– the parameters of the distribution of quantitative indicators – the mean, standard dispersion, the error of mean for variables distributed according to the normal law; median value, first and third quartiles for variables distributed according to the law, other than normal;

– the frequency of the deviation of indicators from physiological norm;

– the maximum value of indicator in the group;

– the results of the assessment of between-group differences using Student's criteria for normally distributed variables and the Mann-Whitney test for variables with distribution other than normal at the significance level αequal to 0.95.

The evidences of harm to health are:

– the establishment of clinical signs and the data of laboratory, instrumental and functional tests on the basis of systemic analysis in the group of exposed persons with identical diagnoses and having reliable biologically justified connections with exposure (exposure markers);

– the registration of the functional disorders of critical organs and systems, for which the risk was assessed as unacceptable. Thus, the frequency of these disorders significantly exceeds that in the comparison group;

– scientific data on the similar diseases occurring in the conditions of similar exposure.

The data of physical examinations are the final "instrumental" stage of the collection of evidence base. Upon its completion the whole system of proof which is shown by logic diagram and presented in Fig. 7.2. is analyzed and built on the basis of the analysis of links between the separate elements in the form of logical variables.

The mathematical equivalent of logical scheme is represented by equation

$$U = \sum_{i=1}^{N_{\Phi}} U_i^{1-2} \left(\sum_{j=1}^{N_{заб}} U_{ij}^{2-6} + U_i^{2-3} \sum_{j=1}^{N_{заб}} U_{ij}^{3-6} + \left(\sum_{k=1}^{N_{кп}} U_{ik}^{2-5} + U_i^{2-4} \sum_{k=1}^{N_{кп}} U_{ik}^{4-5} \right) \sum_{j=1}^{N_{заб}} U_{kj}^{5-6} \right), \quad (7.7)$$

where U_i^{1-2} = "The existence of source(s) of impact, forming the exposure of *i*-th factor is proved" $i = 1..N_F$, N_F – the number of analyzed factors. Evidences are: significant ground level concentrations typical for a source of contaminants in the atmospheric air in the places of permanent residence, which are obtained on the results of calculations of dissipation according to standardized procedures and confirmed by the results of instrumental studies; above permitted standard values of physical factors from the known sources of exposure; increased concentrations of chemical contaminants in potable water, etc.;

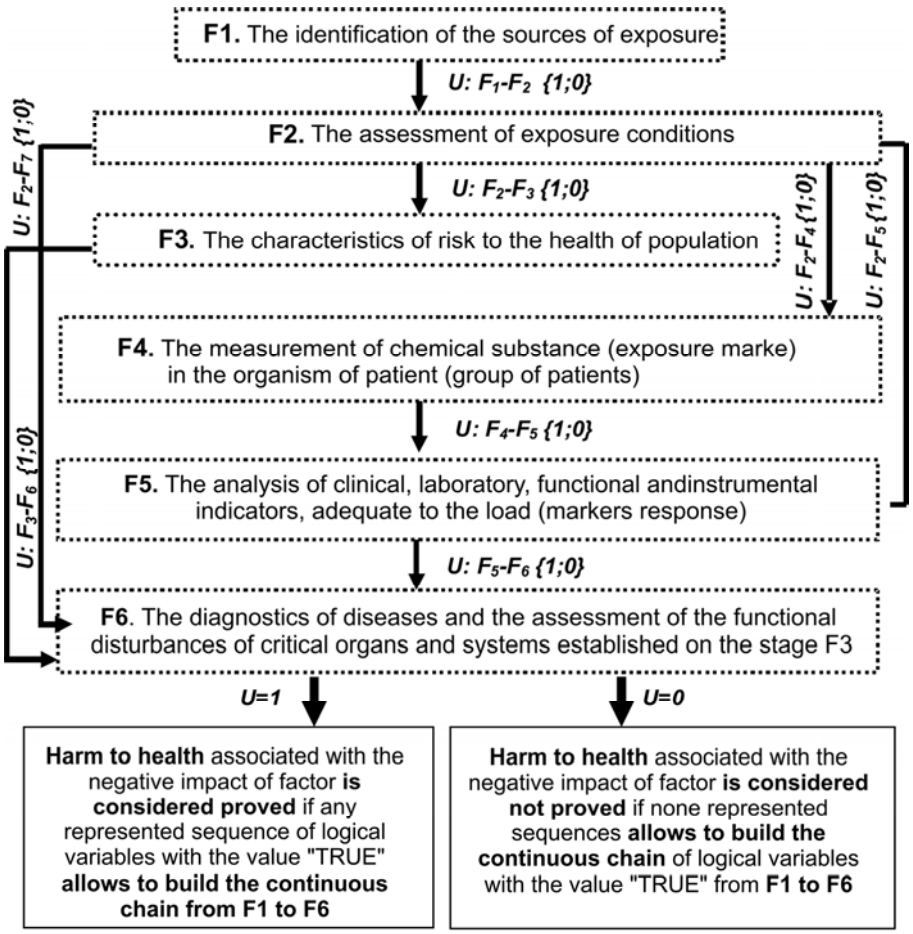

Fig. 7.2. The logic diagram of proving harm to health associated with the exposure of the negative chemical factors of living environment

U_i^{2-3} = "The proved relationship of the exposure of i-th factor with risk to the health of population formed by it" i = 1..N_F, N_F – the number of analyzed factors. Proof is unacceptable carcinogenic and/or non-carcinogenic acute and/or chronic risk to the health of population, calculated according to the approved methods using the criteria recognized in the Russian Federation;

U_i^{2-4} = "Proved relationship between the exposure of i-th factor and the content of appropriate chemical compound in the organism », i=1 .. N_F. Proof is the presence of reliable relationship between the indicators established by the methods of mathematical statistics. Linkage should be biologically plausible, supported by the data of scientific and methodical literature and other independent researches;

U_{ik}^{2-5} = "The proved negative impact of the exposure of i-th factor on the k-th indicator of clinical, laboratory, functional and instrumental studies" k = 1..N_{kl}; N_{kl} – the number of the indicators of clinical, laboratory, functional and instrumental studies. Proof is the presence of reliable relationship between the indicators established by the methods of mathematical statistics. Connection should be biologically plausible, supported by the data of scientific and methodical literature and other independent researches;

U_{ij}^{3-6} = "The proved correlation of health risk of the *i*-th factor with the *j*-th indicator of health" $j = 1..N_{zd}$; N_{zd} – the number of health indicators. Proof is the presence of diseases attributable to critical organs and systems identified at the stage of health risk assessment during epidemiological studies or clinical trials in the group of investigated patients. Frequency of occurrence of diseases should significantly exceed those in the comparison group;

U_{ij}^{2-6} = "The proved negative impact of exposure of *i*-th factor on the *j*-th indicator of health" $j = 1..N_{zd}$; N_{zd} – the number of health indicators. Proof is the presence of reliable relationship between the indicators of exposure and the prevalence of diseases established by the methods of mathematical statistics. Connection should be biologically plausible, supported by the data of scientific and methodical literature and other independent researches. Usually, only the diseases attributable to critical organs and systems revealed at the stage of health risk assessment are considered;

U_{ik}^{4-5} = "The proved negative impact of content of *i*-th factor in the organism on the k-th indicator of clinical, laboratory, functional and instrumental studies" $k = 1..N_{kl}$; N_{kl} – the number of indicators of clinical, laboratory, functional and instrumental studies. Proof is the presence of reliable relationship between the indicators established by the methods of mathematical statistics. Connection should be biologically plausible, supported by the data of scientific and methodical literature and other independent researches;

U_{kj}^{5-6} = "Proved correlation between the impairment of the *k*-th indicator of clinical, laboratory, functional and instrumental studies with the *j*-th indicator of health" $j = 1..N_{zd}$; N_{zd} – the number of health indicators. The proof is the presence of reliable relationship between the indicators established by the methods of mathematical statistics. Connection should be biologically plausible, supported by the data of scientific and methodical literature and other independent researches.

Harm to health associated with the negative impact of factor is considered proved if any represented sequence of logical variables with the value of "True" allows building the continuous chain from the source of harmful exposure up to establishment of the fact of disease and/or identification of functional disorders of critical organs and systems.

Harm to health associated with the negative impact of factor isn't considered proved if none of represented sequence allows building the continuous chain of logical variables with the value of "True" from the source of harmful exposure up to establishment of the fact of disease and/or identification of functional disorders of critical organs and systems. The conclusion about proof or lack of proof of harm caused by risk factors must be made.

It should be noted that the proposed system analysis allows proving the harm to health associated with the factors of living environment on the group and individual levels.

Conclusion on the proof of harm associated with the harmful effects of factor(s) is made on the basis of system analysis of all the obtained data on sources of hazard, human exposure (exposure of group of people), exposure markers, response markers and revealed diagnosis, taking into account the results of assessment of other factors capable to cause the similar health impairments.

7.5. The practice of establishment and evidence associated with the negative impact of environmental factors of harm to public health

The above algorithm and methods of the establishment and proof of harm to health of population were used for scientific substantiation and informational support of a number of management decisions – from the establishment of responsibility measures to the preparation of plans and programs of sanitary-hygienic and medical and prevention activities.

Thus, the assessment of harm to health was made during the investigation of the complaints of the population of large industrial city on unsatisfactory quality of potable water in terms of contamination.

It was established that the water of the superficial source of water supply is characterized as the water of quality class "3B" (very contaminated) and has a specific combined pollution index of 3.0. For the prevention of the microbial contamination of potable waters, the organization, exploiting the plumbing systems, performs the hyperchlorination of water supplied to the population. Instrumental studies have revealed the presence of highly toxic organochlorine compounds in potable water. About 80% of the population of city in the number of 78.000 of people used the water containing chlorine (residual free and residual fixed), trichloromethane, chloroform, tetrachloromethane, dichloroethane, dihlorbrommetan and several other organochlorine contaminants, including at the levels above hygienic standards. For a long time in the conditions of exposure to organic derivatives of chlorine there were about 60.000 of people. This number includes more than 7200 of children who resided and attended the preschool and school institutions in the zone of one and the same water supply system.

The assessment of population health risk associated with the water quality of the network of domestic water supply, conducted in accordance with the R 2.1.10.1920-04 "Guidance on the assessment of population health risk at exposure of chemical substances" on the basis of long-time average annual data (2006–2009) allows revealing that the total individual carcinogenic risk is in 4.6 times higher than the acceptable level. Major contribution to the formation of acceptable carcinogenic risk (93.5%) is made by chloroform. The given level of risk corresponds to the probability of more than 30 cases of malignant tumors among the population of the city during their lifetime because of the content of organochlorine compounds in town water. The unacceptable level of the non-carcinogenic risk of disorders was established for blood system (hazard index up to 1.8), liver (hazard index up to 1.45), central nervous system (hazard index up to 1.33), kidney (hazard index up to 1.28) and endocrine system (hazard index up to 1.28). The results of hazard identification established that the increased level of chlorine in the water may be the cause of pathology of immune system and can to grate on the mucous membranes. The priority risk factor is the chloroform.

The application of the method of gas chromatography allowing to identify and quantify the organic chlorine derivatives in the blood at the level of 0.0001–0.00001 mg/dm^3, in the course of in-depth examination of 243 children from the zone of exposure established the presence of one or several organochlorine derivatives of each child. Thus, the chloroform is identified in the blood of 98.8% of children. Carbon tetrachloride was present in the blood of all the examined children, dihlorbrommetan – in 97.9%, dibromochloromethane – in 59.6%, 1,2-dichloroethane – in 51.5% of patients. The organochlorine contaminants were not identified at the level of method sensitivity in the comparison group. The ambient air contains no chemical impurities, i.e., the inhalation route of the exposure of contaminants was excluded. It was not possible to explain the accumulation of impurities entering in blood with the food due to the fact that the children of comparison group (children from the settlement, located near the investigated area) were characterized by the analogous structure of nutrition, but did not have the contaminants in the organism. Thus, the presence of organochlorine compounds was considered as the proof of chronic exposure of water risk factors in the blood of children.

Because the critical organs and systems in the case of the oral exposure of chloroform dihlorbrommetan, dibromochloromethane, etc. are the immune and nervous systems, digestive organs, blood system, as the evidence of harm is considered the frequency of the diseases of precisely these systems. The data analysis of the system of compulsory health insurance showed that the daily medical aid appealability of children under the age of 3–7 years from the exposure zone due to gallstone disease, other diseases of gallbladder, the lesions of gallbladder, biliary tract and pancreas at the diseases classified in other rubrics (K 80-87) in 4.64 times higher on the territories of comparison. Morbidity due to such nosological forms as immunodeficiencies and other disturbances involving the immune mechanism is in 4.01 times higher,in 8.58 times higher for conjunctivitis (H10-13), in 7.21 times higher for disorders of vegetative nervous system and other disturbance of nervous system. The presence of reliable cause-end-effect relationship between the risk factors caused by water quality of potable water supply system and the occurrence of diseases of the blood system,

blood-forming organs and immune system (*OR* = 3.78), nervous system (*OR* = 2.29), eye and its adnexa (odds ratio – *OR* = 7.45) as well as digestion organs diseases (*OR* = 4.2) was established.

The presence of associations between exposure markers and laboratory, functional and other indicators of child health and the infringement of functions of those or other organs and systems were considered in order to confirm the connections between diagnoses (diseases) and the risk factors.

Thus, the statistically significant cause-and-effect relationships between the increased levels of 1,2-dichloroethane, chloroform and carbon tetrachloride in the blood and biochemical indicators of cellular and functional liver damage was proved in the exposed children. The results of epidemiological studies confirmed the linkage between these factors and the increasing in activity of liver enzymes (*OR* = 13.5). The significant relationship between the content of revealed organochlorine compounds in the blood with the indicators of the activation of oxidative processes (as the consequence of damage of the liver cell membranes) and the disturbance of the intensity of anti-oxidative processes in the organism was established. Epidemiological studies have confirmed the linkage between the elevated levels of 1.2-dichloroethane in the blood and the increasing of the activity of oxidative processes (*OR* = 15.65). The changes in indicators of anti-oxidative activity in 10% of children are caused by the increased content of dibromochloromethane and carbon tetrachloride in the blood. The statistically significant cause-and-effect relationships between the increased content of chloroform in the blood and the disturbance of detoxification processes in the organism was established.

The significant cause-and-effect relationships of changes in cell (phagocytosis, T-lymphocytes) and humoral (immunoglobulins and cytokines) immunity with the concentrations of organochlorine compounds were established in the blood of examined children. Thus, it is proved that the content of dihlorbrommetan and dibromochloromethane in the blood has a negative effect on the state of phagocytosis; and the presence of carbon tetrachloride in the blood – on the factor of cell activation CD25 +. The suppression of CD95 + is associated with the content of dibromochloromethane in the blood and the increase of interferon-gamma – with the presence of dichloroethane in the blood. The reduction of phagocytic number and relative phagocytosis under the influence of chloroform and dichloroethane as well as the dependence of deficiency of IgG and IgA from the availability of chloroform in the blood was reliably established.

Thus, practically all the steps of the proposed algorithm of the formation of evidence base of harm to health were implemented:

– the source of hazard is identified – potable water, hyperchlorinated due to low quality of source of potable water supply;

– risk factors are defined – the organochlorine contaminants: chloroform, carbon tetrachloride, dichloroethane, dihlorbrommetan and several other;

– calculated on the basis of long-time average annual instrumental data the population health risks exceeded the levels that are qualified as permissible (acceptable). Main contributions to the health risks were made by chloroform and carbon tetrachloride. Critically affected organs and systems were the digestive organs, blood and nervous system. Chloroform was the additional factor of carcinogenic risk;

– exposure proved by the registration of chemical impurities specific to oral exposure in the blood of exposure population, especially children. At that, the frequency of the registration of impurities in the examined contingent was extremely high (practically 100%); the impurity levels were significantly higher than in the comparison group, that was outside the exposure;

– the presence of impurities in the blood has significantly changed the system of laboratory parameters of homeostasis; thus, the linkages "contaminants in blood – laboratory data" established by the methods of mathematical statistics were biologically plausible, and adequate to existing scientific data and were stable.

Evidence base used in the judicial process of Sanitary Service Territorial Administration against the economic entity which provides the potable water supply to the municipal settlement. The development of sanitary and hygienic measures is prescribed to legal entity and the transition on another source of water supply – to the local government authorities.

Harm to health was revealed and proved for the population permanently resided in the zone of influence of large industrial enterprise on the production of electrical cable. The complaints of population on inadequate living conditions, including on the unpleasant phenol-cresol smell were the basis for sanitary and epidemiological investigation.

The analysis of the data of inventory statements and draft standards for maximum admissible discharges of enterprises generating the industrial unit in one of neighborhood units of a large industrial city, showed that the sources of only single enterprise have the discharges in the ambient air of settlement of phenol and o-, m- and p-cresol with the mass capable generating the substantial ground level concentrations of these impurities in the ground level layer of the atmosphere.

The instrumental studies of ambient air quality in the points of the placement of preschool institutions (DDU) showed the exceedances of surface concentrations on phenol up to 3.6 TLV_{ae} (Threshold Level Value acute exposure) and up to 2.7 TLV_{ce} (Threshold Level Value continuous exposure); on the amount of cresol – 1.7 TLV_{ae} (Threshold Level Value acute exposure); and 2.0 PDK_{ce} (Threshold Level Value continuous exposure).

In the conditions of the chronic exposure of tricresol and phenol the risk was qualified as unacceptable: the hazard index of the development of the pathology of nervous system at the exposure of the complex of contaminants amounted to 10.02 (the contribution of tricresol – about 99.77%); central nervous system – up to 9.23 (the contribution of phenol – up to 65.34%); blood system – up to 12.08 (the contribution of phenol – up to 82.78%); liver – 2.3 (the contribution of phenol – up to 94.08%), kidney – up to 2.7 (the contribution of phenol – up to 86%).

The zoning of territories on the indicators of risk (Fig. 7.3) established that not only the children's educational institutions are located on the sites of increased risk to the health of population, but also resident houses, in which the bulk of children attending these preschool institutions (PSI) are resided.

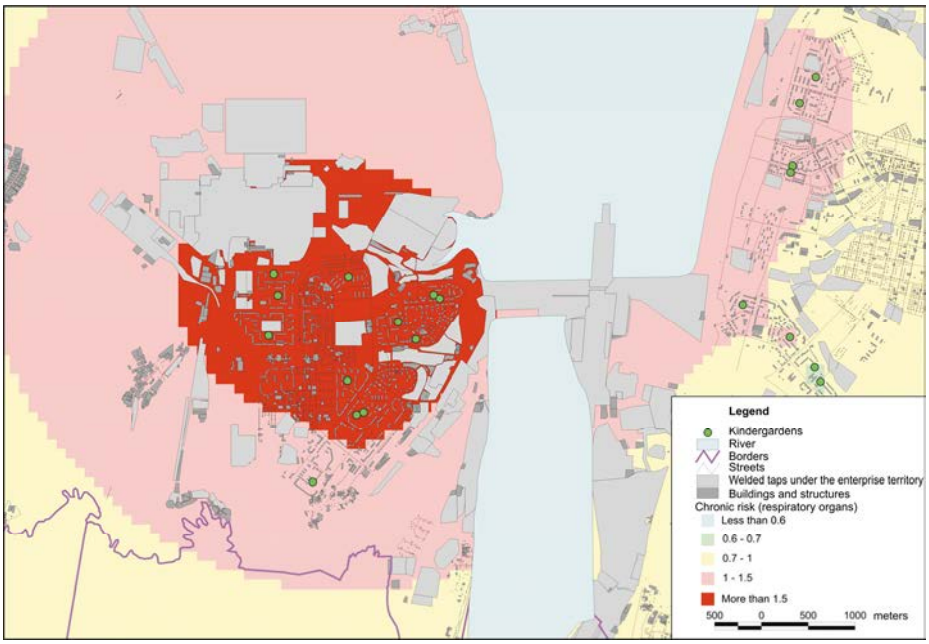

Fig. 7.3. The zoning of influence territory of electro-cable plant according to the level of chronic inhalation risk accepted in relation of respiratory diseases and the point of placement of preschool institutions

Based on the data of scientific literature, it was established that phenol and its derivatives at their extended entering in the organism disturb the oxidative phosphorylation and other fermentative processes, irritate the skin and mucous membranes. Gonadotoxic, embryotoxic and teratogenic effects were detected in this class of substances. The program of medical and biological investigation was formedresident house based on the analysis of toxicological profiles of substances. Children under the age of 4–7 years, permanently residing and attending the preschool institutions (PSI) in the zone of unacceptable inhalation risk were considered as the most vulnerable group. Laboratory diagnostic inspection was performed in accordance with the strict observance of ethical standards set out in the Declaration of Helsinki of 1975 with additions in 1983.

The presence of investigated impurities in the blood of children living permanently in the conditions of exposure was revealed at levels significantly higher than the levels of comparison: for phenol – in 1.6 times, meta- and para-cresol – up to 1.2 and 7.4 times respectively (p<0,05) (Table 7.6).

The complex of the bias of laboratory and cytogenetic indicators characterizing the development of negative effects is allocated at the comparative analysis (with reference to age-related physiological norms and indicators in the control) of results of in-depth laboratory investigation of children: a) the activation of process of lipid peroxygenation in the organism (increase of hydroperoxides of lipids, malonic dialdehyde level) having the dependence on the increased level of phenol ($0.13 \le R^2 \le 0.45$; $7.2 \le F \le 33.8$; $p = 0.000$); b) the intensification of antioxidant system activity (increase of total antioxidant activity level) having the dependence on the increased level of phenol and m-cresol ($0.18 \le R^2 \le 0.36$; $29.26 \le F \le 30.97$; $p = 0.000$); c) the activation of cytolytic process (increase of ACAT activity), having the dependence on the increased level of phenol ($R^2 = 0.11$; $F = 6.73$; $p = 0.012$); d) the disturbance of the synthesis of blood-coagulation factors by the liver (reduction of duration of bleeding) having the dependence on the increased level of phenol ($R^2 = 0.46$; $F = 154.25$; $p = 0.000$); d) the presence of inflammatory response (increase in the content of leukocytes and segmentonuclear neutrophils), having the dependence on the increased levels of phenol in the blood ($R^2 = 0.59$; $F = 79.29$; $p = 0.011$); cytogenetic changes (the qualitative changes of chromosomes by the type of the variants of polymorphism, genetic instability in exfoliative buccal epithelium cells presented by the increased frequency of the infringement of nuclear apparatus) having the dependence on the increased level of phenol and o-, m-cresol ($0.10 \le R^2 \le 0.20$; $6.13 \le F \le 11.85$; $0.000 \le p \le 0.028$), contribution of the present compounds in the formation of polymorphic changes amounted to 10–20% ($0.000 \le p \le 0.028$); e) the activation of oxidative processes on the level of cell DNA (increase of 8-hydroxy-2-deoxyguanosine level), having the dependence on the increased level of phenol and o-, m-cresol in the blood ($0.15 \le R^2 \le 0.25$; $7.22 \le F \le 10.25$; $0.000 \le p \le 0.021$), the contribution of the present compounds in formation of oxidative damage on the level of cells DNA amounted to 15–25% ($0.000 \le p \le 0.028$).

Table 7.6

The concentrations of chemical substances in the blood of children permanently residing in the zone of unacceptable risk formed by the exposure of phenol and its derivatives

Parameter	Phenol	M-cresol	P-cresol
Mean value for the the study group (n = 76) mg/dm^3	0.0699±0.0070	0.560±0.0482	0.0126±0.0022
Maximal value, mg/dm^3	0.1901	3.260	0.550
The share of children with the level of contaminant in the blood above the comparison value,%	79.7	58.0	11.6
Mean value for the comparison group, mg/dm^3	0.0437±0.0034	0.4411±0.0327	0.0037±0.0005
Reliable difference of the control	0.011*	0.026	0.003

Model parameters of dependence between the level of phenol and cresol in the blood of children and the change of some marker laboratory parameters are shown in Table 7.7.

Table 7.7

The parameters of "exposure marker – effect marker" dependence models

Exposure marker	Effect marker	The direction of changes in the rate	*b*0	*b*1	R^2	*F*	*p*
M-cresol	Hemoglobin	Reduction	-3.73±0.019	2.08±0.054	0.78	79.69	0.000
M-cresol	Leukocytes FBC	Reduction	-2.32±0.022	0.77±0.079	0.11	7.55	0.008
P-cresol	Antioxidative activity	Reduction	-0.2±0.0	58.29±20.115	0.73	168.90	0.000
P-cresol	Direct bilirubin	Increase	-1.81±0.0	14.72±0.0	0.63	107.23	0.000
P-cresol	MDA	Increase	-0.2±0.0	58.29±0.0	0.73	168.90	0.000
Phenol	RDWc	Reduction	-0.57±0.076	15.34±16.707	0.21	14.08	0.000
Phenol	Absolute number of eosinophils	Reduction	-2.09±0.069	14.79±14.412	0.24	15.17	0.000
Phenol	Antioxidative activity	Reduction	-0.73±0.043	8.75±8.765	0.13	8.73	0.004
Phenol	Eosinophilic-lymphocyte index	Increase	-0.43±0.0	48.24±0.0	0.79	66.12	0.000

The established complex of the disturbance of immunologic indicators characterizing the development of negative effects at the increased level of m-cresol, o-cresol and/or phenol in the blood, consist of: a) the disturbance of cellular link of immunity – the decrease of phagocytosis activity, inhibition of expression of T-helpers and T-activational cells ($0.24 \le R^2 \le 0.78$; $0{,}000 \le p \le 0.008$); b) the disturbance of the humoral link of immunity – inhibition of IgM content ($R^2 = 0.76$, $p < 0.05$); c) the presence of specific sensitivity to the components of load factor (increase in the content of antibodies to phenol); d) the disturbance of neuro-humoral regulation according to the criteria of content of cortisol and serotonin, reliable in relation to the control group, etc.

Physical examination, followed by the laboratory tests revealed that children from observation group have 1.5 times more frequently the pathology of nervous system (75.7 vs. 49.1%, $p \le 0{,}001$) with the predominance of vegetovascular dystonias in its structure (40.1 vs. 35.2%; $p = 0.49$) than children in comparison group. Neurosis-like syndrome (25.0%) was reveal in more than a third of children (35.6%), while in comparison group, this pathology was detected in 2.3 times less frequently (10.7%, $p < 0.01$). Were established the cause-and-effect relationships of child morbidity from the zone of exposure with increased levels of phenol in the blood: diseases of nervous system ($R^2 = 0.03$; $F = 6.19$; $p = 0.01$), diseases of circulatory organs ($R^2 = 0.99$; $F = 2479.17$; $p < 0.001$), diseases of digestive ($R^2 = 0.22$; $F = 68.10$; $p < 0.001$), and urinary system ($R^2 = 0.43$; $F = 169.52$; $p < 0.001$).

The results of in-depth surveys and the data of special questioning allowed making the conclusion that 7% of children have the whole set of features allowing to include the disease into the class of determined by the factors of living environment (i.e., all criteria of the evidence of connection the harm to health with factors of living environment were respected):

– every patient permanently resided in the zone of increased exposure and attended the preschool institutions in the same area;

– phenol and one of the isomers of cresol at the levels significantly higher than the upper permissible bound of the level of comparison ($M_i > M \pm m$) were identified in the blood of each child; and at every child the number of biochemical and immunological parameters significantly associated with the levels of chemical contaminants in the blood exceeds the upper (lower bound) of physiological norm (i.e., effects were expressed and observed in several persons, they were stable and biologically plausible);

– the diagnosis of "Secondary immunodeficiency state" (D83.9) was revealed taking into account the system of clinical, laboratory parameters and functional assays as well as clinical indicators which have the reliable biologically justified connections with exposure (markers of exposure), i.e. the fact of harm was confirmed by the set of indicators;

– anamnesis data and the results of the questioning of parents did not show the presence of other causes, which could be major in the detected health deteriorations.

Thus, the harm to health on population and in some cases on individual level is considered as proven that was recognized, including, by representatives of industrial enterprise. Following the results of sanitary-epidemiological investigation and examination, the enterprise have considered the possibility of adoption of technologies, eliminating the use of phenol-cresol lacquers and coatings.

Children with health disorders, determined by the factors of living environment, have received the specialized medical care on technologies considering the specifics of impact (Chapter 3).

Investigation on the proof of the relation of the health disorders of population with the level of acoustic discomfort in the zone of influence of large airport was carried out according to the general structural scheme.

Instrumental and calculated data proved that the maximal and average long-term noise levels exceeded the permissible norms for several kilometers along the perimeter of the airport. Territories, which are located in the immediate vicinity to the border of buffer zone of the airport were characterized by the greatest noise pollution (up to 90 dB – maximum noise and 66.6 dB – equivalent noise). In general, the parameters of chronic noise on all the investigated territories exceeded the levels at which, according to the scientific literature, there may be negative effects in the health status of population, including in the respect to nervous and cardiovascular system and hearing organs (Table 7.8).

Table 7.8

Noise levels in the studied territories adjoining to the airport (2007–2012)

Parameter	Th zone of contamination			The territory of comparison (city)	MPL
	The zone of closest approach (1000 m from the runway)	2–4 km from the runway	4–6 km from the runway		
Maximal noise levels in dB*	90.0	78.6	70.2	75.7	70.0
Equivalent levels** in dB	66.57±7.25	61.5±6.02	63.7±6.37	59.9±6.01	55.0

Notes: * – maximal values with 95% probability;
** – average values.

The achievement of the high risk of health disorders, determined by the constant high noise exposure, in residents of territory, possible approached to the airport, was predicted at the age of about 47 years whereas on the territory of comparison the high risk have not been forming according to the calculations. Long-term noise exposure on the territory located along the takeoffs and landings of airplanes under the glide slope (conventional line of airplanes reversals) form the moderate risks to the health of residents to 20 years and the high – to 57–58 years. Displacement from the airport in the investigated limits reduced the risk of health disorders associated with acoustic externally-environmental factor.

The data of population appealability for the medical care and the results of calculation of value of odds ratios (*OR*) as an indicator of the presence of cause-and-effect relationships between the disease and accommodation in the conditions of exposure established that children from the zones of contamination have significantly higher probability to have the circulatory system diseases (*OR* = 1.52), the diseases of central and vegetative nervous system (*OR* = 1.2–1.36) as well as diseases of ear and mastoid process (*OR* = 1.02). The adult population from the zones of increased chemical and noise exposure have the probability of central nervous system disease in 1.9 times higher than on the

comparison territory, generally the frequency of the disorders of nervous systems is in 1.7 times higher. Data were well corresponded with the results of health risk assessment. Significantly more higher levels of cognitive impairments (0.01 cas./1000 in the absence of such disorders in the zone of comparison) than on the comparison territory, and the higher prevalence of vegetative nervous system disorders (0.72 cas./1000, at 0.22 cas./1000 in the zone of comparison) were revealed in children from impact zones. The diagnosis of "conductive and neurosensory hearing loss," was set in the year of study only to children from the zones of increased noise contamination according to the data of Federal Compulsory Medical Insurance Fund (FOMS). Cases of conductive and neurosensory hearing loss for the analyzed year according to the data of Federal Compulsory Medical Insurance Fund (FOMS) were reported only in adult residents of 18–50 years permanently residing on the border of buffer zone (6 cases), or 0.19 cas./1000 pers. In individuals older than 50 years and residing in close proximity to the border of buffer zone, this diagnosis was recorded with a frequency of 2.78 cas./1000 at the indicator in comparison zone of 0.02 cas./1000. Thus, in the course of sociological survey 13.2% of respondents from observation zone and 2.3% from zone of comparison indicated that they were experiencing the extreme anxiety caused by aircraft noise; residents of territories close to the airport, on the daily basis pay attention to the noise generated by airplanes in 2.5 times more frequently than on the comparison territory ($p<0.05$); generally it was marked the high level of tolerance of residents of noisy territories to the aircraft noise, arising for prolonged period of living in the investigated territory.

The study of the functional state of auditory analyzer by the method of audiometry in the children of observation group allowed establishing the decrease of the level of auditory perception from 1.0 to 7.0 dB, relatively to the comparison group, preferably at frequencies of 125–1500 Hz ($p\leq0.05$). The most significant decrease in the level of hearing loss up to 9.7 dB and 7.3 dB was registered in children permanently residing and attending kindergardens in the areas of the highest acoustic discomfort.

In the course of the medical examinations, functional and instrumental studies of children from the zones of observation and comparison it was established that in the structure of revealed diseases in children from zones of the highest noise exposure (of observation group) the functional disorder of nervous system was predominated. That indicator is in 1.8 times higher than that in comparison group. The diseases of nervous system were revealed in 50.7% of children, the disorders of vegetative nervous system (G90.0) – in 13.7% of children. In children attending preschool educational facilities in the zone of maximum noise exposure, the various forms of sleep disorders were revealed in 9.5% of cases, that is 2.0 times higher than in children from the comparison zone ($p<0.05$). The diseases of cardio-vascular system were found in observation groups in 41.2% cases, that is 1.4 times more frequently than in comparison group (29.2%) ($p<0.05$).

The confirmation of risks' implementation caused by the noise factor was especially expressed in the adult population. Thus, the analysis of the morbidity of adult population up to 50 years showed that the priority nosological forms of the diseases of analyzed zones in decreasing order are hypertensive disease, the disorders of vegetative nervous system and symptoms of high blood pressure, in the absence of the diagnosis of hypertension. The highest morbidity rates probably caused by noise factor, were reported in the zone of closest approach to the airport by the following nosological forms: the symptoms of high blood pressure, in the absence of the diagnosis of hypertension, hypertensive disease, cognitive and neurosensory hearing loss. Morbidity rates according to the data of nosological forms significantly exceeded those in comparison zone. The cases of conductive and neuro-sensory hearing loss for the analyzed period (2011–2012) according to the data of Federal Compulsory Medical Insurance Fund (FOMS) were reported only in adult residents at the age of 18–50 years permanently residing in the investigated zones and zones of comparison not further than 1000 m from the runway.

The analysis of the morbidity of adult population over the age of 50 years showed that the priority nosological forms of disease of analyzed zones are the hypertensive disease, chronic ischemic heart disease and stenocardia (Table 7.9).

Table 7.9

The incidence rate of adult population over the age of 50 years, probably caused by influence of noise factor, sl. / 1000

Parameter	The zone of closest approach (1000 m from the runway)	2–4 km from the runway	4–6 km from the runway	The territory of comparison (city)
Hypertensive disease	**3.48±0.005**	**0.99±0.001**	0.77±0.011	0.51±0.002
Chronic ischemic heart disease	**1.88±0.004**	0.62±0.002	0.93±0.012	0.63±0.002
Stenocardia	**0.2±0.001**	0.16±0.001	0	0.10±0.001
Conductive and sensory neural hearing loss	**0.98±0.003**	**0.05±0.001**	0	0.01±0.0
The disorders of autonomic nervous system	**0.02±0.0**	0.01±0.0	0	0.01±0.0

Notes: the significance of differences with the territory of comparison ($p \leq 0,05$) is highlighted by the bold print.

The study of the functional state of auditory analyzer by the method of audiometry in the children of observation group allowed establishing the decrease of the level of auditory perception from 1.0 to 7.0 dB, relatively to the comparison group, preferably at frequencies of 125–1500 Hz ($p \leq 0.05$). Thus, in children at the age of 4–7 years permanently residing and visiting the preschool institutions in the zone of closest approach to the runway, the lower level of auditory perception at the frequency of 125 Hz was 23.5 dB. Thus, in 65% of children, this indicator fluctuated between 23.5 to 17.0 dB, despite the fact that in children from the comparison group (quiet zone) the average indicator was 13.8 dB.

Thus, the harm was proved by:

– the identification of expressed risk factor and accommodation (long term occupancy) of people under the exposure of the given factor;

– established health risk level exceeding the acceptable bounds, in conditions of registered noise exposure;

– the registration of the increased level of morbidity of children and adult population predominantly by the diseases of nervous system, cardiovascular system and hearing organs;

– the availability of reliable connections between increased morbidity of population and environmental factors;

– the identification of significantly more frequent cases of increasing of the lower level of auditory perception in children from zones of increased noise load.

The proof of the implementation of risks is another argument in the favor of the expansion of practice of this methodology in the tasks of hygienic assessment. In-depth medical, biological and epidemiological studies are labor-intensive, expensive types of activities which may not always be applied in the practice of health surveillance, investigations and examinations. Risk assessment using reliable, verified mathematical models and correctly completed exposure assessment in many cases can significantly facilitate the decision-making, including in implementation of constitutionally enforceable right of citizens for compensation of harm to health caused by unfavorable living environment.

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8. HEALTH RISK ASSESSMENT AND MANAGEMENT PRACTICE BASED ON NEW METHODS AND APPROACHES

Currently, the health risk assessment methodology improvement is of such great demand that the terms for practical implementation of new methods and approaches are minimal. During the last 5–7 years we already accumulated a significant experience in the application of methodical developments created within the same terms. The proposed health risk analysis methodology development elements allowed supplementing the information and methodical base for assessment and management of risk associated with the influence of external environmental, occupational and social factors as well as the product hazard factors for the health of citizens.

8.1. External environmental risks at the complex action of hazard factors

The study on the establishment of relationship between the public health disorders and aerogenic chemical and physical factors on the example of Pulkovo airport affected area is performed at the territory of Saint-Petersburg by the specialists of FBSI "Federal scientific center for medical and preventive health risk management technologies" The Administration of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance for Saint-Petersburg according to the program agreed by the parties. The studies included the processing of library materials from the social and hygienic monitoring for 2009–2012, health risks assessment based on the evolution simulation and vectored in-depth medical and biological studies on the detection of harm to health associated with the negative effect of contaminations formed by the airport. The studies were performed in order to assess the sufficiency of size of the sanitary protective zone of facility and to correct it.

The features of the subject of research were as follows:

– airport functioning duration (active development of carriage is dated by the beginning of 30th years in XX century);

– the intensity of air carriage (up to 400–450 flights and landings per day);

– use during a number of years of aircrafts not limited by the noise standards; gradual transition to the "low-noise" airplanes; during the last ten years;

– the vicinity of residential construction: the nearest residential communities are located at the distance of 850–1200 m from the landing strip (area 1 in the study) and 1300–2000 m (area 2 in the study). In general, about 570 thous. of people reside permanently in the conditions exposed to the risk factors associated with the airport activity.

– the availability of the set of different hazard factors from which the priority is given to the chemical and noise contamination of ambient air;

– the necessity of the prospective population safety forecasts, taking into account the further development both of Saint-Petersburg and Pulkovo airport.

The consideration of the listed features during the assessment of health risks for citizens was possible only based on the risk evolution simulation.

The data of instrumental surveys revealed that in the direct vicinity to the boundary of the sanitary protective zone of Pulkovo airport in the residential construction it is possible to register the contamination of atmosphere by chemical impurities measured within the social and hygienic monitoring (nitrogen dioxide, sulfur dioxide, carbon monoxide, suspended substances, benzene, toluene, ethylbenzene, ammonia, benzopyrene, phenol, formaldehyde, hydrogen chloride, xylene, cadmium oxide, manganese, cupric oxide, acetone, lead). Herewith practically all substances are present in the significant concentrations (range from 0.1 to 1.0 of the maximum permissible concentration). It is established that the maximum contamination levels are detected for the impurities which are the components of the aircrafts emissions during the engine warm-up and flights. The hygienic standards exceedance degree was from 1.1 (carbon monoxide) to 10.0 times (sulfur dioxide).

The social and hygienic monitoring data evidenced that the average long-term contamination of ambient air in the area located in the maximum proximity to the landing strip is really higher than at the compared territory under the nitrogen dioxide, sulfur dioxide, suspended substances, benzene, toluene, formaldehyde, manganese, lead, copper. Herewith the accounting of the general applicable criteria of noncarcinogenic chronic inhalation risk evidenced the high health hazard levels (Table 8.1).

Building the health risk increment models at the studied territories due to the negative influence of chemical factors demonstrated that the risk of health disorders in 5 years of exposure in the childhood is 0.088 than without influence this indicator is equal to 0.076. The difference of risks is equal to 0.0012, i.e. the presence of additional hazard risks increases the risk for child to get sick by 1.2%. With the increase of years, the difference between risks formed under and without influence increases significantly making up to 20 years about 8–10%, and to 50 years – more than 20% (Fig. 8.1).

Table 8.1

Average long-term ambient air contamination level and the hazard quotients determined by it in the several areas of investigation

Chemical impurity	Average long-term concentration, mg/m^3			Hazard quotient (*HQ*)			*p*
	Area 1	Area 2	Compared territory	Area 1	Area 2	Compared territory	
Nitrogen dioxide	0.08±0.003	0.051±0.003	0.067±0.003	2.00	1.28	1.67	0.02
Sulfur dioxide	0.044±0.001	0.035±0.002	0.04±0.00001	0.88	0.70	0.80	0.03
Suspended substances	0.298±0.0009	0.204±0.0097	0.267±0.0044	3.97	2.72	3.56	0.03
Carbon monoxide	1.353±0.06	1.099±0.03	1.197±0.07	0.45	0.37	0.40	0.02
Ammonia	0.035±0.002	0.026±0.001	0.027±0.002	0.35	0.26	0.27	0.01
Benzapyrene	1,E-06±5,E-08	1,E-06±1,E-08	1,E-06±1,E-08	0.57	0.52	0.51	0.05
Benzene	0.021±0.0004	0.017±0.0008	0.02±0.0000	0.70	0.57	0.67	0.05
Phenol	0.004±0.0001	0.003±0.0001	0.004±0.0000	0.67	0.50	0.67	>0.1
Hydrogen chloride	0.104±0.002	0.084±0.003	0.100±0.001	5.20	4.20	5.00	0.05
Xylene	0.021±0.0006	0.023±0.003	0.021±0.0008	0.21	0.23	0.21	0.05
Cadmium oxide	0.0001±2,E-06	0.0001±3,E-06	0.0001±1,E-06	5.00	5.50	5.00	>0.1
Manganese	0.002±0.0001	0.001±0.00004	0.001±0.0000	40.00	20.00	20.0	0.01
Cupric oxide	0.0001±0.00001	0.0002±0.00002	0.0001±0.00001	5.00	10.00	5.00	>0.1
Toluene	0.022±0.002	0.019±0.0006	0.018±0.0000	0.06	0.05	0.05	0.03
Acetone	0.16±0.0003	0.146±0.004	0.16±0.0000	0.01	0.00	0.01	>0,1
Lead and its inorganic compounds	0.0002±0.00001	0.0001±5,E-06	0.0001±8,E-06	0.40	0.20	0.20	0.01
Formaldehyde	0,012±0,0005	0,008±0,0005	0,010±0,0002	4.00	2.67	3.33	0.05
Ethyl benzene	0.01±0.0003	0.009±0.0003	0.01±0.0001	0.01	0.01	0.01	>0,1

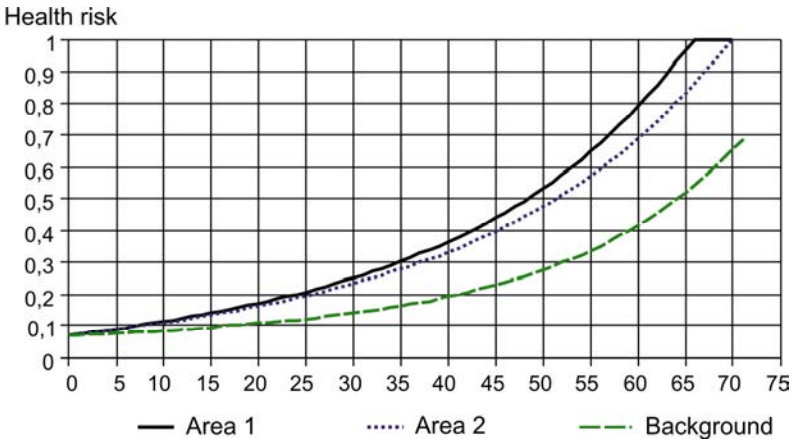

Fig. 8.1. Health risk evolution when exposed to the chemical factors of the ambient air contamination

The health disorders are expressed in the respiratory organs affection (priority risk factors: suspended substances, manganese compounds, toluene, nitrogen dioxide, etc.), cardiovascular system (priority risk factors: suspended substances, nitrogen, carbon dioxide, benzene), central nervous system (formaldehyde, toluene, benzene, phenol), endocrine system (benzene), hematopoietic system (manganese and benzene), digestive organs (toluene) and diseases under a number of other classes.

The priority factors of chemical risks are formaldehyde (about 37% of contributions to the cumulative health disorder risks), aromatic hydrocarbons - benzene and toluene (about 23% of contributions to the cumulative health disorder risks), manganese and its compounds (about 19%) as well as the suspended substances (about 6%).

The analysis of the dynamics of the specified risk indexes formed by the chemical hazard factors evidences that the chronic exposure equal to the exposure established during the study forms the high health risks at the duration of 44–45 years for area No. 1 and a the duration of 56–58 years for area No. 2 (Fig. 8.2).

Except for the expressed load, the increased maximum and average long-term levels of noise which were registered at the levels of up to 90 dB (maximum noise) and 66.6 dBA (equivalent noise), respectively, were established at the investigated territories. At all the investigated territories the noise exceeded the values determined as the thresholds for occurrence of negative effects in the public health condition, including in relation to the nervous and cardiovascular systems as well as the hearing organs.

The building of the risk evolution models for the investigated territories demonstrated that the long-term staying in the conditions of continuous noise influence increases significantly the public health risks. The specified risk indexes at the level of chronic average annual noise exposure of 66.6 dBA achieved:

– the upper limit of range which characterizes the negligible risk ($\tilde{R} = 0{,}05$) at the duration equal to one year;

– the upper limit of range which characterized as the moderate risk ($\tilde{R} = 0{,}35$) – at the duration of exposure equal to 22 years;

– the upper limit of range which characterized as the high risk ($\tilde{R} = 0{,}60$) – at the duration of exposure equal to 32 years.

At other territories in the vicinity of airport where the chronic exposure levels exceeded 60 dBA also the high risks were registered (indexes more than 0.6) but the risks were formed in the later age periods (Fig. 8.3).

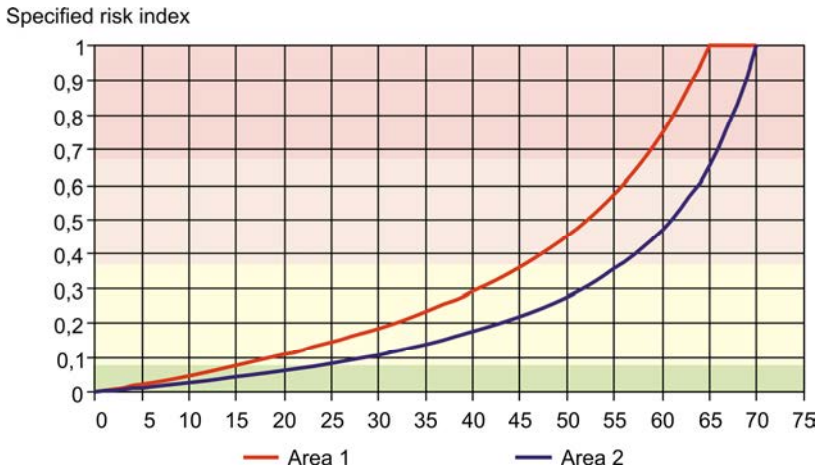

Fig. 8.2. The evolution of specified health risk index in the conditions of chronic chemical contamination of the ambient air by the complex of substances (two areas of investigation in the vicinity of airport)

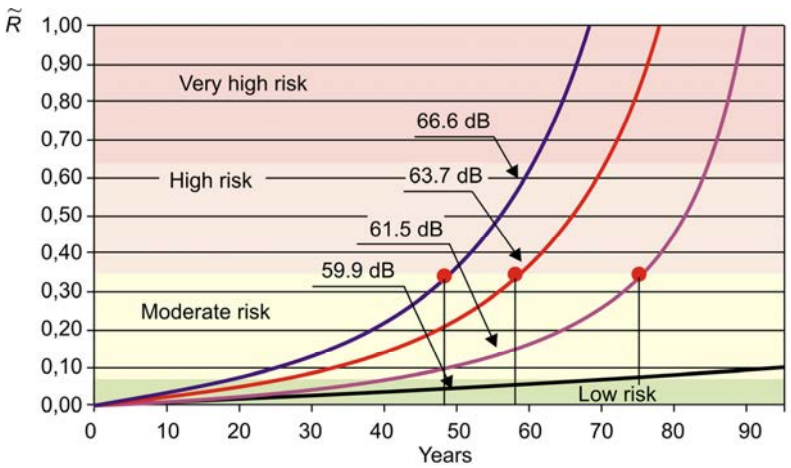

Fig. 8.3. The evolution of integral cumulative risk for development of cardiovascular and nervous systems as well as the hearing organs disorders in the people at the investigated territories when exposed to the noise factor

The integral risk assessments in the airport affected area demonstrated that at the main role of the harmful influence of noise factor the chemical hazard factors increase the total health disorders risk in the exposed population (Table 8.2).

The specified integral risk index evidences that the permanent residence in the conditions of chronic noise exposure at the level of 61–66 dBA and the contamination of ambient air with the complex of chemical impurities formed by the flights of aircrafts and work of the airport ground services results in the formation of the moderate health risks at the duration of exposure of 5–8 years, high health risks – at the duration of exposure of 30–35 years.

With distance from the airport the integral risk level decreases but in this situation the distance of 1200–2000 m does not provide the absence of moderate and high health risks. In addition, the questioning of people conducted within the investigation evidenced

that more than on half (57.5%) of 178 respondents from the area of the nearest to the airport residential construction noted that they every day pay attention to the noise from airplanes and from them about 13.2% feel extremely qualmish and 15% are afraid and shiver from the sound of flying airplane several times a month.

Table 8.2

The specified health risk indexes at the places of the permanent residence of population in the airport affected area

Age, years	Area 1 (66.6 dBA)			Area 2 (61.5 dBA)		
	Index formed by the chemical factors	Index formed by the noise factor	**Integral risk index**	Index formed by the chemical factors	Index formed by the noise factor	**Integral risk index**
0	0.000	0.000	0.000	0.00	0.00	0.00
5	0.015	0.029	0.034	0.013	0.020	0.022
10	0.031	0.066	0.071	0.028	0.043	0.049
15	0.050	0.113	0.128	0.044	0.072	0.081
20	0.072	0.175	0.197	0.062	0.106	0.120
25	0.098	0.258	0.289	0.084	0.150	0.169
30	0.128	0.372	0.413	0.109	0.206	0.233
32	0.142	0.412	0.475	0.120	0.234	0.264
33	0.151	0.460	0.509	0.126	0.248	0.280
34	0.158	0.502	0.545	0.132	0.264	0.298
35	0.166	0.530	0.584	0.138	0.281	0.317
40	0.213	0.755	0.825	0.174	0.382	0.431
44	0.250	…	…	0.209	0.491	0.554
45	0.275			0.219	0.524	0.601
46	0.326			0.255	0.559	0.628
50	0.357			0.278	0.727	0.817
55	0.473			0.356	0.864	…
60	0.646			0.471	0.921	

Note: green – negligible level of risk; yellow – moderate level of risk; orange – high level of risk; red – very high level of risk.

In this relation the decision on the dimensions of the sanitary protective zone of airport requires the accounting of data on the hazard for population and the normative fixation of procedure for the assessment and accounting of risks associated with the noise factor in the airport areas. The health risk structure analysis was performed for the tasks on justifying the sanitary-hygienic and medical-preventive measures which could reduce or mitigate the negative influence of the external environment factors.

In relation to the assessment of the contribution of hazard to the public health risks it is established that in the studied situation the risks are formed mainly as a result of negative noise effect. Herewith, according to the age and increase in the exposure duration the noise factor significance was growing. Thus, the ratio between the specified risk indexes of the sum of chemical factors and noise factor at the territory of the largest proximity to the airport was at the 5 years of exposure 1:1.9; at 10 years – 1:2; at 30 years 1:2.9, etc. Therefore, namely the noise elimination measures, including the transition to the low-noise types of aircrafts, shall be considered as priority in the system of primary preventive sanitary-hygienic measures.

In relation to the health disorders structure under the influence of the set of studied factors it was detected that the priority types of affections are the disorders of cardiovascular and central nervous systems. Herewith the health disorders structure for the citizens of different age is different (Fig. 8.4).

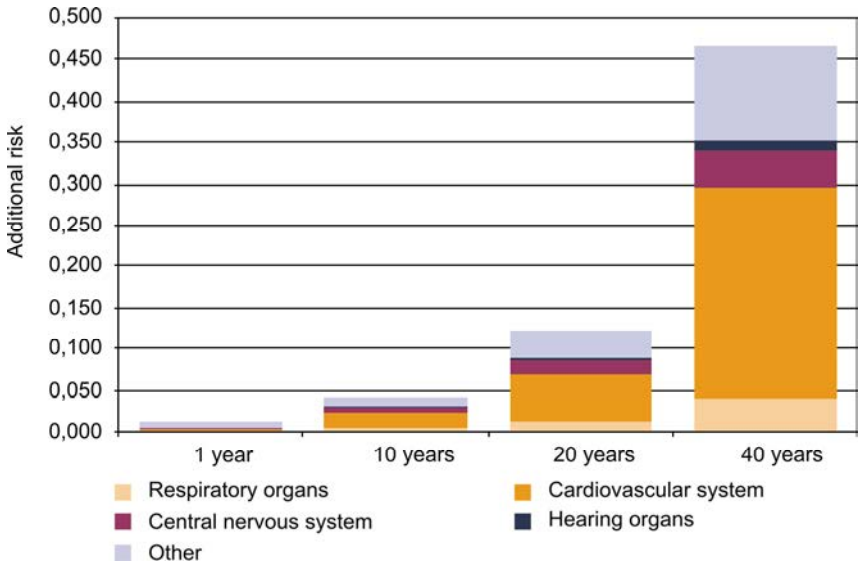

Fig. 8.4. The level and structure of additional risk to the health of citizens permanently residing at the territory of the largest proximity to the airport

In the area of the highest level of chronic exposure the contribution of the risk of cardiovascular system pathologies to the cumulative additional health disorder risk was: in the age of 10 years – about 12%, 20 years – 29%, 40 years – almost 50%. The priorities in these exposure conditions are also the central nervous system affections (contribution during the different periods of life and at the different exposure duration from 5 to 15% to the cumulative integral health risk) and respiratory organs function disorders (contributions from 5 to 10% to the total health risks).

With distance from the airport the noise exposure decreases significantly and the influence of chemical factors is expressed less, the contributions to the risks of cardiovascular system disorders are decreased and the contributions of risks of disorders of respiratory organs, endocrine system, blood and blood-forming organs affections are increased.

The obtained data confirm the necessity to form the targeted medical-preventive programs for population subjected to the negative influence of the living environment factors. Herewith it is necessary to take into account the structure of hazards, the duration of exposure and the age peculiarities of the exposed persons.

The results of health risk assessments in the Pulkovo airport affected area were used as the base for the special medical and biological examinations in the Moskovsky and Kirovsky districts of Saint-Petersburg in 2012 and development of personified recommendations for each examined patient. The same studies were transferred for use during the design of sanitary protective zone of facility.

Together with the Administration of the Federal Service on the Customers' Rights Protection and Human Well-being Surveillance for Sverdlovsk region we conducted the integral assessment of health risk associated with the complex influence of noise, chemical factors and lifestyle. The subject of study was the ambient air of territories located in Nizhny Tagil, drinking water, soil and population: children in the age of 3–7 years (going to the children's educational institutions) and adults (permanently residing in the districts) as well as the noise load on the population in the investigated districts. The study was carried out in the following districts of Nizhny Tagil: "Tekhposelok", "Vagonka", "Tsentr" (which includes the districts Krasny Kamen and Tsentr), the Galyano-Gorbunovsky massive was selected as the compared territory.

As a result of the public health risk assessment associated with chemical factors during the use in the calculation of exposure of the cross-spectrum analysis of design and field data the following is established:

– the highest hazard quotient (*HQ*) at the inhalation exposure is determined for formaldehyde: within 5.48 to 19.25 (the highest *HQ* is established for district "Tsentr"). For other substances *HQ* at the inhalation exposure was as follows: for manganese – from 1.53 to 3.27 (the highest *HQ* is established for district "Vagonka"), benzapyrene – from 1.00 to 1.45, suspended substances – from 1.36 to 1.71 and copper – from 2.08 to 11.57 (the highest *HQ* for these substances is established for district "Tekhposelok"), benzene – 1.41 (for district "Tsentr") and 1.70 (for district "Tekhposelok"); hydrocyanite – from 1.68 to 2.32 (the highest *HQ* is established for district "Tsentr").

In the investigated districts the specified substances for the hazard indexes (*HI*) for the respiratory organs disease – from 15,25 to 33.11; immune system – from 7.44 to 22.10, central nervous system – from 7.34 to 7.49; blood system – from 3.62 to 6.29 and cardiovascular system – from 1.41 to 4.99. The biggest contribution to the hazard index value for the diseases of immune system and respiratory organs is made by the formaldehyde – from 35.95 to 58.13% (for respiratory organs) and from 74.2 to 87.2% (for immune system). The contribution of other substances to the hazard indexes formation was as follows: manganese – from 20.53 to 45.6% (for central nervous system), benzene – from 27.1 to 44.3% (for development processes) and from 18.9 to 29.72% (for blood system), benzapyrene – from 31.4 to 35.9% (for development processes).

The calculated hazard quotients for the oral exposure of substances taken with water and soil are within the permissible values (*HQ*<1). In the conditions of oral intake of contaminants from drinking water and soil the influence of the studied substances formed the hazard indexes (*HI*) for the critical organs / systems <1.

The risk assessment at the combined and complex influence of chemical substances detected that in all the examined districts the inhalation is a priority route for the intake of substances forming the risk to health.

During the assessment of risk to the public health from the exposure to the transport noise according to the guidelines "Public health risk assessment when exposed to transport noise" it was established that in the investigated districts the unacceptable (moderate) level of aggregate risk of diseases of circulation organs, nervous system and hearing organs for population is formed at the average lifespan. For compared territories the levels of health risk disorders under the influence of existing noise exposure do not differ from the background.

During the approbation of methods for assessing the risk associated with the influence of lifestyle factors on the health of population presented in MP 2.1.10.0033–11 "The assessment of risk associated with the influence of lifestyle factors on the health of population" it was established that the regular tobacco smoking factor was recognized as the priority factor having the highest health effect. The action of such factors as alcohol abuse and malnutrition is not critical, i.e. these factors to a minimum degree affect the health of respondents. It is established that the unacceptable level of additional risk of the ischemic heart disease development associated with the tobacco smoking factor effect (provided that the intensity of factor – intake to the body of smoker per day remains unchanged) will be achieved by 58 years with value of 0.00109, and by 61 year it will make up 0.0015. The results obtained during the conducted study characterize completely the selected group of respondents (women in the age of 39–41 years). All the submitted data and conclusions concern namely this group of population of Nizhny Tagil. At the same time the results of study can be considered as the characteristics of tendencies for the formation of health risk associated with the lifestyle at the investigated territory.

As a result of in-depth medical examinations performed by the specialists of "Federal scientific center for medical and preventive health risk management technologies" the implementation of the high risk of immune system diseases is established: we detected the non-specific body sensitization (increase in the relative number of eosinophils, eosinophilic-lymphocytic index), credibly high indicators of phagocytosis (phagocytic index, relative phagocytosis, phagocytic number), increased content of total IgE and intercellular immune

regulation mediators (IL-17, IL-10), credible decrease of content (IgM, IgA, IgG), as well as the increased level of specific sensitization to formaldehyde. The atopic dermatitis was credibly often diagnosed in the district "Tsentr".

The cardiovascular diseases risk from the influence of substances (benzene, hydrogen cyanide, carbon monoxide) is implemented by the functional cardiopathy diagnosed 4.35 times often than in children residing in the compared district. The laboratory and functional studies established the changes in the vegetative myocardium regulation, vegetative regulation disorders, disorder in the function of vascular endothelium ensuring the vascular regulation (increased content of ApoV/ApoA-1, decreased content of nitrogen oxide, increased content of highly sensitive C-reactive protein in the blood serum).

The risk of the central nervous system disorders from the influence of substances (manganese, benzene, hydrogen cyanide): during the clinical and laboratory examination we established the delay in the fine motor skills development, the stress of the compensatory mechanisms of nervous system; the disorder of the exchange of neuromediators regulating the central nervous system suppression.

The implementation of the high risk of respiratory disease from the influence of chemical substances (formaldehyde, copper, manganese) is established in the form of credibly higher than in the compared district levels of the prevalence of the hypertrophy of adenoids and tonsils, tracheitis and bronchitis. Under the results of spirography we detected the decrease in the vital capacity of lungs by 1.3 times, restrictive and obstructive disorders of the external breathing function.

The epidemiological analysis of the results of in-depth studies for the applications of children for medical assistance confirmed the data obtained during the in-depth medical examinations on establishing the changes in the health condition and demonstrated the credible relationships of children diseases with the residence in all the investigated districts: respiratory diseases (*OR*=1.08), diseases of the skin and subcutaneous tissue: *OR*=1.27–1.52; diseases of the circulatory system: *OR*=4,94 (with residence of children in the investigated district "Tekhposelok") and *OR*=5.51 (in the investigated district "Tsentr"); diseases of blood, blood-forming organs and separate disorders involving the immune mechanism – in the district "Tekhposelok" (*OR*=4.01); and in the district "Vagonka": congenital anomalies (developmental defects) (*OR*=4.15); nervous system (*OR*=1.59).

The high risk of immune system diseases from the influence of chemical substances (formaldehyde contribution from 74.2 to 87.2%) is implemented in the form associated with residence in the districts with increased aerogenic risk of additional applications under the separate nosologic forms. They include: atopic dermatitis (*OR*=10.32 – in the district "Vagonka", *OR*=10.32 – district "Tsentr" and *OR*=2.07 – district "Tekhposelok") and urticaria fever (*OR*=10.32 – in the district "Vagonka"). The expected number of additional cases of diseases with atopic dermatitis will make up 119 diseased per year – in the district "Vagonka", 72 – in the district "Tsentr" and 87 – in the district "Tekhposelok"; urticaria fever – 56 diseased per year in the district "Vagonka".

The implementation of the high risk of respiratory diseases from the influence of chemical substances (formaldehyde, copper, manganese) is confirmed in the form of morbidity under the applications with separate nosologic forms associated with the residence of children in the district "Vagonka": the hypertrophy of tonsils (*OR*=14.16), laryngitis, tracheitis (10.61), asthma (35.81) and nasopharyngitis (1.12) – in the district "Vagonka". The additional applications under these nosologic forms will make up: the hypertrophy of tonsils (up to 544 diseased per year), laryngitis, tracheitis (up to 768), asthma (up to 264), nasopharyngitis (up to 256).

The risk of cardiovascular system diseases from the influence of substances (benzene, hydrogen cyanide, carbon monoxide) is confirmed by the credible relationships of morbidity under the applications with cardiomyopathy and residence of children in the districts "Tekhposelok" (*OR*=4.94) and "Tsentr" (*OR*=5.08). The expected number of additional cases of diseases will make up: 11 diseased per year - in the district "Tekhposelok" and 19 – in the district "Tsentr".

The morbidity of children with diseases of blood, blood-forming organs and separate disorders involving the immune mechanism (iron deficiency anemia) is established only in

the investigated district "Tekhposelok" *OR*=4.01). Herewith the health risk for the blood system in all the investigated districts is determined as high.

The mathematical simulation resulted in the description of expected health risk evolution under the influence of living environment and lifestyle factors for the scenario of exposure established in the investigations during the whole life.

The building of model is based on that the body is permanently cooperating with environment and consists of many target organs interrelated with each other. The negative effects risk evolution is described by the system of differential equations which reflects the accumulation of functional disorders associated with the affective action of the environment factors on the background of natural processes in the human body. The accumulation of risk of negative effects for the critical organs/systems due to the influence of factors is taken into account that allows carrying out the forecasting of integral risk of health disorders at any moment of time. The model does not include the factors for which were no credible simulation factors. The simulation included the following factors: carbon monoxide, nitrogen dioxide, suspended substances, ozone, sulfur dioxide, formaldehyde, nickel, noise, chloroform and cadmium in water, lifestyle factor – smoking (influence of factor "smoking" is included to the model from 18 years and the level of nicotine in vivo intake – under the results obtained during the conducted sociological study of the population in Nizhny Tagil).

The example of curve for the change in the integral risk of health disorders in the conditions of harmful complex influence of noise, chemical factors and lifestyle in the investigated districts is shown in Fig. 8.5.

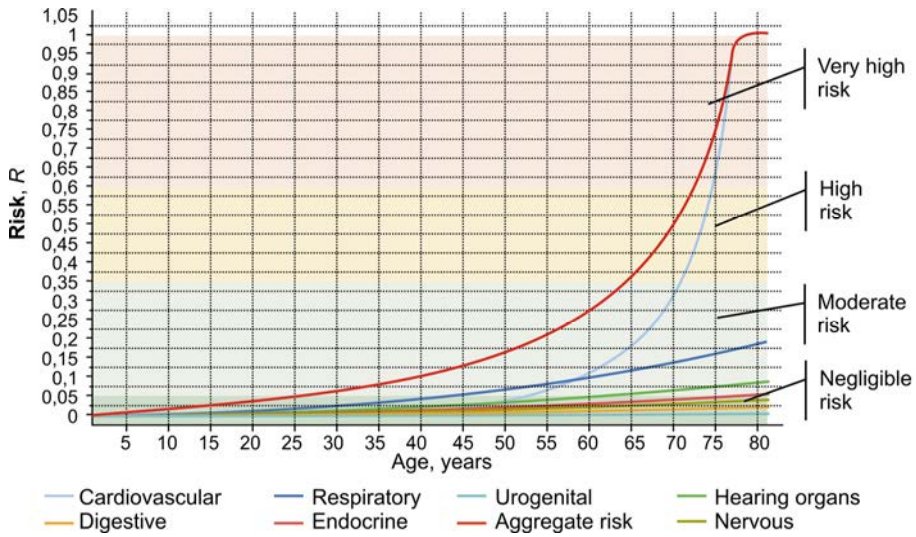

Fig. 8.5. The model of change in the integral health risk at the complex influence of noise, chemical factors and lifestyle in the district "Tsentr"

Under the results of evolution simulation it was established that the integral risk of health disorders in the conventionally clear district "Galyano-Gorbunovsky massive" is considered as the acceptable to the age of 37 years. The complex action of noise, chemical factors and lifestyle forms the unacceptable risk in the district "Tsentr" by the age of 26, and in the district "Tekhposelok" – by the age of 27, in the district "Vagonka" – by the age of 35. The main contribution to the integral risk in all the investigated districts to 56–60 years is made by the expected disorder of the respiratory system functions: up to 56 years – in the district "Tekhposelok", up to 58 – in the district "Tsentr", up to 60 – in the districts "Vagonka" and "Galyano-Gorbunovsky massive", after the specified age – of cardiovascular system. At

the considered exposure scenario the expected lifespan will be reduced: in the district "Tsentr" – by 6 years, in the district "Tekhposelok" – by 7, and in the district "Vagonka" – by 5.

The priority factors under the health disorder criterion for all the investigated districts are the smoking, formaldehyde, suspended substances and noise. The contribution of priority risk factors to the integral risk value in the investigated districts is presented in Table 8.3. In all the districts the largest contribution to the aggregate risk is made by the factor "smoking" (from 37.63 to 70.31%). For the districts "Galyano-Gorbunovsky massive" and "Vagonka" the second place under the contribution to the aggregate risk is taken by formaldehyde (21.26 and 23.50%, respectively). For the districts "Tekhposelok" and "Tsentr" the formaldehyde under the contribution to the aggregate risk occupies the third place and makes up from 17.41 to 18.84% (the second place is occupied by the suspended substances). The noise in the contribution to the aggregate risk in all the investigated districts occupies the fourth place.

Table 8.3

The structure of the contribution of priority risk factors to the integral risk value in the investigated districts, %

Item No.	Factor	Districts			
		Vagonka	Tekhposelok	Tsentr	Galyano-Gorbunovsky massive
1	Smoking	61.33	37.63	40.20	70.31
2	Formaldehyde	23.50	17.41	18.84	21.26
3	Suspended substances	13.48	24.73	20.57	5.16
4	Noise	1.65	11.51	13.90	3.23

According to the results of conducted hygienic study on the assessment of integral health risk in Nizhny Tagil, we developed the recommendations for the bodies of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance and municipal administration on the conduction of preventive measures aimed at the health risk mitigation. These recommendations except for the established priorities for monitoring and supervision include the program of medical-preventive measures and informing of the target groups of population.

8.2. Occupational risks

The harmful production environment factors can cause not only the occupational diseases but also can act as the pathogenetic mechanism of development and progression of common diseases not included into the occupational ones.

The degree of occupational conditionality of health disorders can be established using the occupational risk assessment methodology which is aimed at the establishment of dependence "harmful action – result" that is finally expressed in the determination of the harmful action on the certain workers of certain professional groups. The occupational risk assessment system allows obtaining the quantitative and qualitative characterization of the action of factor of health based on the observation over the factors of working conditions and health of working population much earlier than the negative consequences of this action will be revealed. It is acknowledged that the liquidation of all risks is not always possible. The whole risk assessment procedure is based on the assessment of possible consequences.

In Russia when implementing the risk concept in the labor medicine it is necessary to be guided by the provision that any type of labor and life activity in the production and ambient environment is associated with possibility of harmful effects of health the quantitative assessment of which is determined by the risk value. This approach provides the residual risk

availability. Its allowability (acceptability) is determined by the social, economic and moral (deontological) criteria and possibilities of prevention [Izmerov N.F. et al., 2002].

In relation to labor medicine the occupational risk is considered in the aspect of the establishment of the qualitative and quantitative regularities of the occurrence of occupational and occupationally stipulated morbidity and the development of methods for its diagnostics and mechanisms for its prevention. Herewith the factors of production environment (noise, vibration, chemical and biological substances, temperatures, etc.) and labor process (labor intensity, lifting and transportation of cargo, etc.) are studied as the health affection sources.

The cardinal tasks are not only the detection (identification) of hazardous and harmful to health factors but also the justification of their quantitative levels which in relation to the modern science and practice can be considered as the indicators of harmlessness and danger. The deviation of the production environment and labor activity parameters from these criteria can be used for the quantitative determination of risks and development of preventive measures.

The Research Institute of Occupational Health affiliated to the Russian Academy of Medical Sciences developed the hygienic classification of working conditions (under the leadership of N.F. Izmerov) and executed the manual P 2.2.2006-05 which is officially approved by the Federal Service on Customers' Rights Protection and Human Well-being Surveillance. The manual is used also for the occupational risks assessment.

The following is used in the domestic practice as the risk assessment criteria:

- hygienic (prior);
- health condition (posterior);
- relationship between the health disorders and work.

The assessment of risks and hazards includes three stages.

First stage is a detection of hazards and risks (types of works and production factors).

Second stage is an analysis and assessment of risk (testing and measurement; the determination of exposure (under the measurement or calculation) and risk assessment.)

Third stage is a risk management (the elimination of hazard or its reduction to the minimum permissible level or to the level which in relation to the modern knowledge will not result in the health disorders during the duration of exposure during the whole work experience).

The categories of occupational risk and the urgency of measures on its mitigation are determined during the hygienic (prior) risk factors assessment (classes of labor conditions) (P 2.2.1766-03) (Table 8.4).

Table 8.4

Hygienic (prior) occupational risk assessment

The class of labor conditions	The category of occupational risk	The urgency of measures on the risk mitigation
Optimum – 1	No risk	Measures are not required
Acceptable – 2	Negligible (endurable) risk	Measures are not required but the affected persons require additional protection
Harmful – 3.1	Small (moderate) risk	Measures on the risk mitigation are required
Harmful – 3.2	Moderate (significant) risk	Measures on the risk mitigation within the established terms are required
Harmful – 3.3	High (intolerable) risk	Urgent measures on the risk mitigation are required
Harmful – 3.4	Very high (intolerable) risk	It is forbidden to start or continue the work before the risk mitigation
Hazardous (extreme)	Super high risk and risk for life inherent to this profession	Works shall be performed only according to the special regulations

The key moment during the occupational risk assessment is the establishment of relationship between the influence of risk factor (toxic substance taken into the body, the level of noise and vibration, etc,) and its influence of the health of worker. That is the main attention is paid to the assessment of the level of effect of harmful factor to the workers and assessment of the frequency of disease development in the professional groups.

In Russia during the assessment of risk to the health of workers under the influence of production factors the scheme commonly used in the world is observed. The risk assessment includes the detection (identification) of hazard, exposure assessment and risk characterization.

The hazard identification provides the establishment of factors affecting the health and negative effects from their influence on health and diseases in the development of which these effects can result (i.e. to analyze the routes and biological peculiarities of their influence).

To assess the exposure (risk degree assessment) it is necessary to establish the quantitative indicators of detected occupational risk factors, including the comparison of quantitative indicators to the hygienic labor classification criteria. Herewith the forecast of consequences to health in case of non-observance of hygienic criteria is conducted taking into account the normative levels exceedance value.

The risk degree assessment includes the forecast of probability for the development of occupational and occupationally stipulated diseases in workers. The data of epidemiologic studies, hygienic and clinical observations or developed standards, separate programs and projects are used for this purpose. For example, the electronic interactive directory guide "The occupational risk assessment" (under the editorship of of the member of the Russian Academy of Medical Sciences N.F. Izmerov and professor E.I. Denisov) provides the occupational risk assessment in the form of forecast for the probability of health disorders from the action of production factors. It contains the information about the harmful factors, groups of risk, possible health disorders, their probability or degree of their relationship with work.

The domestic model for the forecasting of the occupational diseases development which is developed by the Research Institute of Occupational Health affiliated to the Russian Academy of Medical Sciences and includes the calculation of the occupational diseases index ($И_{ПЗ}$) exists and is used actively in practice. The calculation of indicator is carried out under the formula

$$И_{ПЗ} = 1/(К_р К_т), \quad (8.1)$$

where $К_р$ – is a risk category under the posterior probabilities; $К_т$ – is a category of severity of occupational disease which is taken from the medical forecast of disease and type of incapacity.

$И_{ПЗ}$ index includes both the probabilistic risk extent and the occupational disease severity degree. The use of reciprocal value of the product of these categories allows the qualitative and quantitative assessment of the most important features of occupational diseases in the form of integral indicator. At the multifactorial effects the index allows assessing of both every disease and their combination because the indexes are summarized in the probability of simultaneous development of forms of occupational diseases. $И_{сум} = \Sigma И_i$ [Izmerov N.F. et al., 2002].

Also the occupational risk index calculation is used:

$$\text{ORI} = \sum_{i=1}^{n} N_i K_i / NL, \quad (8.2)$$

where K_i – is an occupational disease severity category;

N_i – is a number of occupational diseases in each category of severity;

N – is a number of members in group;

L – is a number of years of observation.

The occupational risk structure and degree analysis can be included into the first stage of detection of diseases associated with work. There are many quantitative risk measures. The most often used measures are as follows:

– oddis ratio – *OR*, i.e. the coefficients for the probability of disease and its absence in the exposed and control groups;

– relative risk – *RR*, i.e. the relation of the frequencies of disease in the exposed and control groups;

– etiological fraction – *EF*, i.e. the proportional introduced risk at the expense of action of this factor.

Under the relative risk it is possible to assess the degree of occupational stipulation for the health disorders. The degree of this stipulation depends on the difference of compared groups reflecting the dependences "exposure – effect". Table 8.5 contains the classification of the degrees of occupational stipulation for the health disorders depending on the relative risk.

Table 8.5

The degrees of occupational stipulation for the health disorders depending on the relative risk (compared to control)

The degree of stipulation	Relative risk, *RR*	Etiological fraction, *EF*, %
Absent (zero)	$0 < RR \leq 1$	0
Small	$1 < RR \leq 1{,}5$	Less than 33
Medium	$1.5 < RR \leq 2$	33–50
High	$2 < RR \leq 3.2$	51–66
Very high	$3.2 < RR \leq 5$	67–80
Almost complete	$RR > 5$	81–100

This scale reflects the differences in the frequency of disorders determining the measure of causation, pathogenetic stipulation of the signs of disease [Izmerov N.F., 2002].

Also the risk assessment in the organization is performed taking into account all the expenses conducted in the organizations of sector (subsector) due to the occupational diseases and industrial accidents in the past year. According to the Resolution of the Government of the Russian Federation No. 713 dd. December 1, 2005 (as revised dd. December 31, 2010) the class of occupational risk is determined under the value of integral indicator of occupational risk taking into account the level of occupational traumatism, occupational morbidity and expenses on the insurance security in accordance with types of economic activity of the insured. The occupational risk integral indicator (Ип) calculation is performed; this indicator is determined as the relation of the value of cumulative expenses in the sector (subsector) of economy for the compensation in the past calendar year of harm inflicted to the insured due to he accidents and occupational diseases (the benefits in case of temporary incapacity to work, wage loss indemnity, non-recurrent and monthly insurance payments, expenses for medical, social and professional rehabilitation) to the size of payroll fund in this sector (subsector) of economy for which the contributions to the Social Insurance Fund of the Russian Federation (SIF RF) are charged. The level of SIF RF payments is connected to the level of salary of injured and the duration of payments depends on the severity of injury (occupational disease).

In general, the modern methodical approaches are characterized by the possibility to assess the occupational risk associated with the action of separate chemical, physical, behavioral and other factors. The presence of cause-and-effect relationships between the occupational factors, functional condition and morbidity stimulates the search for methods and means to clarify these possibilities contributing to the more effective forms of preventive work. One of the most prospective directions in the labor medicine is the development of methodology allowing the complex assessment and forecasting of health indicators together with integral parameters of industrial factors and functional stress of the body of workers in response to the work load.

The mathematical simulation of dependence "exposure – effect (response) – work experience" for negative effects and diseases associated with the occupational risk factors contributes to solving the task of quantitative risk assessment for the health of worker, forecasting in the health condition changes dynamics stipulated by the influence of industrial factors.

The results of the use of such type of simulation for the risk of diseases associated with work at one of the mining industry enterprises can be taken as an example. The results of epidemiological analysis demonstrated that for the operators of mining winning machines the relative risk of respiratory diseases during the work in the existing labor conditions is: at the work experience of less than 5 years – *RR*=1.75, etiological fraction *EF*=42.86 % (average degree of occupational stipulation); at the work experience of more than 20 years – relative risk transfers to the next degree of relationship of health disorders with work (2<*RR*≤3,2) and is *RR*=2.67, etiological fraction *EF*=62.50 % (high degree of occupational stipulation). The example of graphical three-dimensional model is shown in Fig. 8.6. Under the results of simulation it was established that during the work in the existing labor conditions (the sylvinite dust concentration – 61.2 mg/m^3) the diseases development risk level already at the first year of work is 0.176 and increases to the 5 years of work experience to 0.208. The number of additional cases of diseases for the investigated group of workers will make up 24 cases to the end of the first year of work and will amount to 29 cases per year after the 5 years of work experience. This is confirmed by the experience determination in the development of chronic rhinitis and rhinopharyngitis (J30-J31).

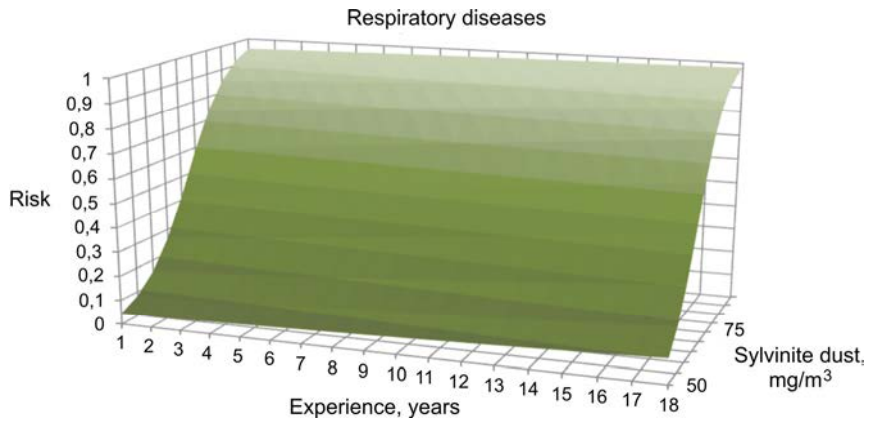

Fig. 8.6. The model of dependence "exposure – experience – response" for the respiratory diseases

The limited abilities of statistical models, mainly the pair ones, do not allow solving completely the task of quantitative assessment of the whole aggregate of negative effects from the side of health associated with the action of factors of labor conditions. The development of existing occupational risk assessment methodology offers the analytical approaches based on the combination of determined and stochastic simulation allowing conducting the numerical (virtual) experiments which are difficult to reproduce in real and, that is more important to the health risk analysis, assessing of the risk of negative effects under the established exposure scenarios [Zaytseva N.V. et al., 2013].

The evolution models which take into account the certain conditions of the work places contamination and reflect the influence of the set of different factors on the risk for development of different health disorders depending on the experience and duration of exposure are the most effective for the health risk assessment tasks The methodical approaches to the health risk assessment based on the evolution models of the negative effects development under the influence of labor conditions factors provide the possibility to trace the dynamics of these effects development on the background of the natural body aging and forecast the health condition for human and subpopulation under the conditions of multifactorial and multi exposure load.

Thus, at the nonferrous metallurgy enterprise at the work places the concentration of chlorine and hydrochloride vapors exceeds the maximum permissible concentration by 9.92 and 6.7 times, respectively; at all the work places the level of noise achieves 81–87 dBA that by 1–7 dBA exceeds the maximum permissible level; the total level of vibration exceeds the maximum permissible level by 1.4 and 1.7 times, the micro climate parameters determine the heating micro climate in summer and cooling – in winter.

The health risk evolution simulation in the conditions of combined harmful action of industrial factors demonstrated that the health disorders risk without the influence of industrial factors is considered as acceptable up to 54 years. The influence of industrial factors on the workers in shop forms the unacceptable risk already by 45 years (Fig. 8.7).

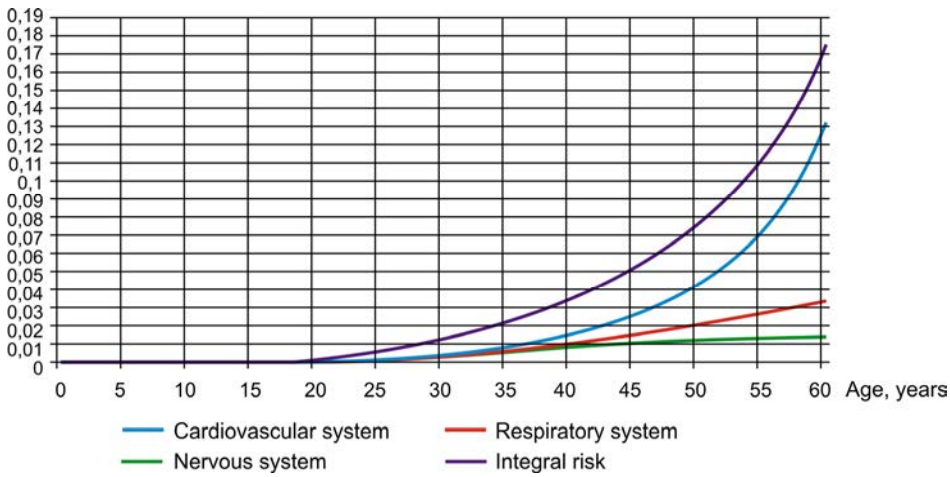

Fig. 8.7. Health risk evolution model when exposed to the industrial factors (shop workers)

When assessing the occupational risk of somatic (non-infectious) diseases which can be associated with labor conditions it is necessary to take into account that the lifestyle factors can contribute to the development of these types of pathology in workers. The human health condition is determined by his lifestyle, exposure to the behavioral risk factors which can intensify the action of industrial risk factors. Namely the social factors can potentiate and increase the influence of labor conditions of health forming the increased risk of occupationally stipulated diseases development. It is necessary to take into account the whole complex of adverse factors of labor conditions and lifestyle affecting the health condition.

Also the development of methodical approaches to the assessment of risk for the health of workers associated with the influence of the separate occupational hazard factors is quite essential. They include the dust factor. The occupational diseases associated with the action of aerosols, pneumoconiosis and pneumosclerosis, chronic dust bronchitis during a number of years occupy the one of the leading places under the frequency among the occupational diseases in Russia.

In the real industrial conditions at the control of the content of predominantly fibrogenic action aerosols (PFAA) in the air of work area it is necessary to take into account all the fluctuations of their content during the work shift that is reflected in GOST R 54578-2011 "Predominantly fibrogenic action aerosols". According to GOST R 54578-2011 at the maximum permissible concentration exceedance MPC_{cc} (mean-shift maximum permissible concentration of dust in the worker breathing zone) it is necessary to calculate the total dust load (DL) on worker, including the fluctuations K_{cc} (actual mean-shift concentration of dust in the worker breathing zone) during the whole period of professional contact with PFAA. DL is a product of the actual mean-shift concentration of dust in the

worker breathing zone, the duration of the contact of worker with PFAA (years), number of work shifts worked in the calendar years under the PFAA influence and pulmonary ventilation rate per shift (m^3).

The obtained DL value is compared to the control dust load (CDL) which is a product of actual mean-shift concentration of dust in the worker breathing zone, the duration of the contact of worker with PFAA (years), the number of work shifts worked in the calendar years under the PFAA influence and pulmonary ventilation rate per shift (m^3).

According to the results of the comparison of actual dust load to the control dust load the labor conditions are included either to the permissible safe or to the harmful class of labor conditions.

According to GOST R 54578-2011 the probability for development of PFAA-induced occupational diseases during the work in the conditions of the first "double" harmful class of labor conditions (3.1+3.2) is not more than 10–15%; during the work in the conditions of the second "double" class (3.3+3.4) – not more than 40–50%. It is feasible to carry out the individual assessment for the risk of occupational lung disease of dust causation based on the analysis of the dust pathology occurrence probability evolution.

The assessment for the individual risk of occupational lung disease associated with the PFAA action is performed based on the calculation of indicator which includes the disease development probability and its severity as the health damage characteristics. The values recommended by the WHO experts (1994) are used as the values of the disease severity coefficients: g=0.4 – for pneumoconiosis; g=0.5 – for chronic respiratory diseases.

It is feasible to carry out the calculation for the probability of the development of the occupational disease of dust causation based on the evolution model analysis. The evolution model is represented in the form of recurrent ratios allowing organizing the iteration calculation procedure under the time steps and reflecting the change in the probability of diseases associated with the deleterious action of dust factor.

$$P_{t+1} = \begin{cases} P_t + \beta\left(\dfrac{qKc_i}{\mathrm{MPC}_i} - \dfrac{1}{3}\right)C, \ \text{если } 0 < P_t + \beta\left(\dfrac{qKc_i}{\mathrm{MPC}_i} - \dfrac{1}{3}\right)C < 1, \\ 0, \ \text{if } P_t + \beta\left(\dfrac{qKc_i}{MPC_i} - \dfrac{1}{3}\right)C \le 0, \\ 1, \ \text{if } P_t + \beta\left(\dfrac{qKc_i}{\mathrm{MPC}_i} - \dfrac{1}{3}\right)C \ge 1, \end{cases} \quad (8.3)$$

where P_{t+1} – is a probability of occupational disease development at the time step t+1;

P_t – is a probability of occupational disease development at the time step t;

β – is a coefficient characterizing the change in the probability of disease at the expense of dust and depending on the level of fibrogenity. For low fibrogenic dusts β =0.0021, for high/moderate fibrogenic dusts β =0.005;

Kc_i – the average concentration of dust for substance i for a period of time corresponding to the time step in the worker breathing zone, mg/m^3;

MPC_i – the maximum permissible concentration of dust for substance i in the worker breathing zone, mg/m^3;

q – is a coefficient which depends on the labor intensity, reflects the probable dose, proportional to the pulmonary ventilation rate per shift and taken as equal to: 0.4 – for light works; 0.7 – for works of average severity; 1 – for hard works.

K – time empirical coefficient corresponding to the time step.

The ratio (8.3) is applicable to the dusts belonging to the one fibrogenity group. If the worker breathing zone contains the dusts belonging to the different fibrogenity groups, it is necessary to perform the separate calculations for each dust group.

The recurrent ratios allow for the gradual calculation of value for the probability of disease at the different time steps, starting from the initial level. The initial level for the probability of the development of occupational disease associated with the deleterious action of dust factor complies with zero experience in the PFAA exposure conditions and is equal to zero:

$$P_0 = 0. \tag{8.4}$$

Based on the ratio (8.3) and initial level (8.4) it is necessary to perform the subsequent calculations at the following time steps: P_1, P_2, P_3, P_4, etc.

The time step selection during the performance of calculation with the use of recurrent ratios depends on the exposure settlement detailing. At the permanent dust exposure during the whole work experience the time step is selected as equal to 1 year. When setting the exposure variable the time step shall comply with the circularity period, i.e. if there are the cycles of changes for the dust concentration values of more than 1 month the step of 1 month is selected, in case of changes during one week or month – 1 day, in case of changes during shift – 1 hour.

The average dust concentration for the period of time (K_{ci}) corresponding to the time step is calculated under the formula

$$K_{ci} = \frac{\sum_{t=0}^{n} K_{ti}}{n}, \tag{8.5}$$

where K_{ti} – is a dust concentration of substance i for hour t, mg/m^3;

n – is a number of hours corresponding to the time step.

The method for the calculation of the probabilities of occupational diseases associated with PFAA action based on the recurrent ratios provides the possibility to take into account the irregular character of the dust factor exposure in time; herewith not only the exposure variables during the shift but also the duration of intervals between the shifts is taken into account.

The following scale is accepted for the occupational risk assessment:

$0–1\cdot10^{-3}$ – small (moderate) risk (in the manual P 2.1.10.1920-04 individual risk during the whole life of more than $1\cdot10^{-4}$, but less than $1\cdot10^{-3}$ is specified as an acceptable for the professional groups);

$1\cdot10^{-3} – 1\cdot10^{-2}$ – average (significant) risk;

$1\cdot 10^{-2} – 1\cdot10^{-1}$ – high (intolerable) risk;

1 – very high (intolerable) risk.

The example for the calculation of the risk of lung dust diseases in workers in the conditions of permanent exposure to the vanadium-containing dusts is specified below.

The calculation is performed for three possible exposure scenarios:

– first scenario K_{cc} =4 mg/m^3 (the level of maximum permissible concentration);

– second scenario K_{cc} =5.5 mg/m^3 (negligibly higher than the level of maximum permissible concentration);

– third scenario K_{cc} =20 mg/m^3 (the five-fold exceedance of exposure level).

The calculation is provided from the beginning of work experience for 20 years at the high level of labor intensity (*q=1*). The value K_{cc} for each scenario is considered as unchanged during the whole work experience (Fig. 8.8). In this case it is feasible to perform for each scenario the calculation with the time step 1 year (*C=1*). The average annual concentration can be determined under the formula

$$K_c = \frac{K_{cc} \cdot n_1 \cdot n_2}{24 \cdot 365}, \tag{8.6}$$

where n_1 – is a duration of shift, hours;

n_2 – number of shifts per year.

At n_1=8 hours and n_2=251 shifts, K_c=K_{cc} 0.23. Then K_c for the first scenario will be equal to 0.92; for the second – 1.265, for the third – 4.6. The average annual dust exposure distribution by time is shown in Fig. 8.8.

The vanadium-containing dusts belong to low fibrogenic that is why β =0.0021. The occupational disease development probability is determined under the ratio

$$P_{t+1} = P_t + 0{,}0021\left(\frac{K_c}{4} - \frac{1}{3}\right)1 \qquad (8.7)$$

with initial value $P_{t=20}$=0.

Because the chronic bronchitis severity is g=0.5, the occupational disease development risk is determined under the formula $R = P_t$ 0,5.

The chart for changes in the risk of chronic toxic bronchitis is shown in Fig. 8.9.

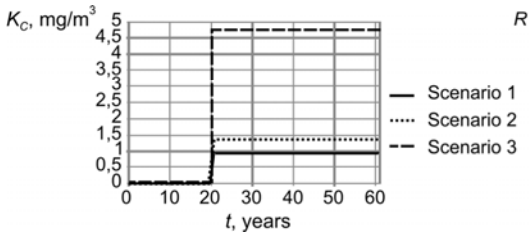

Fig. 8.8. The dependence of average annual concentrations of vanadium-containing slags and dusts in the worker breathing zone on the time and level of exposure

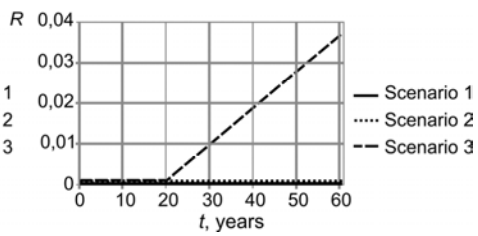

Fig. 8.9. The dependence of the risk of disease with chronic toxic bronchitis on the time and level of exposure

The options of calculation with more frequent time steps are specified below. The time step of 1 day is characterized by the change of exposure with weekly circularity. In this case at the standard working week during the working days (Monday – Friday) the average daily concentration K_c=K_{cc} 0.33, on week-end (Saturday – Sunday) K_c=0. Such setting of exposure is presented graphically in Fig. 8.10; herewith the risk dynamics is presented in the form of broken line (Fig. 8.11).

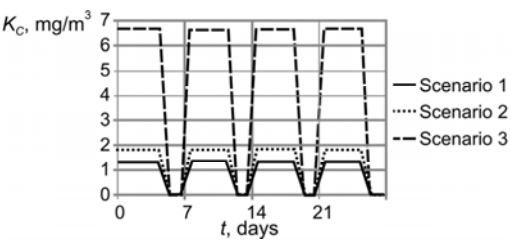

Fig. 8.10. The dependence of the average daily concentrations of vanadium-containing slags and dusts in the worker breathing zone on the time (day-by-day averaging) and level of exposure

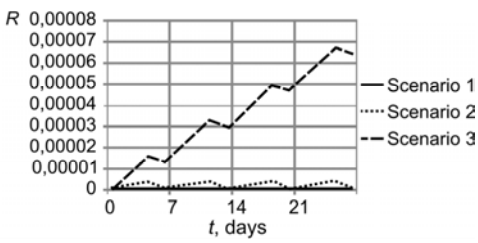

Fig. 8.11. The dependence of the risk of disease with chronic toxic bronchitis on the time (day-by-day averaging) and level of exposure

The figures represent the dynamics of indicators since the beginning of labor activity. Because the average shift exposure is permanent, the performance of calculations with time step of 1 day during the whole calculation period will lead to the results presented in Fig. 8.11.

In case of permanently acting dust factor exposure or at the availability of long experience intervals with permanent exposure it is possible to calculate the risk for occurrence of occupational diseases in worker using the simplified methods. The simplified methods are aimed at the previously prepared tables containing the values for the risk of occurrence of occupational disease in worker depending on the experience and level of exposure in relation to the maximum permissible concentration.

The exposure calculation is performed based on the determination of average annual relative dust load coefficient under the ratio

$$\text{КПН} = \frac{K_{cc}}{\text{ПДК}} \frac{n_1}{24} \frac{n_2}{365} q, \tag{8.8}$$

where DLC – is an average annual relative dust load coefficient;

K_{cc} – is an average shift concentration;

n_1 – is a duration of shift, hours;

n_2 – is a number of shifts per year;

q – is a coefficient which depends on the labor intensity, reflects the probable dose, proportional to the pulmonary ventilation rate per shift and taken as equal to: 0.4 – for light works; 0.7 – for works of average severity; 1 – for hard works.

Based on the DLC value and work experience in the conditions of permanent exposure under the nomographic charts presented in Fig. 8.12–8.15 the value for the risk of occurrence of occupational disease in worker is determined. The disease risk is calculated as the ordinate of line corresponding to DLC (exposure) with abscissa corresponding to the worker experience.

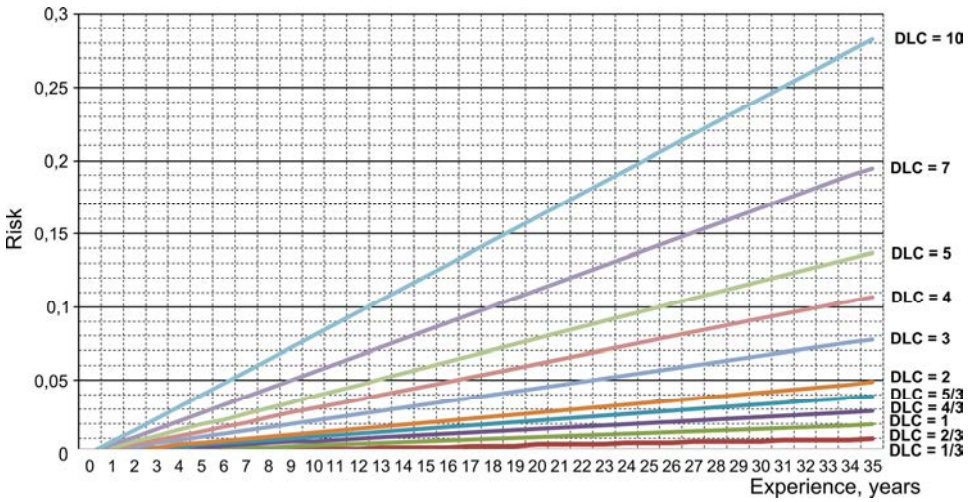

Fig. 8.12. Disease risk values depending on the time and exposure to PFAA (low fibrogenic dusts), disease severity: 0.4

If the calculated DLC value is absent in the submitted nomographic charts, the risk of occurrence of occupational disease in worker is calculated using two adjacent DLC of risk under the formula

$$R = R_H + \left(\frac{\text{КПН} - \text{КПН}_H}{\text{КПН}_B - \text{КПН}_H} \right) (R_B - R_H), \tag{8.9}$$

where DLC – is an average annual relative dust load coefficient;

DLC_H – is a lower value of DLC in table;

DLC_B – is a higher value of DLC in table;

R_H – the risk of occupational disease development corresponding to the lower value of DLC in table (DLC_H);

R_B – the risk of occupational disease development corresponding to the higher value of DLC in table (DLC_B).

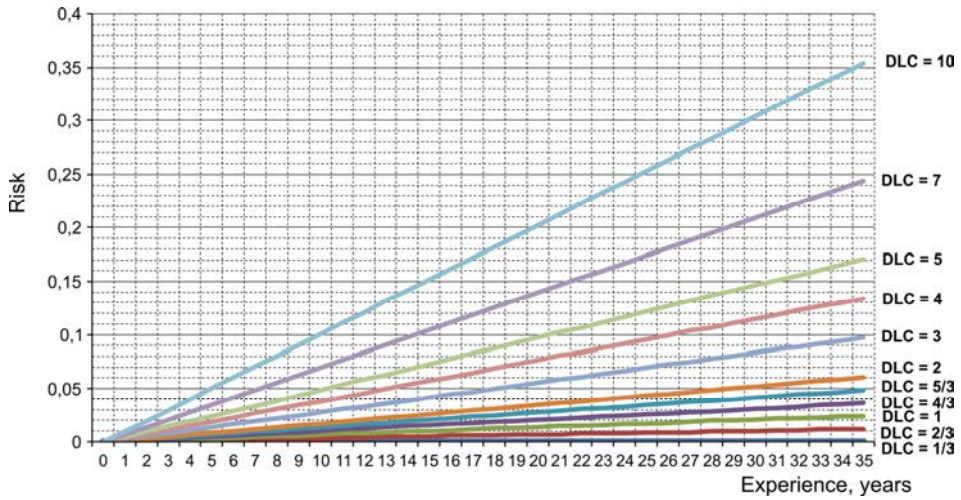

Fig. 8.13. Disease risk values depending on the time and exposure to PFAA (low fibrogenic dusts), disease severity: 0.5

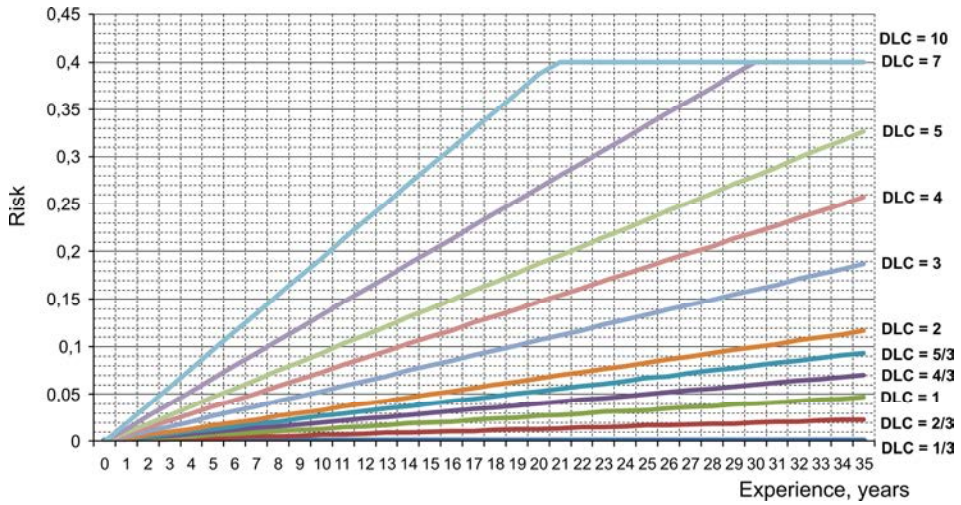

Fig. 8.14. Disease risk values depending on the time and exposure to PFAA (high/moderate fibrogenic dusts), disease severity: 0.4

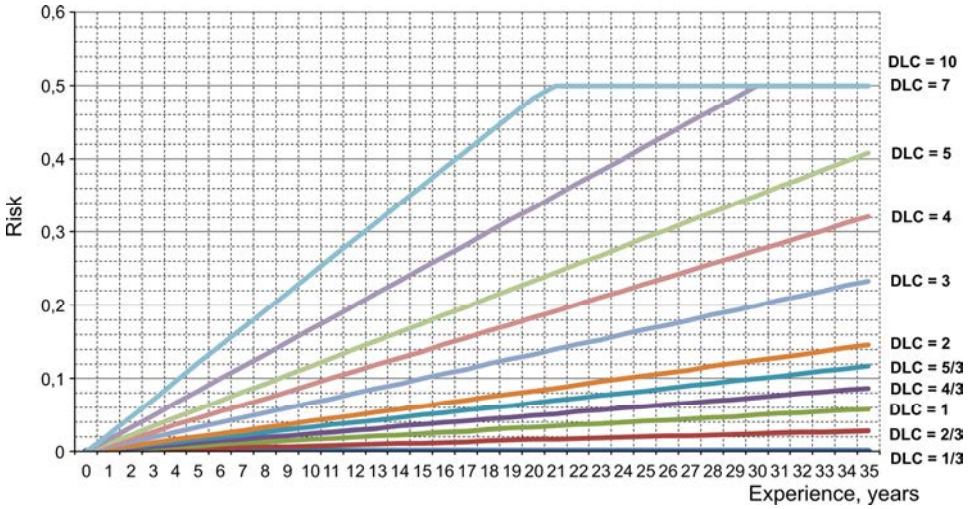

Fig. 8.15. Disease risk values depending on the time and exposure to PFAA (high/moderate fibrogenic dusts), disease severity: 0.5

If the total experience of worker can be divided into the periods which differ under the dust factor exposure level, the calculation for the risk of occupational disease development in worker is performed as the sum of risks for the separate periods:

$$R = R^1 + R^2 + R^3 + \ldots , \tag{8.10}$$

where R^1, R^2, R^3, … – is a risk of occupational disease development during the different periods of work experience.

If during the labor activity the worker has long break, the decrease of the accumulated risk of occupational disease development in worker is possible. The values by which the individual risk of occupational disease development is decreased are taken from table 8.6 according to the required time period.

The occupational risk assessment results are the base for the development of measures on the workers health risk management. The risk management is based on the different actions and, as a rule, their combinations on the prevention, mitigation, transfer of risk and the risk consequences compensation. The management includes the making of decisions and actions on the selection and implementation of the technical, medical and social preventive measures. For the effective risk management it is necessary to take into account such factors as the effect occurrence probability, severity of consequences, reversibility of effects, risk control possibility and clearness of benefit.

The risk management shall be based on the preliminary analysis of its formation and assessment: hygienic characterization by the exceedance of maximum permissible concentration / maximum permissible level under the criteria of P 2.2.2006-05 "Manual on the hygienic assessment of working environment and labor process factors. Criteria and classification of labor conditions" and the forecast of probability for the development of occupational and occupationally stipulated disease (assessment of the category of its risk and severity (under the standards or epidemiological data)) [Izmerov N.F. et al., 2002]. The urgency and scope of preventive measures depend on the occupational risk degree.

During the risk management it is necessary to be guided by the following principle: the minimization of risk shall be carried out at the optimum cost/benefit ratio. When selecting the risk management measures it is recommended to be guided by the priorities determined at the international and national levels [ILO. Ambient factors in the workplace, 2001; R 2.2.1766-03].

Table 8.6

The decrease of disease risk from the break in work under the dust factor influence

Experience, years	Disease probability reduction (severity 0.4)		Disease probability reduction (severity 0.5)	
	Low fibrogenic dusts	High/moderate fibrogenic dusts	Low fibrogenic dusts	High/moderate fibrogenic dusts
1/12	-0.00002	-0.00006	-0.00003	-0.00007
1	-0.00028	-0.00068	-0.00035	-0.00085
2	-0.00056	-0.00132	-0.0007	-0.00165
3	-0.00084	-0.002	-0.00105	-0.0025
4	-0.00112	-0.00268	-0.0014	-0.00335
5	-0.0014	-0.00332	-0.00175	-0.00415
6	-0.00168	-0.004	-0.0021	-0.005
7	-0.00196	-0.00468	-0.00245	-0.00585
8	-0.00224	-0.00532	-0.0028	-0.00665
9	-0.00252	-0.006	-0.00315	-0.0075
10	-0.0028	-0.00668	-0.0035	-0.00835
11	-0.00308	-0.00732	-0.00385	-0.00915
12	-0.00336	-0.008	-0.0042	-0.01
13	-0.00364	-0.00868	-0.00455	-0.01085
14	-0.00392	-0.00932	-0.0049	-0.01165
15	-0.0042	-0.01	-0.00525	-0.0125
16	-0.00448	-0.01068	-0.0056	-0.01335
17	-0.00476	-0.01132	-0.00595	-0.01415
18	-0.00504	-0.012	-0.0063	-0.015
19	-0.00532	-0.01268	-0.00665	-0.01585
20	-0.0056	-0.01332	-0.007	-0.01665
21	-0.00588	-0.014	-0.00735	-0.0175
22	-0.00616	-0.01468	-0.0077	-0.01835
23	-0.0064	-0.01532	-0.008	-0.01915
24	-0.00668	-0.016	-0.00835	-0.02
25	-0.00696	-0.01668	-0.0087	-0.02085
26	-0.00724	-0.01732	-0.00905	-0.02165
27	-0.00752	-0.018	-0.0094	-0.0225
28	-0.0078	-0.01868	-0.00975	-0.02335
29	-0.00808	-0.01932	-0.0101	-0.02415
30	-0.00836	-0.02	-0.01045	-0.025
31	-0.00864	-0.02068	-0.0108	-0.02585
32	-0.00892	-0.02132	-0.01115	-0.02665
33	-0.0092	-0.022	-0.0115	-0.0275

The urgency of risk mitigation measures is determined according to the occupational risk category. The Research Institute of Occupational Health affiliated to the Russian Academy of Medical Sciences developed the summarized characteristics of the occupational risk categories and required preventive and social protection measures for the different classes of labor conditions under the criteria of guide R 2.2.2006-05.

The following is distinguished among the risk mitigation measures: organizational and technical measures, use of personal protective equipment, therapeutic and preventive measures (TPM), periodical medical examinations (PME), as well as the time forms of protection - work-rest distribution (WRD), shortened working day (SWD), additional leave (AL), premature retirement insurance (PRI). The effective risk mitigation measure is a complex of preventive measures aimed at the preservation of health and increase of workers body resistance to the action of industrial environment factors and detection of initial signs of changes in the health condition. The periodical medical examinations (PME) shall contribute to this objective.

The use of "Guidelines on the occupational risk assessment under the data of periodical medical examinations" allows distinguishing the three zones of the risk of occupational disease and determining the direction and urgency of the risk management measures:

– safe zone – the experience exposure is low and probably is not dangerous and acceptable; the argued data on the health disorders are not available yet, but the certain attention is required;

– border zone – the experience exposure exceeds the permissible and becomes dangerous because the health disorders occur in some number of workers; it requires the close attention;

– hazardous zone – the experience exposure is extremely high and the frequency of occupational diseases is high and unacceptable under the medical and social damage.

It should be noted that the development of diseases and their clinical complications occurs during the intensive activity of workers. It is stated that one of the most important conditions for strengthening and preservation of health of workers is an available and high-quality medical and preventive services [Occupational pathology: national manual, 2011].

Thus, at the machine building enterprise the workers are exposed to the industrial factors which exceed the hygienic standards. The exposure to these factors can result in the development of occupational diseases as well as cause the permanent functional in vivo changes, changes in the human biological media that can lead to the increased level of morbidity with temporary loss.

When carrying out the extended medical examination including the additional clinical and laboratory studies (standardized biochemical and immunological parameters, ultrasonographies (US) of the abdomen and thyroid, spirography (SPG) allowing assessing the status and function of organs and systems, a wider range of pathology than during the conduction of medical examination, is established according to the current regulations (Table 8.7).

Table 8.7

The comparative analysis of morbidity for the machine building enterprise workers under the results of periodical and extended medical examination

The class of disease	The share of workers with detected diseases (%) in accordance with results		Additional morbidity, %
	PMO	of extended medical examination	
The diseases of the digestive system	8.3	40.0	31.7
The diseases of the respiratory system	2.3	13.9	11.6
Musculoskeletal disorders	7.1	13.9	6.8
Dermal diseases	4.7	6.9	2.2

As a result of the extended medical examination of workers it is possible to detect the early manifestations of the affections of the organs and systems that will allow preventing or detecting the industrially stipulated diseases at the early stages. The studies performed by FBIS "Federal Scientific Hygiene Center named after F.F. Erisman" of the Federal Service on Customers' Rights Protection and Human Well-being Surveillance on the assessment of the hemodynamics of workers as the indicator for the functional condition of cardiovascular system being the important limitation for the achievement of end adaptive result, i.e. the adaptation of human to the industrial conditions, demonstrated the feasibility of the use of hemodynamics indicators for conducting the express assessment of the functional condition of the worker body [Shushkova T.S., 2013].

During the study of the health condition of workers at the metallurgical enterprise it was established that among the workers exposed to the set of industrial factors with the increase of experience there is an increase in the share of persons with deviations under the results of laboratory examinations. Thus, during the ultrasound assessment of the vasomotorial function of the brachial artery endothelium in the sample of endothelium-dependent vasodilation the share of persons with deviations in the endothelium function indicators is maximum in the experience subgroup of 5–10 years, the most severe manifestation of endothelial dysfunction

are established in the same experience subgroup. The obtained results indicate the adaptation stress in the workers with small experience with formation in future of arterial hypertension on the background of the disorders of regulatory systems This is confirmed by the increase of the registration of clinical manifestation in workers depending on the experience (Table 8.8).

Table 8.8

The experience dynamics of the share of workers at the metallurgical enterprise with clinical manifestations and deviations under the results of laboratory examinations

The share of workers	Work experience, years		
	up to 5	6–10	more than 10
– with deviations in the results of laboratory examinations, %	30.0	42.8	66.6
– detected diseases, %	21.6	42.9	53.5

In the structure of total morbidity of workers contacting with industrial factors the respiratory system pathology occupies the priority (first) place and is credibly higher than the respiratory organs diseases in persons not contacting with industrial factors. The recommendations on the early diagnostics of occupationally stipulated diseases in workers are provided for the risk management, taking into account the certain labor conditions and determination of markers demonstrating the interrelation with aerogenic load.

For professions with the increased hazard of the development of occupational and occupationally stipulated diseases established at the risk assessment stage the scientific institutions develop the recommendations on extending the scope of clinical and laboratory studies within the periodical medical examination. A number of studies developed the algorithms for forecasting the health disorders of workers in the different sectors of industry based on the determination of dose-experience ranges of health disorders and the features of exposure to the priority industrial environment factors, clinical-functional and laboratory markers of exposure to the industrial factors that can be recommended to use during the conduction of periodical medical examinations [Zheglova A.V., 2009; Vlasova E.M. et al., 2012; Vlasova E.M. et al., 2012; Zemlyanova M.A et al, 2013; Shlyapnikov D.M. et al., 2012].

The main industrial factors affecting to any extent the workers of oil extraction enterprise are the noise, total vibration, electromagnetic radiation, severity of labor process, micro climate and different chemical substances present in the air of working zone. The effect of industrial factors has the intermittent character. The main industrial factors exceeding the permissible levels are the noise and harmful chemical substances. In addition, some workplaces do not comply with hygienic requirements under the work process severity indicators. At some workplaces the level of noise achieves 87–91 dBA that by 7–11 dBA exceeds the maximum permissible level.

For the oil extraction enterprise workers there was established the risk of diseases of the circulatory system (*OR*=2.8, 95% *CI* 1.30–3.66) and biochemical markers (total cholesterol, LDL cholesterol) which are an important mechanism in the cardiovascular pathology development. The main approaches to the detection of risk groups among the workers of enterprise within the periodical medical examination are offered based on the results of examination.

The important element of the occupational risk management is a creation of corresponding procedure on making the managerial decisions aimed at the correction of already existing and applicable in practice risk management measures and assessment of efficacy of the decisions made.

The workers health risk management program can be used as the procedure for making the managerial decisions. The risk management program is a systemic approach to the ensuring of safety and occupational hygiene at the workplace due to the liquidation or mitigation to the extent reasonably practicable of industrial risks and hazards in order to prevent the occupational traumatism, occupationally stipulated and occupational diseases.

The program can be considered as the base for the further processing of system for managing the risks of occupational and occupationally stipulated diseases of workers.

The system for managing the risks of occupational and occupationally stipulated diseases of workers will allow managing the risks and making the maximally quickly decisions on the corrective measures conduction. It is more convenient to structure the measures within the occupational risks management system under the following principle: organizational measures, measures on mitigating the effect of the risk factors of occupational diseases, medical preventive measures, informing about the risks and methods for their mitigation and prevention.

The following composition of system is proposed as an example:

– the determination of hazards (risk factors);

– the monitoring of the condition of industrial environment and health of workers;

– the development of managerial decisions on mitigating the risk of occupationally stipulated and occupational diseases.

It should be noted that the management of risks associated with work shall be integrated into the system for the management of production, the management of personnel, the management of labor protection and ecology issues. This relationship is important for ensuring the integrity of organizational structure and health risks management. The main element of risk management is the cooperation at the level of enterprise between its management, workers and their representatives through the system of established rights, responsibility and liabilities.

One of the measures for controlling the labor conditions forming the risk of diseases associated with work for making the future managerial decisions is the conduction of laboratory and instrumental control at the workplaces (production laboratory control).

The optimization of production laboratory and instrumental control at the workplaces under the occupationally stipulated diseases occurrence hazard criteria can be used as one of the risk management measures.

The possibilities to change the ratio of production laboratory control are regulated by the item 4.1 of СП 1.1.1058-01; namely, the limitation of frequency by not more than two times compared to the rated indicators is provided.

Herewith, to establish the ratio of conduction and scope of laboratory instrumental studies when carrying out the production laboratory control the occupational risk criteria were not applied up to the present time. The guidelines on the production control planning taking into account the degree, extent and credibility of cause-and-effect relationship of health disorders with work are developed within the production control improvement [MR 2.2.2.0021–11].

The specified approaches are tested on the example of powder metallurgy enterprise but they can be applied to any production.

When testing of these recommendations at the productions of items using the powder metallurgy method during the assessment of cause-and-effect relationships between the exposure of the unfavorable factors of manufacturing process and the frequency of the occurrence of the separate types of responses from the side of the health of workers with the use of epidemiological methods of study it was established the presence of credible relationship between the labor conditions and respiratory diseases which are stipulated by the increased content of heavy metals in the air of working zone (*OR*=3.55 with 95% *CI* 1.04 – 14.41; *EF*=53.9 %) that corresponds to the high level of the risk of occupationally stipulated diseases. In addition, the credible relationship of the arterial hypertension development with the noise effect is detected (*RR*=2.9 with 95% *CI* 1.14 – 7.2; *OR*=3.6 with 95% *CI* 1.3 – 10.3). Taking into account the credible relationship of health disorders with labor conditions, it was proposed to change the ratio of studies in the production control program. Thus, at the workplaces of press operators it is proposed to increase the ratio of measurements for the content of zinc compounds in the air of working zone – up to 1 time per month, and to conduct the studies of iron and aluminum 1 time per year; at the workplaces of operators of computer-controlled machines it is recommended to change the ratio of measurements for the production noise level from 1 time per year to 1 time in every 3 months.

Therefore, we accumulated the certain experience in managing the risk for the health of workers both in the field of control and minimization of the risk factors effect and in the field of preventive measures.

In general, the assessment and management of health risks associated with occupational factors is one of priority directions of the risk analysis. The regulatory legal and methodical base existing in the Russian Federation requires the harmonization with the internationally recognized approaches. At the same time the domestic hygienic science accumulated the sufficient potential for improving the methodical approaches to the occupational risk assessment, specially its quantitative characteristics, formation and implementation of the state and corporate systems for managing the risk to the health of workers.

8.3. Socially determined risks

The macrosocial determinants of the health of population in the regions of the Russian Federation have the significantly different values. For example, at the total growth of per capita gross regional product throughout the Russian Federation the differentiation of the Russian regions under this indicator is still significant. The value of this indicator in the regions with the highest level (Sakhalin region – 978.4 mln. rubles, 2012) exceeds the indicator of region with the lowest level (the Republic of Ingushetia – 52.1 thous. rubles, 2012) almost by 20 times.

The top five of the most trouble-free regions stably consists of Tyumen region, the Chukotka Autonomous District (AD), Moscow, Sakhalin region and the Republic of Sakha (Yakutia). The economy of 5 of 4 listed regions is based on the resource-extraction sector – oil and gas extraction (Tyumen and Sakhalin regions, the Republic of Sakha), gold extraction (Chukotka AD, the Republic of Sakha), and extraction of diamonds (the Republic of Sakha). The growth of indicator was observed recently in all the regions of the first five areas. The list of the subjects of the Russian Federation with the lowest and highest level of per capita gross regional product is actually permanent (the Republic of Ingushetia, Chechen Republic, the Republic of Kalmykia, the Kabardino-Balkarian Republic, the Karachayevo-Cherkessian Republic).

In 2012 the average for the Russian Federation contribution of macrosocial factors to the negative deviation of indicators for the mortality and morbidity of population from the average throughout the Russian Federation was respectively 18.8% and 12.5%. However, due to the different manifestation of social and economic problems in the regions the degree of effect of the different groups of factors to the formation of health disorders in the population of regions is no equal.

The main macrosocial factors affecting the medical and demographical situation in the country are the total level and potential of the social and economic development of territories, social standards of living and living conditions of the population (Table 8.9).

Complete algorithm for the assessment of risk associated with the action of macrosocial risk factors was tested on the example of 14 industrially developed cities of the Russian Federation in 2008–2012.

Under the results of factorial analysis of macrosocial indicators for the cities of the Russian Federation 6 groups of macrosocial factors (Table 8.10) which characterize the following were distinguished: *F1* – the total level of the social-economic development of territory, *F2* – the territory economic development potential level, *F3* – medical infrastructure development level, *F4* – provision with medical staff, *F5* – the territory social welfare level, *F6* – the social standards of living.

Based on the mathematical simulation the following models describing the relationship of health indicators and macrosocial factors in the large cities of the Russian Federation were obtained:

$$y_{31} = 0.07 - 0.34\, F_2 - 0.342\, F_4, \qquad (8.11)$$

where y_{31} – is a morbidity in relation to the endocrine system diseases and malnutritions, F_2 – is the territory economic development potential level, F_4 – is a provision with medical staff, $R^2 = 0.371$;

Table 8.9

Priority macrosocial factors determining the health of population in Russia [State Report, 2012]

The priority groups of social and economic factors	Main health indicators associated with the social and economic factors	The contribution of social and economic factors to the negative deviation of the public health indicator from the average indicator for the Russian Federation
Per capita gross regional product Average monthly calculated nominal salary The number of population with incomes below the minimum living wage. The total area of residential premises in average per one citizen. The specific weight of total area not equipped with water supply and sewage systems. The specific weight of total area not equipped with central heating. The area of residential premises per one citizen. The cost of fixed assets under the types of economic activity. The specific weight of rundown and damaged dwelling. The cost of the fixed set of consumer goods and services. Expenses for healthcare. Expenses for education.	The mortality of population from all causes. Infant mortality. Expected lifespan at birth. The mortality of population from external causes (including the poisonings, suicides, traffic accidents). Mortality from the contagious and parasitic diseases Mortality from the circulatory diseases. Mortality from the malignant neoplasms. Morbidity in relation to the contagious and parasitic diseases (adults, children). The diseases of skin and subcutaneous tissue (children). The pathology of pregnancy, delivery and postpartum period. Injuries, poisonings and other consequences of external causes. Neoplasms. The diseases of blood, blood-making organs and separate disorders involving the immune mechanism. Congenital abnormalities	The mortality of population – 18.8% in average Morbidity – 12.5% in average

Table 8.10

The macrosocial factors of risk to the health of population in the cities of the Russian Federation distinguished under the results of factorial analysis

Item No.	Name	Indicator with the load of more than 0.5
1	2	3
F1	The level of the social and economic development of territory	Per capita gross regional product (rubles)
		Average monthly calculated nominal salary (rubles)
		The number of doctors (thous. of persons per 1000 of population)
		The number of enterprises and organizations (at the end of the year; under the state registration data) (per capita)
F2	The territory economic development potential level	The availability of fixed assets (per capita)
		Investment to fixed capital in the actually active prices (thous. rubles per capita)
		The relation of average monthly calculated nominal salary to the living wage at the territory
F3	The medical infrastructure development level	The number of hospitals (units per 1000)
		The number of hospital beds (per capita)

End of Table 8.10

1	2	3
F4	Provision with medical staff	The number of nursing staff (per 1000 of persons)
		The capacity of medical outpatient polyclinical institutions (per capita visits during one shift)
F5	The territory social welfare level	The total area of residential premises in average per one urban citizen
		The number of registered crimes (per capita)
F6	The living standards of the population	Per capita average living wage value (rubles per month)
		The average size of calculated pensions (rubles)

$$y_{22} = 0.013 + 0.334\ F_3 - 0.546\ F_4, \quad (8.12)$$

where y_{22} – is a morbidity in relation to the diseases of blood and blood-forming organs, F_3 – is a medical infrastructure development level, F_4 – is a provision with medical staff, $R_2 = 0.497$;

$$y_{24} = 0.08 + 0.344\ F_1 + 0.333\ F_3 - 0.397\ F_4, \quad (8.13)$$

where y_{24} – is a morbidity in relation to the diseases of nervous system and sensory organs, F_1 – is a total level of the social-economic development of territory, F_3 – is a medical infrastructure development level, F_4 – is a provision with medical staff, $R^2 = 0.409$;

$$y_{26} = 0.183 - 0.308\ F_2 - 0.569\ F_4, \quad (8.14)$$

where y_{26} – is a morbidity in relation to the diseases of digestive organs, F_2 – is a territory economic development potential level, F_3 – is a medical infrastructure development level, F_4 – is a provision with medical staff, $R^2 = 0.473$;

$$y_{34} = 0.03 + 0.315\ F_1 - 0.503\ F_4, \quad (8.15)$$

where y_{34} – is a morbidity in relation to the class "congenital anomalies (developmental defects)", F_1 – is a total level of the social-economic development of territory, F_4 – is a provision with medical staff, $R^2 = 0.416$;

$$y_{36} = 0.17 + 0.27\ F_1 - 0.484\ F_4, \quad (8.16)$$

where y_{36} – is a morbidity in relation to the class "injuries and poisonings", F_1 – is a total level of the social-economic development of territory, F_4 – is a provision with medical staff. $R^2 = 0.380$.

The obtained parameters of models can be used to calculate the health risk associated with macrosocial factors at the level of urban settlements.

The results of calculation of risk associated with the action of macrosocial factors on the health of population on the example of urban settlement are presented in Table 8.11.

Table 8.11 demonstrates that for all the specified classes of diseases the value of risk associated with the action of macrosocial factors on the health of population is less than $1 \cdot 10^{-6}$ that corresponds to the level of minimal risk.

were used as the empirical base for testing the algorithm of assessment of risk associated with the influence of behavioral factors on health. The total scope of selected aggregate is 264 persons. The sampling included only the representatives of work professions subjected to the effect of harmful industrial environment factors. The method for selecting the units of observation is targeted, the main selection criterion is an employment in the harmful labor conditions.

The following was implemented and conducted at the enterprise: the complex medical examination of workers, the analysis of the statistics of the applications of workers for medical assistance (method – copying of data on morbidity from the database of the Federal Compulsory Medical Insurance Fund), sociological questioning (method – distributive questioning at the workplace). To characterize the social and economic status of workers, the regime and ration of their nutrition, the level of motion activity, the availability of vicious habits, the peculiarities of hygienic and medical behavior.

Table 8.11

The calculation of risk associated with the action of macrosocial factors on the health of population on the example of urban settlement

The class of diseases	$y_{текущ.}$	$y_{порог.}$	$\Delta y = y_{текущ.} - y_{порог.}$	$p = \Delta y/100000$	g	R^2	$R = pgR^2$
Endocrine system diseases	0.0504	0	1.2220	0.000012	0.00183	0.371	$3.42 \cdot 10^{-10}$
The diseases of the blood and blood-forming organs	0.0038	0	0.2528	0.0000025	0.00106	0.497	$2.02 \cdot 10^{-11}$
The diseases of nervous system and sensory organs	0.049	0.7423	-0.6933	-0.0000069	0.00238	0.409	$-6.74 \cdot 10^{-9}$
The diseases of the digestive system	0.0789	0	1.4856	0.000014	0.00469	0.473	$1.75 \cdot 10^{-9}$
Congenital anomalies (developmental defects)	0.0111	0	0.2799	0.0000027	0.00710	0.416	$3{,}30 \cdot 10^{-10}$
Injuries and poisonings	0.0608	0	0.2417	0.0000024	0.03219	0.308	$6{,}03 \cdot 10^{-9}$

The results of complex medical and social study conducted at the oil extraction plant

At the priority risk factors identification stage it was determined that the most significant lifestyle factors among the workers of the enterprise are the tobacco smoking and alcohol abuse. In general, the specific weight of actively smoking workers is 42.7%, including 35.4% (95% of CI: 29.6–40.8) of respondents are permanently smoking. In relation to sex, the men prevail among the regular smokers (40.0%), women – 16.0% (V = 0.39 at $p \leq 0.05$). The average smoking experience in the group of regular smokers was 17.5 years. In this category the respondents in average smoke 17 cigarettes per day; herewith the maximum number of smoked cigarettes is in the age group of 36–45 years (20 cigarettes), and minimum – for the groups of respondents in the age from 18 to 25 years and from 26 to 35 years (14 cigarettes per day). Average nicotine content in cigarettes is 0.6 mg/cigarette. In addition to the practice of active tobacco smoking this aggregate of respondents in 96.3% of cases is subjected daily to the passive smoking from the side of the members of family, friends and colleagues at work.

During the last 12 months 76.6% (95% of CI: 71.5–82.0) of respondents consumed the alcoholic drinks with different frequency. The most prevailing alcoholic drinks under the frequency of consumption are: beer – 9.7 % (the frequency of consumption 1–2 times per week (95% of CI: 4.8–15.3)), vodka (same frequency – 8.9 % (95% of CI: 4.8–14.5)), brandy – 5.0 % – from one to several times per week (95% of CI: 2.4–11.3) and whiskey – 5.6 % – several times per moth (95% of CI: 0.8–8.1). The average quantity of pure alcohol consumed at one time in relation to beer was 33.2 g, champagne – 15.6 g, wine including the fortified wine - 21.3, strong alcoholic beverages – 77.5 g.

The analysis demonstrated that under the chances relation criterion the risk of the development of cardiovascular diseases for the group of actively smoking workers was 1.21 (1.13; 2.01), for smoking respondents with the experience of smoking of more than 5 years – 2.33 (1.18; 4.21), with experience of more than 10 years – 2.53 (1.19; 5.63).

The risk of respiratory diseases development also increased depending on the fact of smoking and experience of the tobacco products consumption. For the group of actively smoking workers the value of indicator was 1.77 (1.05; 2.98), for regularly smoking respondents with the experience of smoking of more than 5 years – 2.59 (1.19; 5.63), with the experience of smoking of more than 10 years – 2.23 (1.18; 4.21).

Among the workers who consumed the alcohol during the last twelve months the value of indicator *OR* in relation to the cardiovascular diseases development was 2.52 (1.31; 4.82). For respondents consuming the non-recurrent share of pure alcohol of more than 56.25 g –

2.12 (1.33; 5.75), more than 62.5 g – 3.76 (1.08; 13.03). In relation to the endocrine system diseases the value of indicator *OR* for the group of respondents consuming the non-recurrent share of pure alcohol of more than 56.25 g was 3.74 (1.12; 8.9). Also the statistically credible dependence between the development of digestive system diseases and the strong alcoholic beverages consumption is observed.

The conducted analysis demonstrated that the most critical organs and systems of human body suffering from the action of factors of tobacco smoking and alcohol abuse are, first of all, the cardiovascular diseases, the diseases of digestive and endocrine systems as well as the respiratory diseases.

The calculation of individual risk for the ischemic heart disease development from the action of tobacco smoking factor (Table 8.12) demonstrated that the value of individual risk for the ischemic heart disease development increases depending on the average daily concentration of nicotine in the human body as well as from the regular smoking experience.

Table 8.12

Risk for the ischemic heart disease development at the action of insulated factor "smoking"

Age, years		Average daily intake of nicotine, mg	Age of beginning of smoking, years (in average for group)	Risk of ischemic heart disease	
				without the action of factor	of factor
18–25	25	3.97	16	3,9E-08	7,0E-08
	35			2,4E-07	4,5E-07
	45			1,4E-06	2,8E-06
26–35	35	6.43	19	2,4E-07	4,4E-07
	45			1,4E-06	2,7E-06
	55			9,1E-06	1,6E-05
36–45	45	12.13	19	1,4E-06	4,6E-06
	55			1,4E-06	3,8E-06
	65			9,1E-06	2,4E-05
46–55	55	9.45	22	9,1E-06	2,1E-05
	65			4,6E-05	8,0E-05
	75			0.000285673	0.000494347
56 and older	in 60	27.00	24	1,9E-05	4,6E-05
	in 70			0.000138227	0.080684728
	in 80			0.000707888	0.001735591

Table 8.12 contains the median values of forecasted ischemic heart disease development risk under the influence of factor "active smoking" (at its permanent intensity). It is established that at the separated action of factor in the age group of 46–55 years (at the average daily intake of nicotine of 9.45 mg) the risk of ischemic heart disease development is unacceptable after 20 years, and in group older than 56 years (at the average daily intake of nicotine of 27 mg) – after 10 years.

Thus, both the macrosocial and behavioral factors can have not only the separated by also the combined effect resulting in the formation of more essential population and individual health risks.

8.4. Risks associated with the use of consumer products

When justifying the safety of consumer products the risk assessment is required at the implementation of two directions: during the justification of separate risk-based standards; during the assessment of the risk of products in general.

General risk assessment principles are formulated in the manual on the procedure of Codex Alimentarius in the section V "Risk analysis working principles". Regardless of that the document concerns only the food products the principles are applicable to all the types of products:

– the scope and objective of the certain risk assessment shall be clearly established according to the risk assessment policy;

– experts responsible for the risk assessment shall be selected transparently based on their professional knowledge, experience and the independence of interests. The procedure for the selection of these experts shall be documented, including the public declaration on any possible conflict of interests. The experts from different regions shall participate completely in the expert consultations;

– the risk assessment shall be carried out in accordance with "declaration of principles concerning the risk assessment role..." and shall provide four stages of risk assessment (hazard identification, hazard characterization, assessment of effect (exposure) and risk characterization);

– the risk assessment shall be based on all the available scientific data. It shall use the available quantitative information to the maximum possible extent;

– when assessing the risk it is necessary to use the correct data from all the parts of the world. The most important are the data of epidemiological supervision, analytical data and exposure data. The risk assessment conduction shall not be postponed without any reason while waiting for data, however if such data are obtained the risk assessment shall be revised;

– the limitations, uncertainties and assumptions affecting the risk assessment shall be considered in detail at each stage of risk assessment and shall be documented;

– the risk assessment shall be based on the realistic exposure scenarios, taking into account the different situations which are determined by the risk assessment policy. The groups of population with high sensitivity and mostly susceptible to the risk are taken into account. When carrying out the risk assessment it is necessary to take into account the probability of occurrence of acute, chronic (including the long-term) and other cumulative and/or combined unfavorable consequences to health (depending on the certain situation).

– the risk assessment report shall contain any limitations, uncertainties and assumptions as well as their influence on the risk assessment. The opinion of minority shall be also reflected. The expert on the risk prevention and mitigation, but not the experts on the risk assessment bears the responsibility for decisions on the effect of the uncertainty on measure concerning the risk prevention and mitigation;

– the risk assessment conclusion, including, if possible, the risk calculation shall be presented in the form easy for the understanding of persons managing the risk, it also shall be brought to the attention of other experts on the risk assessment and concerned parties to form the general notion of it in them.

The principal risk assessment algorithm which ensures the commonality of procedure regardless of the group, type and kind of products is shown in Fig. 8.16.

The algorithm includes the following stages:

– hazard identification providing the risk factors establishment, the characterization of effects (responses) of their influence, including for the most susceptible groups of population;

– the assessment of the dependence "exposure – effect (response)" providing the determination of the types and parameters of mathematical models for assessing the influence of factors of risk for the certain products established at the hazard identification stage, including the inactive levels;

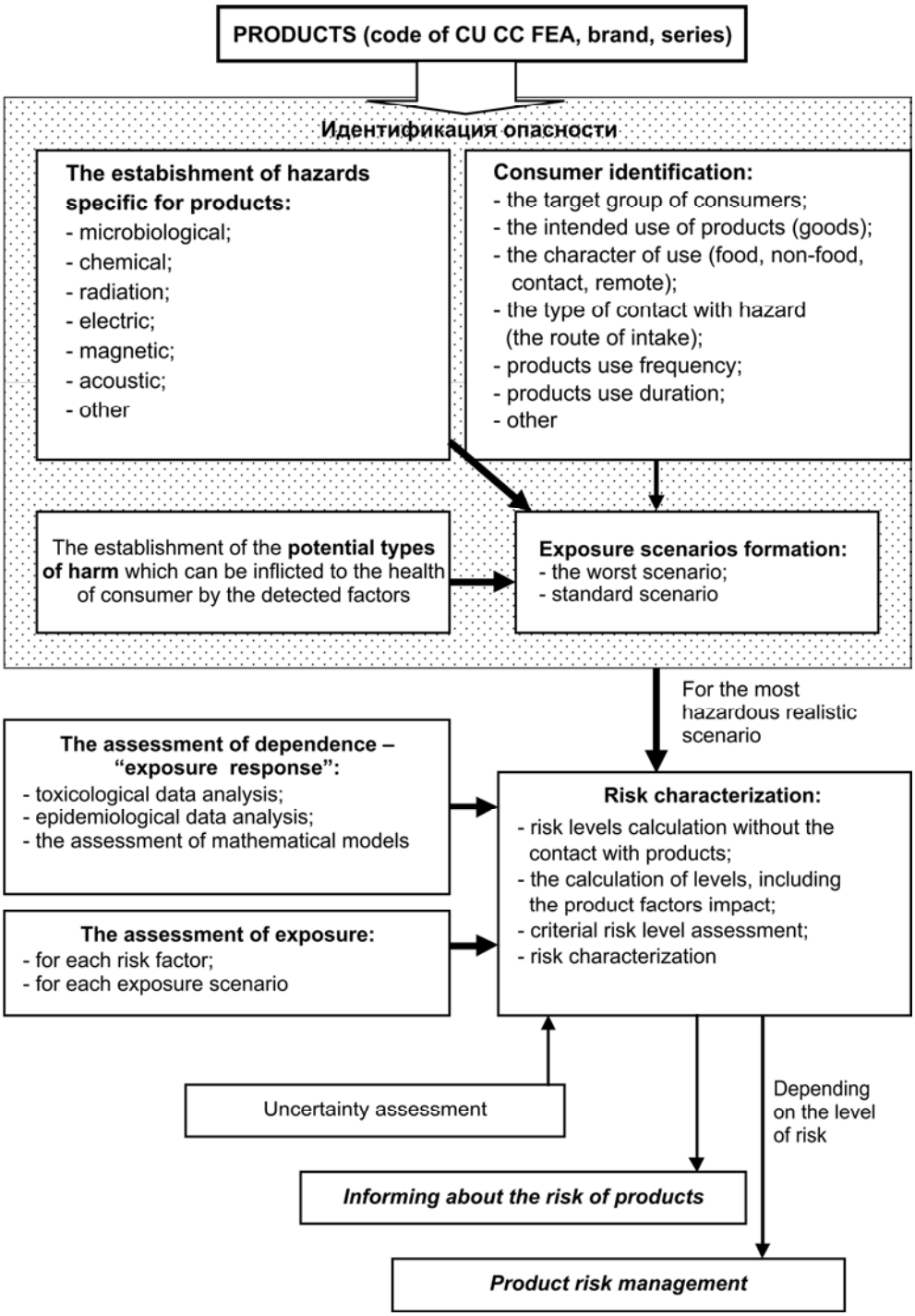

Fig. 8.16. Products risk assessment algorithm

– exposure assessment providing the formation of exposure scenarios for the groups of risk, taking into account the maximum, optimum and actual levels of consumption (use) of products (goods), measurement and/or calculation of intensity and the duration of exposure for each scenario of the use of products (goods);

– risk characterization, taking into account the individual and population indicators of the risk of health disorders in consumers, the inclusion of the risk value into the certain class (category), the assessment of its compliance with acceptable level.

The risk assessment stages are interconnected.

The risk assessment results are documented and used as the basis for making the decisions on the risk management and informing about the risks of the products of all the concerned parties.

Under the presented algorithm at the products design and compliance assessment stage the risk is evaluated for the sample having the typical characteristics and used for the specified purpose. At the products marketing stage the risk is evaluated for the certain type, kind and brand of goods of the certain series from the certain manufacturer.

The hazard identification for the certain type of products is performed based on the technical documentation for products, test reports and/or based on the specially performed measurements, studies and tests, information about the hazardous risk factors of products contained in the internationally recognized databases, reports and relevant sources of scientific literature. Herewith it is mandatory to conduct the expert evaluation of the sources of information and data under the criteria of credibility, completeness and adequacy to the tasks solved.

In virtue of that the certain products (goods) can be characterized by the one or several hazard factors each of them shall be considered as well as the aggregate action of all hazardous factors.

When identifying the chemical factors of the products hazard it is necessary to determine the certain chemical substance, its aggregative state (solid, liquid, gaseous), the degree of interrelationship and/or ability to migrate from the product to other significant parameters. It is necessary to detect all the chemical substances with which the consumer can contact and which can cause the health disorders in human. The specific and subspecific belonging of agent, taxonomy and other features are established at the biological factors identification. When identifying the physical factors of the products hazard it is necessary to establish the characteristics for each factor which can determine the specificity of negative effect (for example, noise rating curves, spectrum of) non-ionizing radiation, the type of ionizing radiation, etc.).

It is important to take into account the specificity of the groups of consumers, including the groups most susceptible to the risk, namely:

– young children (0–3 years), the disabled of the 1–2 disability groups, pregnant and nursing women (category "very susceptible groups of consumers");

– children in the age of 3–14 years, persons with limited physical or mental abilities, immunity compromised persons, elderly people (older than 65 years), persons which do not have the proper experience for handling of products (category "susceptible consumers").

The most complete and various exposure scenarios are justified for these groups, taking into account the physiological peculiarities, susceptibility to effect, behavioral practices, etc.

The probable types of health disorders which can be caused by the use of products are established for each detected chemical, biological or physiological goods hazard factor.

In the summarized form the probable types of negative health effects formed by the chemical, biological and physical factors of the consumer products (goods) hazard are presented in Table 8.13.

The sources of data on the negative effects of chemical substances are the toxicological profiles described in the relevant scientific literature, internationally recognized databases, for example, IRIS, ATSDR, reports of international organizations, for example, WHO, ICPS, EFSA, Codex Alimentarius, etc. The data on the effects of biological factors are contained, as a rule, in the scientific reports on the results of epidemiologic studies and

scientific medical literature. The most reliable sources of information about the effect of physical factors to health are the databases and reports of the International Agency for Research on Cancer, International Electrotechnical Commission, International Non-Ionizing Radiation Committee.

Table 8.13

The probable types of negative effects from the side of health formed by the chemical, biological and physical factors of the consumer products hazard

The type of products	Risk factor		Exposure route	Probable responses from the side of health
Food products	Chemical		Peroral	Non-microbial poisonings (poisonings with products poisonous by their nature (mushrooms, plants, products of animal origin), poisonings with impurities of some metals, poisonings with nitrites, poisonings with products temporarily became poisonous (potato with solanine, fish during the breeding season, etc.)), disorders from the side of gastrointestinal tract, kidneys, liver, immune system, blood system, nervous system, development processes, endocrine system, milt, cardiovascular system, reproductive system, musculoskeletal system, teeth, eyes, systemic effects, carcinogenic effects
	Biological			Toxinfections, mycotoxicosis, bacterial poisonings, helminthosis, virus infections, persistency of antibiotic-resistant bacteria
	Radiation			Carcinogenic and other effects
Non-food products	Chemical		Inhalation	Disorders from the side of cardiovascular system, kidneys, liver, central nervous system (CNS), respiratory organs, reproductive system, blood system, immune system, disorders of development processes, endocrine system, eyes, mucous membrane, milt, skeletal system, systemic effects, carcinogenic effects
			Peroral	Disorders from the side of gastrointestinal tract, kidneys, liver, immune system, blood system, CNS, development processes, endocrine system, milt, cardiovascular system, reproductive system, musculoskeletal system, teeth, systemic action, carcinogenic effects
			Percutaneous	Dermal and mucous membrane disorders
	Biological		Inhalation	Respiratory disorders
			Peroral	Poisonings, toxinfections, mycotoxicosis, bacterial poisonings, carcinogenic effects
			Percutaneous	Dermal and mucous membrane disorders
	Physical	Noise		Disorders from the side of CNS, cardiovascular system, hearing organs
		Electro-magnetic radiation		Disorders from the side of CNS, cardiovascular system, endocrine system, skin and mucous membranes, eyes, carcinogenic effects
		Radiation factor		Carcinogenic factors

The optimum is the maximum possible clarification of the type of health disorder - deviations from the value of certain laboratory indicator (as the indicator of pre-nosologic early changes in health), functional disorder, diagnosis of disease. Such concretization is important for the solution of two tasks - assessment of the health disorder severity and formation of evidence basis for effect of the studied factor specific for the products. The examples of higher detailing of health disorders when exposed to the factors of products are specified in table 8.14.

Table 8.14

The examples of established health disorders associated with the hazard factors of consumer products

Goods (products)	Hazard factor	Health disorder
Milk	Listeria	Listeriosis
Ice cream		
Fermented meat		
Smoked fish		
Perfumery products	Phthalates (diethylphthalate)	Effect to lungs (respiratory function, asthma), Fetal development disorder in pregnant women (disorder of work of reproductive organs of future baby - feminizing effect to the genital organs of boy, cryptorchiism), infertility of men (decrease of testosterone, seminal fluid quality deterioration) and women, decrease in immunity, effect to nervous system (migraine), oncology (breast cancer), hormone system (excessive weight)
	Musks	Endocrine system function disorder (hormone exchange disorder)
	Parabens	Breast cancer
	Methylisothiazolinone	Fetal development disorder during pregnancy
Cellular phones	Electromagnetic radiation	Developmental delay in children, increased risk of encephaloma, CNS (Parkinson disease, memory loss, sluggishness of reaction, depressive manifestations), effect to immune system (immunogenesis disorder, cellular immunity T-system inhibition), endocrine system (sexual activity reduction, stimulation of hypophysial-adrenaline system, spermatogenesis inhibition), cardiovascular system (lability of heart rate and arterial pressure, phase changes in the peripheral blood composition)

The extremely significant during the hazard identification is the accounting of the routes of intake for the contact of consumers with the health risk factors of products.

The combination of data on the types of hazard, probable health disorders, and methods for the contact of consumer with the risk factors allows forming the exposure scenarios. Thus, when identifying the chemical hazard of products the preliminary exposure scenario describes how the influence of the studied chemical substance occurs, taking into account the substance transportation mechanism, routes of intake of substance to human body (peroral, inhalation, dermal), its physical and chemical properties, toxicological effect, including at the cellular, organic and genetic levels.

When identifying the biological hazard it is important to assess how the contact of human with the studied biological agent occurs, taking into account the type of products (food/non-food) and routes of its intake (peroral, inhalation, percutaneous). It is necessary to account the ways of the consumption of products usually consumed together with the studied goods; the ability of product to act as the substrate for microorganisms; the

duration of storage; conditions of production, storage, transportation, use of detergents and disinfectants, etc.

When identifying the physical hazard of products the preliminary principal scenario shall describe how the contact of human with hazardous agent occurs (electric current, electromagnetic field, radioactive radiation, etc,) and take into account the peculiarities of spatial and time distribution of factor, frequency and other characteristics.

When assessing the risk of products, it is necessary to describe the maximum possible number of the real exposure scenarios. However the risk assessment can be performed for scenarios which can lead to the most severe and most probable negative effects (shortest path to injury). The typical scheme for forming the scenario for risk assessment on the examples of goods from the group "Toys" is shown in Fig. 8.17.

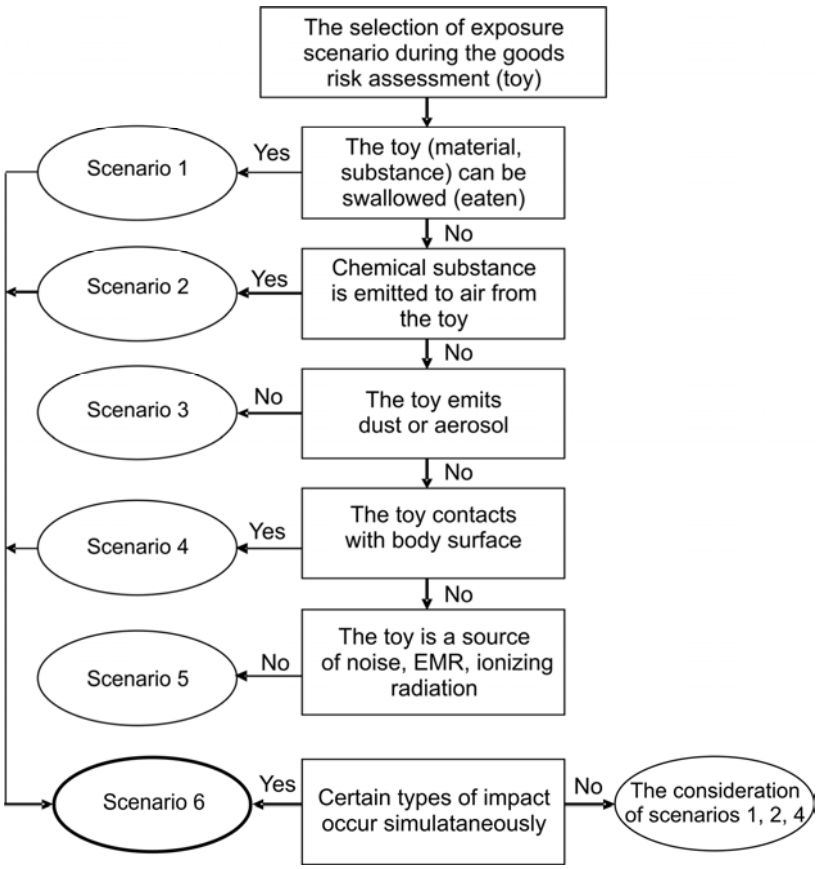

Fig. 8.17. The selection of scenario during the products risk assessment

It is necessary to pay attention to the fact that practically all the documents of international level provide the assessment of the aggregate (integral) risk of products, regardless of that the methodical issue is developed extremely insufficiently. Therefore, the integral risks assessment practice is extremely limited.

It should be noted that the products risk assessment process can be ended already at the hazard identification stage, if:

– the factors which can impose the hazard for the life and health of consumer at the targeted use are detected;

– the credible information about the certain types of health disorders associated with the products hazard factor is not available.

The relationship between the detected hazard factors and probable health disorders requires the formalizing and mathematical description which is performed at the stage "The assessment of dependence "exposure – effect (response)"". At this stage of risk assessment it is necessary to use the results of toxicological studies on animals, clinical studies of effect, as well as the data of priority epidemiologic studies. Herewith the source of information shall be relevant (internationally recognized, if possible), the information shall characterize the dependence of clearly identified negative health effects from the certain levels of the risk factors exposure; it is necessary to specify for which risk group this dependence can be applied, it is necessary to specify for which ranges of the values of factors this dependence can be applied.

If there is no information about the parameters of the model of "exposure – effect (response)" dependence, it is allowed conducting the special toxicological or epidemiologic studies. In this case the complete information about the studies shall be submitted in the annex to the products risk assessment report.

As a rule, today in the majority of cases during the risk assessment the pair models "factor – response" obtained as a result of toxicological or epidemiological studies are used. In this relation extremely difficult is the task of integral risk assessment because the summarizing of effects can be extremely complicated and even impossible in a number of cases. Therefore, the risk assessment is limited by the assessment of the most hazardous scenario.

But even the most correct and repeatedly confirmed model of "effect – response" relationship allows obtaining the reliable risk characteristics provided that the accurately assessed exposure is available. In this relation the exposure assessment stage in the common algorithm receives the special significance.

The assessment of exposure to the hazardous factor of products, i.e. the measured or calculated quantity of agent which contacts with border organs of human (lungs, digestive tract, skin, etc.) requires the information about the intensity of factor (this is a parameter characterizing the products themselves), the time of non-recurrent contact of consumer with products, the degree of contact (for example, about the body surface area contacting with goods) (parameters characterizing both the products and consumer); about the duration or frequency of use of the certain type of products by the certain consumer, group of consumers (parameter characterizing the consumer).

The data on the factor intensity are obtained during the targeted instrumental measurement, calculations, during the analysis of technical documentation for products, scientific reviews, reports, guides, databases.

The frequency of exposure, the probable duration of the use of the certain type of products, and degree are assessed under the data of special studies or data from literature, statistical materials, the results of sociological studies, data on the characteristics of products, the service life of products, the rates and scopes of consumption of goods, etc. The expert evaluations can be applied in a number of cases. It should be noted, that the global society pays a significant attention to the collection, processing, and the analysis of data allowing correctly assessing the exposure to the hazardous factors of products. The special manuals concerning exclusively the products exposure assessment are developed (for example: "Exposure assessment of microbiological hazards in food: Guidelines, MRA Series"); "Guidance Document on Pesticide Residue Analytical Methods, 2007)", etc.

Annually the large-scale exposure assessment studies are performed by the specialized centers, institutes and other organizations oriented to the scientific support of the risk assessment, including the products risk assessment. Such scientific centers include: The Risk Assessment Institute of the German Federal Republic, Applied Nutrition and Food Products Safety Risk Analysis Center (USA), Grain Manufacture Risk Management Center (Uganda), Budapest Central Food Products Research Institute (Hungary), Risk and Substance Assessment Center (the Netherlands), Food Products Safety and Toxicology Institute of the Danish Food Products and Veterinary Administration (Denmark), Joint Scientific and Research Center of European Commission (Belgium), Food Products Chemistry Institute of Gratz Technological University (Austria), National Food Products and Veterinary Research Institute (EELA) (Finland), etc.

Table 8.15 contains the example of the results of study for the time of the oral contact of the children of different age with one or another type of toys. Such data allow making the justified calculation of the dose of chemical substance taken by the child during the manipulations with toy and, therefore, perform the correct risk assessment. Same studies are carried out in relation to the dermal effects assessment when the areas of body contacting with products are established (for example, finger paints), the assessment of the exposure of noise, electromagnetic radiation, etc.

Table 8.15

The example of data on the duration (taking into account the frequency) of oral contact "child - toy"

The age of child (months)	Goods	The time of oral contact "child – toy"			
		minutes per hour		minutes per month	
		average	95% percentile	average	95% percentile
3–11	Soft plastic toys	0.13	0.69	1.3	6.9
	Soft plastic butterfly teethers, rattles	0.19	0.44	1.69	4.4
	Butterfly teethers, rattles made of hard plastic	1.8	6.5	18	65
12–23	Soft plastic toys	0.18	0.88	1.8	8.8
	Soft plastic toys, butterfly teethers, rattles	0.02	0.1	0.2	1.0
	Toys, butterfly teethers, rattles made of hard plastic	0.56	1.8	5.6	18
24–36	Soft plastic toys	0.07	0.21	0.7	2.1
	Soft plastic toys, butterfly teethers, rattles	0.02	0.01	0.2	0.4
	Toys, butterfly teethers, rattles made of hard plastic	0.21	0.94	2.1	9.4

The methodical aspects of the assessment of exposure to the chemical substances and biological agents present in the food products are developed quite thoroughly. The existing methods combine the data on the consumption of food products by population (the structure of nutrition) with data on the contamination of food products by the chemical impurities of different origin (the concentrations of chemical substances). Herewith the methods used cover the whole range of possible exposure scenarios – from the "worst" to the probably real scenarios. Two main approaches to the assessment of exposure from the chemical substances contaminating the food are used, – *deterministic* (pointwise assessment, multilevel approach), *probabilistic* (probabilistic assessment). Currently the majority of documents reflect the use of stage-by-stage (multilevel) approach to the exposure assessment in relation to the chemical factors of food products.

In case of the microbiological risk assessment, the assessment of exposure is aimed at the establishment of actual or expected quantity of pathogenic microorganisms taken to the human body as a result of the consumption of contaminated food products as well as the quantitative and/or qualitative assessment of probability for the presence and level of content of pathogenic microorganism in the certain volume of food products or water. During the exposure assessment it is necessary to determine the level of food products contamination with the studied microorganism, taking into account its life cycle as well a the time, frequency and duration of its effect to the selected population.

When assessing the health risk from the effect of *noise* the exposure assessment includes the determination of the rated noise parameters at this moment of time and duration of its effect as well as the assessment of daily weighted noise as the measure for the contact of population with harmful factor. The indicator L_{den} (the equivalent level of average daily weighted noise) which can be determined taking into account the day and

night noise levels is accepted as the main unit of the active noise levels during the risk assessment.

When assessing the health risk from the effect of *electromagnetic radiation* the exposure assessment includes the determination of the electromagnetic characteristics of affecting range at this moment of time and duration for the preservation of the certain levels of electromagnetic radiation as well as the assessment of the weighted level of electromagnetic radiation as the measure for the contact of population with harmful factor. It is possible to carry out the exposure assessment trough the theoretical assessments (calculations).

In general, the selection of approach to the products exposure assessment is determined by the type, scope and characteristics of the used data on the chemical, biological and physical products hazard factors, data on the quantity, frequency and duration of the use/consumption of products by the consumer.

The characterization stage includes the calculation of indicators, semi-quantitative and/or quantitative risk assessment and its classification with the permissibility assessment. It should be noted that currently this stage causes the largest number of discussions and differs by a large number of methodical approaches and diversity of the assessment criteria. In general, the task of the stage is to calculate correctly the probability for the health disorder (harm) occurrence, determine the severity of consequences, assess the risk in relation to the combination of both and include the obtained value into the certain established qualification risk category for making the managerial decision in future.

The Consumer Product Safety Commission (CPSC) provides the following risk assessment process description: "For the purposes of this manual we determine the risk as the probability of that the damage or harm are inflected or can be inflicted by the substance, technology or activity". Respectively, the result of risk characterization performed by the experts of this commission is the establishment of the safe levels of chemical and other factors of products, taking into account the consumer health risk criteria. At the withdrawal of products the CPSC distinguishes three levels in the risk characterization in order to determine the risk of products representing the "significant risk". Three risk classes are based on two risk factors, i.e. the severity of harm/diseases and the probability of origin.

During the risk characterization it is necessary to use the value of conventionally taken acceptable risk – the probability of event the negative consequences of which are so negligible that for the obtained benefit from the risk factor a human or a group of humans or a society in general are ready for such risk.

In the majority of cases the probability and severity of the occurrence of negative effect (health disorder) are evaluated by experts. Herewith the assessments have qualitative (very low, high, medium, high, etc. probability; low, medium, high, etc. severity) or semi-quantitative character (probability from 0 to 1E-04; from 1E-04 to 1E-03; more than 1E-03, etc.). As a rule, the risk is characterized qualitatively, in accordance with the probability and severity combination matrix: high, medium, low.

Such risk characterization and calculation system is provided, for example, by the "Manual on characterizing the microbiological risk of food products" [WHO, FAO, 2009], "Manual on the information system for informing about the risk of non-food products" *(decision of EU Commission 2010/15/EU),* and some other documents.

However for the products the other risk assessment algorithm is used when the levels of factors obtained as a result of hazard identification and exposure assessment are compared to the permissible values of these factors (safety standards). In case of the exceedance of the established standards the risk is acknowledged as unacceptable and the measures on its mitigation are considered. If the established standard is observed, the risk is acknowledged as acceptable (permissible). Such approach is provided by the guideline documents of *Codex Alimentarius,* when the reference dose is used as the risk characterization criterion. If the established exposure of chemical substance does not exceed the permissible level (*ARfD* – at the short-term intake, *ADI* – at chronic), the risk is characterized as acceptable. Herewith it is taken into account that the permissible levels of exposure are established based on the health risk assessment, including the modifying factors and uncertainty factors. The values of the maximum permissible levels of content (MRL) in the separate food products are used as the

criteria when characterizing the risk of pesticides and the residual quantities of veterinary drugs in the food products. It is considered that the content of pesticides and residual quantities of veterinary drugs in the food products not exceeding these values provides the health risk level not exceeding the permissible one. This provision is based on that the consumption of food products with content of these chemical substances at the level not exceeding the maximum permissible level will provide their daily dose of not more than ADI justified under the acceptable risk criteria.

When assessing the effect of the mixtures of components for the characterization of risk it is necessary to use as the risk assessment criteria either the group permissible daily doses if they are established or the toxicity equivalency factors (TEF) for their calculation. In the European Union the human health risk assessment at the combined multifactorial chemical exposure is performed using the step-by-step approach (Tiered approach) to the risk characterization – from step 0 (approximate assessment at the minimum volume of information) to step 3 (complete assessment with use of relevant probabilistic models). For the substances having the genotoxic or carcinogenic action the safe levels are not established.

In this case for the risk assessment it is necessary to use the exposure border indicators (MOE) which represent the relation of the established exposure to the lowest exposure causing the effect. The MOE value of 10000 or more is considered as the low level at which no risk management measures are required.

When discussing the criterial basis for the products risk assessment it should be noted that in a number of cases the decision on the acceptable risk levels is made by the manufacturer himself. Herewith it is required to observe the principles of "rationality", "attainability" and "feasibility" which orient the manufacturer to the maximum possible in the existing scientific-technical and economic conditions reduction of the risk of products for consumer not establishing the clear criteria of its reduction. In general the criteria of acceptability, permissibility and the classification of the risk of products still remain the most problematic and require both the scientific justification and political decisions. But in addition it is not the obstacle for the development and improvement of the scientific and methodical base for the risk assessment in general.

Advantages and practice for the use of the products risk analysis and its management based on the evolution models

In the international methodology development the risk evolution methods specified in the section 2.4 are adapted to the tasks on the products risk assessment. In relation to the goods (products) the evolution model of the health risk accumulation is the mathematical description of change in the condition of the health of consumers exposed to the set of harmful factors inherent to the products during the long time [Kamaltdinov M.R., Kiryanov D.A., 2013; Zaytseva N.V. et al., 2011, 2013]. Herewith the iteration calculation procedure allows considering the following:

– the peculiarities of the distribution of exposure to the different factors in time taking into account the products use conditions and their service characteristics;

– risk accumulation processes in time associated with the negative effect of factors on the body functions;

– the additivity of the effects of the sets of different factors on the different body systems;

– the integration of the risks of the different types of negative effects for health at the influence of different factors.

The approach is innovative and allows solving the whole range of tasks which cannot be solved by the use of traditional approaches.

The building of the health risk accumulation evolution model for the consumers of products is performed based on the pair dependences reflecting the influence of factors inherent to the products on the human health and published in the scientific editions. The pair dependences are included into the health risk accumulation evolution model for the consumers of products with the use of algorithms of their adaptation to the forms of calculation.

During the evolution simulation the following is considered:

– the risk of the occurrence of noninfectious noncarcinogenic disorders in the functions of the body organs and systems when exposed to the chemical (noncarcinogenic substances) and/or physical factors (noise, electromagnetic radiation);

– the risk of occurrence of carcinogenic effects (malignant neoplasms) caused by the action of chemical (carcinogenic substances) and/or physical (ionizing and non-ionizing radiation) factors during the contact of consumer with products;

– the risk of the occurrence of contagious and parasitic diseases when exposed to the biological agents (mainly for the food products).

The risk evolution models are based on the pair models.

The implementation of the assessment of dependence "exposure – effect (response)" results in the models describing this dependence of the adequately assessed products. The description of models shall contain the characterization of their types, quantitatively determined coefficients, including the threshold levels justified under the health risk criteria. The certain models shall allow calculating the indicators characterizing the probability of negative effects stipulated by the effect of the products hazard factors to health for the risk groups established at the hazard identification stage.

The risk evolution simulation application allows setting the integral health risk assessment at the next stages and characterizing the products as the source of different risk factors as well as assessing the accumulation of risks during the use of different products, including for the different groups of consumers.

Risks associated with the food products consumption

The analysis of the risk of food products to health provides the risk assessment procedure conduction with the further development of recommendations including the justification of such measures as the development of risk-based standards (safety criteria).

The implementation of methodical approaches specified in the chapter 2 is presented on the examples of justification of the safe levels of microbiological (*L. monocytogenes*) and chemical (antibiotics of tetracycline group, ractopamine, nitrates) factors of food products.

L. monocytogenes

At the hazard identification stage it was established that *L. monocytogenes* is a gram-positive facultative anaerobe, asporous bacteria. The bacteria belongs to the group of psychrotrophs, i.e. it is able to propagate actively a low temperatures (4–10 °C) and can grow at the temperatures from 0 to 45 °C (temperature optimum is 37 °C) and pH from 4.4 to 9.4 and water activity 0.9 in the NaCl solution [Miller A.J., 1992].

L. monocytogenes is widely spread in the environment and is extracted from different objects, including the soil, waste water, plants, silo, faeces and water.

Due to the resistance to the high salinity of water and acidity which distinguishes *L. monocytogenes* from the majority of other asporous bacteria being the activators of alimentary infections the microorganisms are able during the long time to service in the unfavorable environmental conditions [McCarthy S.A., 1990; Ryser E.T., Marth E.H., 1991].

L. monocytogenes is detected at the different stages of the food products production [Ryser E.T., Marth E.H., 1991, 1999] and is able to survive for a long time in the food products, processed plants, living conditions and environment, specially when stored in the refrigerator or freezing chamber.

The ability of *L. monocytogenes* to survive in food and model systems is widely studied that results in the multiple models describing the effect of different environmental factors on the survivability of bacteria [Buchanan R.L., Golden M.H., 1994, 1995, 1998; Buchanan R.L. et al., 1993, 1997].

In addition that *L. monocytogenes* is often detected in the products not passed the cooking both of vegetable and animal origin the contamination can occur also after it.

L. monocytogenes is very often extracted in the products processing conditions characterized by the low temperatures and high humidity in such food products as milk, cheese (specially soft ones), ice cream, raw vegetables, fermented raw meat and boiled sausages, raw and boiled poultry meat, raw meat products, raw and smoked seafood

[Buchanan R.L. et al., 1989; Farber J.M., Peterkin P.I., 1991; Ryser E.T., Marth E.H., 1991, 1999; FDA/FSIS, 2001].

However the existing data on the listeria detection, for example, in the meat products, are quite contradictory and evidence on the different levels of *L. monocytogenes* detection (from 0,5 to 30–40 % of samples in quantities from 0,1 to 10^3 CFU/g and more); herewith the use of different methods for the listeria strains identification significantly complicates the comparison of obtained data and essentially complicates the analysis of situation [Beumer R.R. et al., 1996].

Regardless of a large number of foreign publications concerning the *L. monocytogenes* extraction at the different food enterprises the data on the listeria detection at the enterprises of food industry in the Russian Federation are extremely low. Based on the available information it was established that the process cycles permanently contaminate the objects of production environment with Listeria species; the frequency of listeria detection on the surface of equipment was 71.4%, inventory - 29.2% that of course can lead not only to the contamination of raw materials but also to the contamination of finished meat products. The frequency of *L. monocytogenes* detection in the washouts from the process equipment and inventory was 9.7% that evidences the intensive circulation of listeriosis activator at the meat processing enterprises [Sheveleva S.A., Karlikanova N.R., 1999].

The contamination of raw milk with listeria is explained mainly by the contamination with faeces. The raw milk quality analysis data during a number of years demonstrated that the frequency of *L. monocytogenes* detection varies mainly within 1–12% of the number of investigated samples. The delivery of such raw materials to the plant stipulates the gradual accumulation of activator and massive contamination of premises at the enterprise, equipment, inventory, creating the conditions of the secondary contamination of the finished diary products [Karlikanova N.R. et al., 1999; Efimochkin N.R., 2007].

The sources of exogenic raw milk contamination are the feeds including the hay and feeding concentrates: the frequency of *L. monocytogenes* detection in them varies from 1 to 8.7% [Farber J.M. et al., 1989; Husu J.R., 1990] and the probability of such method of the raw milk contamination is very high even if there are no sick animals at the farms. This in turn can result not only in the presence of activator in the prepared raw materials but also in the contamination of containers to which the milk on the farms is collected, dishware, inventory, etc. [Karlikanova N.R. et al., 1999].

The studies on the detection of listeria in the raw milk samples obtained at the farms of the central region of the Russian Federation (more than 60 samples) demonstrated that 5.7% of them contain *L. monocytogenes* in the quantity of up to 100 CFU/cm^3. The listeria were detected on the background of high level of the milk microbial contamination the sanitary and hygienic characteristics of which evidenced the unsatisfactory conditions for the milk raw materials production and storage [Karlikanova N.R. et al., 1999].

The role of raw milk in the transfer of activator at the milk processing enterprises is very high. The contamination of dairy products and first of all of cheese as a rule occurs after the milk pasteurization during the manufacturing process: *L. monocytogenes*, coming to the factory with cheese and milk can stay and propagate there stipulating the secondary contamination of products.

It is established that the *L. monocytogenes* bacteria have high ability to propagate in the temperature conditions of refrigerator that is why during the storage of contaminated food products the CFU number of *L. monocytogenes* can be increased significantly.

The study of the wide range of products stored in the refrigerators of patients suffering from listeriosis in the USA demonstrated that *L. monocytogenes* was detected at least in one sample in 64% of patients, the strains of bacteria detected in the food products and patients were the same in 33% of cases [Pinner R.W., 1992].

However, because the exposure of population to *L. monocytogenes* is much higher than the morbidity with listeriosis the hazard of intake of small quantities of bacteria is discussed actively, specially among the population without the immunity reduction [ICMSF, 1994; Farber J.M. et al., 1996].

The gates for infection are the mucous membrane of the gastrointestinal tract and tonsils. At the adequate immune reaction of body and production of the sufficient quantity of

subpopulations of T-lymphocytes and activation of macrophagocytes the further development of infection does not occur. At the reduced reactivity *L. monocytogenes* penetrate by lymphogenic way to the organs of reticuloendothelial system (liver, milt, lymph nodes) and by hematogenic way - to adrenal glands, kidneys, CNS where their further propagation occurs. The listeria are able to penetrate through the blood-brain and placental barriers that in the first case results in the affection of the brain tunic and substance, and in the second case - to the development of septic and granulomatous process in the fetus.

Within the hazard characterization it was established that the listeriosis stipulated by the intake of *L. monocytogenes* with food products is relatively rare but severe disease with the predominant affection of the susceptible groups of population. The microorganism widely spread in the environment and food products is regularly taken to the body in low concentrations. Regardless of the wide range of food products which can be contaminated by *L. monocytogenes*, the outbreaks and sporadic morbidity are predominantly associated with the food products ready for consumption.

Annually the morbidity with listeriosis varies from 0.0 to 11.3 cases /mln. of population [Notermans S. et al., 1998] and, for example, in Europe in 2003 it was 0.3–7.5 cases/mln. of population (EC, 2003), in Australia – 3 cases/mln. of population. Under the data of program FoodNet U.S. CDC from 1996 to 1998 the morbidity was annually about 5 cases of listeriosis per one million of population.

In the Russian Federation the listeriosis is officially registered since 1992. Since this time annually from 30 to 100 patients are detected that corresponds to 0.02–0.067 disease incidences per 100 000 of population. Annually the growth of morbidity is observed: thus, if in 1996 in Moscow only 12 cases were registered (10 of them in children), in 1999 – 23 cases (12 in children). It is necessary to take into account that the registered morbidity (in many cases it is associated with that the listeriosis diagnostics were not conducted properly untill now, the monitoring of infection was carried out not in all the subjects of the Russian Federation and the number of laboratories able to identify *L. monocytogenes* and its antibodies is small) is significantly lower than real. The lethality from listeriosis for the period of 1992–1999 was 17.4% [Mukhina L.B., Dmitrieva E.Yu., 2003].

The characterization of hazard for the occurrence of listeriosis associated with the food products is complicated by the absence of clear definition of the disease incidence. The main number of applications to the medical institutions is associated with severe disease incidences requiring the medical interference. However, it is more feasible to consider the cases of contagion as the colonization of microorganism in the hosting body (attachment to the mucous membrane and their growth) which can result in the asymptomatic forms, gastroenteritis with fever, the severe forms of disease or death.

The mortality in cases of invasive listeriosis among the hospitalized patients is 20–30%. According to the data of the Centers for Disease Control and Prevention in 2000 among all the activators of alimentary infections controlled by the organization the *L. monocytogenes* occupied the second place under the frequency of lethal outcomes (21%) and the first place under the frequency of hospitalization (90.5%).

The decisive role in the development of *L. monocytogenes* infection is played by the human immune system condition, the dose and virulence of activator are less significant [Gellin B.G., Broome C.V., 1989].

L. monocytogenes are the facultative intracellular parasites; herewith the immune reaction of the hosting body is carried out mainly with the help of cellular mechanisms, and any inborn or received T-lymphocytes function disorder is a prerequisite for the infection development, that is why the persons with different immune deficiencies are the most susceptible to the risk of disease: pregnant women, newborns, elderly people, HIV positives, oncological patients, patients with diabetes mellitus, renal and heart failure, chronic alcoholic intoxication, after the transplantation of organs.

It should be noted that currently the humoral immunity in case of the listeriosis development, in particular, the conversion process, is understudied. It is established that in response to the *L. monocytogenes* contagion the human body produces the antibodies to

listeriolysin O, interlines A and B, autolysin and some other proteins. During the mass screening of population the antibodies to listeria are determined in 22–53% of healthy people.

L. monocytogenes are the "opportunistic microorganisms" that explains the variety of light and hidden forms of listeriosis and often the bacteria carrying; the clinically manifested disease is developed only at the weakening of resistance factors.

L. monocytogenes can cause a wide range of symptoms. In adults, including the non-pregnant women, these symptoms include bacteremia, meningitis and encephalitis [Rocourt J., Cossart P., 1997].

In pregnant women which make one third of all the cases of listeriosis in adults that is explained by the *L. monocytogenes* affinity to the tissues of alvus and placenta the contagion can result in the amnionitis and infection of fetus which leads to the abortion, stillbirth or premature delivery.

Often the severe forms of listeriosis occur either in the very early age or after 60 years.

The frequency of listeriosis occurrence in the men and women is practically the same.

The majority of the cases of listeriosis are sporadic but a part of such cases can have the previously unknown sources of activator [Broome C.V. et al., 1990; Farber J.M., Peterkin P.I., 1991]. The source and route of infection are usually unknown but the food contaminated with *L. monocytogenes* is considered as the main way for the transferring of infection and the cause of 99% of the cases of listeriosis [WHO, 1988; Mead P.S. et al., 1999].

L. monocytogenes often are present transitory in the human intestine. The share of population in the samples of faeces of which the *L. monocytogenes* are detected is from 0.5 to 29% [Farber J.M., Peterkin P.I., 1991]. In average, 2–10% of population are the carriers of bacteria without the manifestations of any health disorders [Skidmore A.G., 1981; Farber J.M., Peterkin P.I., 1991; Schuchat A. et al., 1991; Mascola L. et al., 1992; Rocourt J., Cossart P., 1997; Slutsker L., Schuchat A., 1999].

The availability of a large number of carriers, to the opinion of Farber J.M. and Peterkin P.I. (1991) evidences that the presence of *L. monocytogenes* in faeces is not mandatory for the infection presence confirmation. The role of healthy carriers is still not clearly established but the study of the outbreak of listeriosis in California in 1985 demonstrated that the outbreaks of disease can be potentiated by the secondary transfer through the faeces containing the *L. monocytogenes* [Rocourt J., 1996].

The pregnancy increases the risk of listeriosis development however it is not considered as the prerequisite factor to the development of carrying. Healthy pregnant women can be the carriers of *L. monocytogenes*, but can give birth to the healthy children. Asymptomatic carrying among the pregnant women can achieve 40% [Lamont R.J., Postlethwaite R., 1986].

The classification of symptoms associated with *L. monocytogenes* is based on the hosting body condition, the route of the transfer, the severity of course and the duration of the incubation period (Table 8.16) [FAO/WHO, 2004].

It is considered that more than 20% of population belong to the group with high risk of listeriosis development [Buchanan R.L. et al., 1997; Lindqvist R., Westöö A., 2000]. In case of severe infection development in adults and children the listeriosis is usually followed by some other disease [Gray M.L., Killinger A.H., 1966; WHO, 1988; Linnan M.J. et al., 1988; Shelef L.A., 1989; Broome C.V. et al., 1990; Lorber B., 1990; Schuchat A., 1991] which results in the affection of immune system, for example, cancer, diabetes, alcoholism, viral hepatitis, AIDS; in the people using the immunosuppressive agents as well as in the elderly people. The healthy children and immune competent adults have low risk of the severe listeriosis development.

It is established that in many cases of the outbreaks of listeriosis the light forms of disease characterized by diarrhea, fever, headache and myalgia were registered [Riedo F.X. et al., 1994; Salamina G. et al., 1996; Dalton C.B. et al., 1997; Aureli P. et al., 2000], herewith the outbreaks of disease were associated with the intake of high doses of *L. monocytogenes* with food in the healthy individuals and the symptoms of gastroenteritis disappeared in a few days.

Table 8.16

The classification of health disorders associated with *L. monocytogenes*

The type of listeriosis	The route of transfer	The severity of disease	Incubation period
Occupational infection	Initially the dermal listeriosis occurring after the direct contact with tissues of infected animal	The light degree of severity; self-eventuated cases	1–2 days
Neonatal infection	The contagion of newborns infected by mothers during the delivery or cross-infection between the newborns	Can be very severe resulting in the development of meningitis or death	1–2 days (the early beginning of infection) usually in case of prenatal contagion 5–12 days (late beginning of infection) in case of cross-contagion
Infection during pregnancy (prenatal infection)	Food contaminated with *L. monocytogenes*	The light degree of severity like flue or asymptomatic in mother but resulting in the spontaneous abortions, the death of fetus, stillbirth and newborn meningitis	Usually occurs in the third trimester
Infection in adults (except for pregnant women)	Food contaminated with *L. monocytogenes*	The asymptomatic or light degree of disease severity, with the further development of meningitis; mainly occurs at the decrease in immunity or in elderly people	1 day – 3 months (mainly 20–30 days)
Alimentary infection (gastroenteritis with fever)	Food with high level of contamination by *L. monocytogenes* ($>10^7$/g)	Vomiting and diarrhea, the possible development of bacteremia, usually the self-eventuated cases	<24 hours after the consumption of food contaminated with *L. monocytogenes*

According to the WHO data, the food plays the main role in the propagation of listeriosis. At that the most important is the food ready for consumption which supports the growth of *L. monocytogenes*: log storage in the conditions of refrigerator as well as consumption without further treatment against the listeriosis activator [Pinner R.W. et al., 1992; Rocourt J., 1996; Nø rrung B. et al., 1999; FDA/FSIS, 2001], i.e. the products intially passed the corresponding treatment and further contaminated or subjected to the cross-contamination at the sales outlets or in living conditions.

The different types of soft cheese, processed meat, salami, pasteurized milk, non-pasteurized milk, raw vegetables, etc. are considered as the most often sources of the outbreaks of listeriosis. [FDA/FSIS, 2001].

The data on the outbreaks and sporadic cases of morbidity with listeriosis associated with the consumption of food products European commission health & consumer protection directorate-general opinion of the scientific committee on veterinary measures relating to public health on Listeria monocytogenes) are presented in Table 8.17, 8.18.

Among the registered outbreaks of listeriosis from 1985 to 2005 with the known data of the *L. monocytogenes* content in 1 g of product the outbreak in 1998–1999 in Finland should be noted associated with the consumption of butter in which 10 CFU/g of *L. monocytogenes*/1 g of product were detected. Herewith the number of diseased was 18 persons, with 4 lethal outcomes. Therefore, it can be assumed that the content of 10 CFU/g of *L. monocytogenes*/1 g of product can be considered as the minimum infecting dose.

According to the known data of sporadic morbidity (Table 8.18) the minimum infecting dose can be considered 10^3 CFU of *L. monocytogenes*/g of product.

Table 8.17

The outbreaks of listeriosis associated with the food products consumption

Country	Year	Product	The quantity of *L. monocytogenes* in 1 g of product	The number of cases (deaths)
USA	1985	Soft cheese	10^3–10^4	142 (48)
Switzerland	1983–7	Soft cheese	10^4–10^6	122 (34)
Great Britain	1987–9	Paste	10^2–10^6	More than 350
Australia	1990	Paste	10^3	9 (6)
Australia	1991	Smoked mussels	10^7	4
France	1992	Pork tongue in aspic	10^4–10^6	279 (85)
France	1993	Pork fillet	10^2–10^4	33
USA	1994	Chocolate milk	10^9	45*
Sweden	1994–5	Smoked fish	10^2–10^6	8 (2)
Italy	1997	Maize flour	10^6	748*
Finland	1998–9	Butter	10^1–10^4	18 (4)
Switzerland	2005	Cheese	32 000 CFU/g	10 (3)

N o te : * – predominantly the fever and diseases of gastrointestinal tract.

Table 8.18

The sporadic cases of listeriosis associated with the food products consumption

Country	Year	Product	The quantity of *L. monocytogenes* in 1 g of product	The number of cases (deaths)
USA	1985	Turkish sausages	10^3	None
England	1988	Soft cheese	10^7	None
Finland	1989	Pickled mushrooms	10^6	None
Italy	1989	Sausage	10^6	Unknown
Belgium	1989	Ice cream	10^3–10^6	None

In order to exclude the contamination with *L. monocytogenes* the programs of HACCP (Hazard Analysis and Critical Control Points) as well as the measures aimed at the improvement of sanitary conditions in the food industry are implemented which resulted in the decrease of morbidity with listeriosis in USA from 7.9/mln. of population in 1989 to 4.4/mln. of population in 1993 [Tappero J.W. et al., 1995]. Also the decrease of morbidity with listeriosis in Great Britain was observed simultaneously with the introduction of preventive measures [Fyfe W.M. et al., 1991; McLauchlin J. et al., 1991]. Also it is known about the reductions in the levels of morbidity with listeriosis as a result of the implementation of such programs in the other European countries and Australia [Jacquet C. et al., 1995]. Thus, due to the preventive measures carried out at the food industry enterprises in France it was possible to reduce the morbidity with listeriosis during 1987–1997 by 68% [Goulet V. et al., 2001]. However, starting from this time the level of morbidity remains quite permanent [CDC, 2000]. The annual level of morbidity according to the data of Notermans S. et al. (1998) is within the range from 0.1 to 11.3 of cases/mln. of population. The later studies conducted in the EU countries demonstrate some decrease of morbidity rate which in 2000–2001 varied from 0.3 to 7.8 of cases/mln. of population [De Valk H. et al., 2003].

Also the analysis of existing permissible levels of *L. monocytogenes* content in the food products was performed at the hazard characterization stage.

According to the requirements of technical regulations of the Customs Union and Unified sanitary requirements of the Customs Union the content of *L. monocytogenes* in 25 g of product is not allowed [Unified sanitary-epidemiological and hygienic requirements, 2010; The technical regulations of the Customs Union 021/2011], that corresponds to the permissible level of the content of bacteria 0,04 CFU *L. monocytogenes*/g for all the investigated groups of products.

CAC/GL61–2007 ("Guidelines On The Application Of General Principles Of Food Hygiene To The Control Of *Listeria Monocytogenes* In Foods") is the main document of Codex Alimentarius containing the requirements to the permissible levels of *L. monocytogenes* in food. According to CAC/GL61–2007 the value for the criterion of the permissible content of *L. monocytogenes* in the food products is selected in accordance with probability for the growth and propagation of bacteria in the investigated group of products. Thus, for the food products not supporting the growth and propagation of *L. monocytogenes* in virtue of their physical and chemical properties the permissible level for the content of bacteria is established as 100 CFU *L. monocytogenes*/g, and for the food products in which the growth and propagation of *L. monocytogenes* is possible – 0,04 CFU *L. monocytogenes*/g. The content of *L. monocytogenes* in the fish and fruit and vegetable products is rated under CAC/GL 21–1997 ("Principles for the establishment and application of microbiological criteria for foods") according to the established requirements to the production and use of HACCP system.

The EU countries in accordance with EC Regulations EC 1441/2007 (Commission regulation (EC) No. 1441/2007 of 5 December 2007 amending Regulation (EC) No. 2073/2005 on microbiological criteria for food stuffs) established the criteria for the content of *L. monocytogenes* for the food of children and therapeutic foods (0,04 CFU *L. monocytogenes*/g), for other food products in which the growth and propagation of *L. monocytogenes* is possible (100 CFU *L. monocytogenes*/g – during marketing, 0,04 CFU *L. monocytogenes*/g – before marketing by the manufacturer), as well as for other products not supporting the growth and propagation of *L. monocytogenes* (100 CFU *L. monocytogenes*/g).

The models "dose – response" were used to assess the population health risks associated with the intake of *L. monocytogenes* with food products. In the context of this study the dose means the quantity of microorganisms taken through the gastrointestinal tract. The negative effect from the side of health was considered as the probability of contagion, the development of disease or death. As a rule, same models are built using the known statistical functions of the probability distribution, and the coefficients of dependences are determined from the results of epidemiologic studies. It should be noted that the considered models describe the dependences "dose – response" at the level of population, the probability of disease is not evaluated at the individual level. During the risk assessment it is necessary to pay attention to the characteristic of investigated population, specially to the immune status.

One of the most simple and often used models is the exponential model with one parameter [Haas C.N, 1983; Rose J.B. et al., 1991]:

$$P_i = 1 - \exp[-r_i N_i], \tag{8.17}$$

where P_i – is a probability of disease after the consumption of product i; N_i – is a consumed dose of microorganisms CFU *L. monocytogenes*/day; r_i – is a parameter corresponding to the probability of disease when exposed to the single microorganism. The function curve (8.17) is presented in Fig. 8.18 in the semilogarithmic scale.

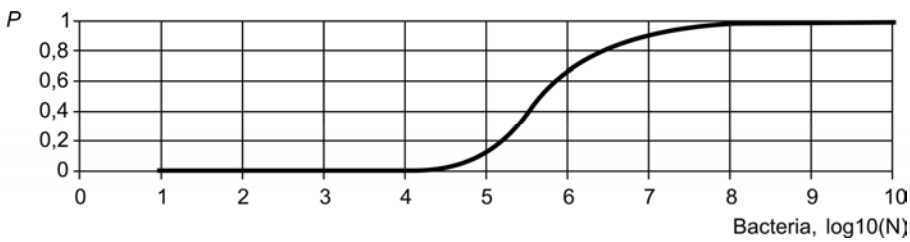

Fig. 8.18. Exponential model

The equation (8.17) is widely used for the assessment of the probability of disease stipulated by the influence of *Listeria monocytogenes* [FAO/WHO, 2004]. The known coefficients under the three types of products were used in the calculation of risk of disease for the people with normal immunity:

1) smoked fish: $r_1 = 5,6 \cdot 10^{-10}$ [Lindquist R., Westoo A., 2000];

2) chocolate milk: $r_2 = 5,8 \cdot 10^{-12}$ [FAO/WHO, 2004];

3) salad "tuna – corn (vegetables)": $r_3 = 1,8 \cdot 10^{-8}$ [FAO/WHO, 2004].

The daily dose of microorganisms N_i was calculated at the exposure assessment stage.

When assessing the risk of disease after the consumption of the several types of products the probability additivity supposition $P = \sum_i P_i$, permissible at the small values P_i was used.

The coefficient $r = 3,15 \cdot 10^{-7}$ was used to calculate the probability of disease in the people of susceptible group [FAO/WHO, 2004].

The exposure assessment was performed based on the average daily intake of the groups of food products considered as the most probable sources of *L. monocytogenes* [FAO/WHO, 2004] by the different groups of population and the permissible content of *L. monocytogenes* in the food products.

The several options of daily intake for the following categories of food products are proposed for the population of the Russian Federation: vegetables, fruit, fat products, dairy products, meat products, fish (seafood) used for the assessment of exposure of *L. monocytogenes* based on the data of 2005–2010 (Table 8.19–8.21).

Table 8.19

The recommended daily consumption of food products by the population of the Russian Federation for 2010*

The group of food products	Recommended consumption for the whole population (g/day)
Vegetables	383.0
Fruit	273.9
Fat products	30.0
Dairy products	931.5
Meat products	205
Fish (seafood)	60.2

Note: * – the recommended volumes of the food products consumption are according to the Order of the Ministry of Health and Social Development of the Russian Federation No. 593n dd. August 2, 2010 "On the approval of recommendations on the rational norms of food products consumption meeting the modern requirements of healthy nutrition".

Table 8.20

The actual daily consumption of food products by the adult population of the Russian Federation for 2005**

The group of food products	Actual consumption by the adult population (g/day)
Vegetables	196
Fruit	112
Fat products	62
Dairy products	555
Meat products	143
Fish (seafood)	24

Note: ** – according to the data of the "State policy concept in the field of healthy nutrition for population of the Russian Federation for the period to 2005".

Table 8.21

The optimum average daily set of food products for pregnant and nursing women* (g, gross weight) completely meeting their physiological needs in the nutrients and energy**

The group of food products	Optimum average daily set for pregnant women (g/day)	Optimum average daily set for nursing women (g/day)
Vegetables	500	500
Fruit	320	320
Fat products	62	62
Dairy products	590	690
Meat products	170	170
Fish (seafood)	70	70

Note: *** – "Recommended sets of products for the nutrition of pregnant women, nursing mothers and children in the age of up to 3 years".

Based on the presented data, and also taking into account the permissible content of *L. monocytogenes* at the final point of the food production (0,04 CFU *L. monocytogenes*/g) and maximum permissible content of *L. monocytogenes* in the food product ready for consumption and entered the market (100 CFU *L. monocytogenes*/g) as the most often discussed standards for the content of bacteria in the food products [FAO/WHO, 2004] 12 exposure scenarios were developed:

– at the recommended daily consumption of food products by the adult population with the content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 1 and 2 respectively);

– at the actual daily consumption of food products by the adult population with content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 3 and 4 respectively);

– at the consumption in accordance with optimum average daily set of food products for pregnant women (vegetables and fish) and recommended daily consumption of other food products with content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 5 and 6 respectively);

– at the consumption in accordance with optimum average daily set of food products for pregnant women (vegetables and fish) and actual daily consumption of other food products with content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 7 and 8 respectively);

– at the consumption in accordance with optimum average daily set of food products for nursing women (vegetables and fish) and recommended daily consumption of other food products with content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 9 and 10 respectively);

– at the consumption in accordance with optimum average daily set of food products for nursing women (vegetables and fish) and actual daily consumption of other food products with content of *L. monocytogenes* at the level of 0,04 and 100 CFU/g (scenarios 11 and 12 respectively).

The pregnant and nursing women were considered as the susceptible groups of population.

The maximum daily intake of *L. monocytogenes* with food products is presented in Table 8.22–8.24.

According to the results of the simulation of dependence "dose – response" at the risk characterization stage the cumulative probabilities of the listeriosis development were obtained for 12 exposure scenarios (Table 8.25).

The level of the cumulative risk of the listeriosis development for adults at the permissible content of *L. monocytogenes* in the food products as 0,04 CFU/g was $2{,}77^{-07}$ and $1{,}42^{-07}$ taking into account the recommended (scenario 1) and actual (scenario 3) consumption of food products, respectively, the main contribution to the value of cumulative risk is made by vegetables (99,6 and 99,3 %, respectively).

Table 8.22

The maximum daily intake of *L. monocytogenes* with food products taking into account the recommended daily consumption of food products in the Russian Federation for 2010

The group of food products	CFU number *L. monocytogenes* (scenario 1)	CFU number *L. monocytogenes* (scenario 2)
Vegetables	15.32	38300
Fruit	10.956	27390
Fat products	1.2	300
Dairy products	37.26	93150
Meat products	8.2	20500
Fish (seafood)	2.408	6020

Table 8.23

The maximum daily intake of *L. monocytogenes* with food products taking into account the actual daily consumption of food products in the Russian Federation for 2005

Group of food products	CFU number *L. monocytogenes* (scenario 3)	CFU number *L. monocytogenes* (scenario 4)
Vegetables	7.84	19600
Fruit	4.48	11200
Fat products	2.48	6200
Dairy products	22.2	55500
Meat products	5.72	14300
Fish (seafood)	0.96	2400

Table 8.24

The maximum daily intake of *L. monocytogenes* with food products taking into account the optimum average daily set of food products for pregnant and nursing women (g, gross weight) completely meeting their physiological needs in the nutrients and energy

The group of food products	Pregnant women		Nursing women	
	CFU number *L.monocytogenes* (permissible content of *L. monocytogenes* in the food product 0,04 CFU/g)	CFU number *L. monocytogenes* (permissible content of *L. monocytogenes* in the food product 100 CFU/g)	CFU number *L.monocytogenes* (permissible content of *L. monocytogenes* in the food product, 0,04 CFU/g)	CFU number *L.monocytogenes* (permissible content of *L. monocytogenes* in the food product 100 CFU/g)
Vegetables	20	5000	20	5000
Fruit	12.8	3200	12.8	3200
Fat products	2.48	6200	2.48	6200
Dairy products	23.6	5900	27.6	6900
Meat products	6.8	1700	6.8	1700
Fish (seafood)	2.8	700	2.8	700

Table 8.25

The cumulative probabilities of the listeriosis development at the different scenarios of exposure to *L. monocytogenes*

The group of food products	Vegetables	Dairy products	Fish	Cumulative risk
Scenario 1	2.76^{-07}	2.16^{-10}	1.35^{-09}	2.77^{-07}
Scenario 2	**6.89^{-04}**	5.40^{-07}	3.37^{-06}	**6.93^{-04}**
Scenario 3	1.41^{-07}	1.29^{-10}	5.38^{-10}	1.42^{-07}
Scenario 4	**3.53^{-04}**	3.22^{-07}	1.34^{-06}	**3.54^{-04}**
Scenario 5	2.76^{-07}	7.43^{-06}	1.35^{-09}	7.71^{-06}
Scenario 6	**6.89^{-04}**	**1.86^{-03}**	3.37^{-06}	**2.55^{-03}**
Scenario 7	1.41^{-07}	7.43^{-06}	5.38^{-10}	7.57^{-06}
Scenario 8	**3.53^{-04}**	**1.86^{-03}**	1.34^{-06}	**2.21^{-03}**
Scenario 9	2.76^{-07}	8.69^{-06}	1.35^{-09}	8.97^{-06}
Scenario 10	**6.89^{-04}**	**2.17^{-03}**	3.37^{-06}	**2.86^{-03}**
Scenario 11	1.41^{-07}	8.69^{-06}	5.38^{-10}	8.83^{-06}
Scenario 12	**3.53^{-04}**	**2.17^{-03}**	1.34^{-06}	**2.52^{-03}**

For the conditions of scenarios developed taking into account the optimum average daily set of product for pregnant women (vegetables and fish), the daily consumption of other products by the adult population and the permissible level of the content of *L. monocytogenes* in the food products 0.04 CFU/g (scenarios 5 and 7) the cumulative risk of listeriosis development was 7.71^{-06} (scenario 5) and 7.57^{-06} (scenario 7), herewith the main group of products forming the risk to health are the dairy products, the contribution to the cumulative value of risk is 96.4 and 98.2% for scenario 5 and 7 respectively.

Cumulative values for the risk of listeriosis development for scenarios 9 and 11 (optimum average daily set of food products for nursing women (vegetables and fish) supplemented by the daily consumption of other products by the adult population, taking into account the permissible level of content of *L. monocytogenes* in the food products 0.04 CFU/g) was 8.97^{-06} and 8.83^{-06}, the dairy products stipulate 96.9% (scenario 9) and 98.4% (scenario 11) from the cumulative risk value.

In the exposure scenarios which are based on the recommended and actual consumption of food products and permissible level if content of *L. monocytogenes* 100 CFU/g (scenario 2 and 4 respectively) the cumulative risk is equal to 6.93^{-04} and 3.54^{-04} respectively. The main share of cumulative risk (99.4 and 99.7 % for scenarios 2 and 4 respectively) is associated with the intake of vegetables.

For the conditions of scenarios developed taking into account the optimum average daily set of product for pregnant women (vegetables and fish), daily consumption of other products by the adult population and the permissible level of the content of *L. monocytogenes* in the food products 100 CFU/g (scenarios 6 and 8) the cumulative risk of listeriosis development was 2.55^{-03} (scenario 6) and 2.21^{-03} (scenario 8), herewith the main group of products forming the risk to health are the dairy products, the cumulative value of risk to health is 72.9 and 84.2 % for scenario 6 and 8 respectively.

Cumulative values for the risk of listeriosis development for scenarios 10 and 12 (optimum average daily set of food products for nursing women (vegetables and fish) supplemented by the daily consumption of other products by the adult population, taking into account the permissible level of content of *L. monocytogenes* in the food products 100 CFU/g) was 2.86^{-03} and 2.52^{-03}, the dairy products stipulate 75.9 % (scenario 10) and 86.1 % (scenario 12) from the cumulative risk value.

The minimum contribution to the levels of cumulative risk of listeriosis development is made by the fish products from 0.01% (5.38^{-10}) (scenarios 5 and 7) to 0.49 % (3.37^{-6}) (scenario 2).

The characterization of risk of the listeriosis occurrence was conducted based on the system of criteria for the health risk acceptability (Table 8.26).

Table 8.26

Listeriosis occurrence risk characterization for the different exposure scenarios

Scenario	Listeriosis occurrence risk level	Assessment criterion	Characteristics
1	$2.77 \cdot 10^{-7}$	$\leq 1 \cdot 10^{-6}$	Negligible, not differing from usual daily risks (*de minimis* level), do not require any additional mitigation measures; the levels are subject to the periodical control ony
2	$6.93 \cdot 10^{-4}$	$1 \cdot 10^{-4}$–$1 \cdot 10^{-3}$	Unacceptable for population; requires development and conduction of palnned measures on its mitigation
3	$1.42 \cdot 10^{-7}$	$\leq 1 \cdot 10^{-6}$	Negligible, not differing from usual daily risks (*de minimis* level), do not require any additional mitigation measures; the levels are subject to the periodical control ony
4	$3.54 \cdot 10^{-4}$	$1 \cdot 10^{-4}$–$1 \cdot 10^{-3}$	Unacceptable for population; requires development and conduction of planned measures on its mitigation
5	$7.71 \cdot 10^{-6}$	$1 \cdot 10^{-6}$–$1 \cdot 10^{-4}$	Maximum acceptable risk; are subject to continuous control; the additional measures on its mitigation can be conducted
6	$2.55 \cdot 10^{-3}$	$\leq 1 \cdot 10^{-3}$	Unacceptable for population (*de manifestis* risk); if it is reached it is necessary to provide the recommendations for persons making the decisions on the implementation of urgent measures for the risk mitigation
7	$7.57 \cdot 10^{-6}$	$1 \cdot 10^{-6}$–$1 \cdot 10^{-4}$	Maximum acceptable risk; are subject to continuous control; the additional measures on its mitigation can be conducted
8	$2.21 \cdot 10^{-3}$	$\leq 1 \cdot 10^{-3}$	Unacceptable for population (*de manifestis* level); if it is reached it is necessary to provide the recommendations for persons making the decisions on the implementation of urgent measures for the risk mitigation
9	$8.97 \cdot 10^{-6}$	$1 \cdot 10^{-6}$–$1 \cdot 10^{-4}$	Maximum acceptable risk; are subject to continuous control; the additional measures on its mitigation can be conducted
10	$2.86 \cdot 10^{-3}$	$\leq 1 \cdot 10^{-3}$	Unacceptable for population (*de manifestis* level); if it is reached it is necessary to provide the recommendations for persons making the decisions on the implementation of urgent measures for the risk mitigation
11	$8.83 \cdot 10^{-6}$	$1 \cdot 10^{-6}$–$1 \cdot 10^{-4}$	Maximum acceptable risk; are subject to continuous control; the additional measures on its mitigation can be conducted
12	$2.52 \cdot 10^{-3}$	$\leq 1 \cdot 10^{-3}$	Unacceptable for population (*de manifestis* level); if it is reached it is necessary to provide the recommendations for persons making the decisions on the implementation of urgent measures for the risk mitigation

The results of risk assessment demonstrated that for all the exposure scenarios developed taking into account the maximum permissible content of *L. monocytogenes* in the food product ready for consumption and available at the market (100 CFU *L. monocytogenes*/g), the listeriosis occurrence risk is assessed as unacceptable for population. The high risk levels are formed at the expense of the intake of *L. monocytogenes* with vegetables for adult population and additionally with dairy products for the pregnant and nursing women.

In the exposure scenarios with the use of the permissible content of *L. monocytogenes* at the final point of food production (0,04 CFU *L. monocytogenes*/g) the level of risk for the health disorders associated with the intake of *L. monocytogenes* with food products is characterized as negligible (scenarios based on the optimum and actual daily consumption of food products by the population of the Russian Federation) and acceptable (scenarios based on the optimum average daily set of products for pregnant and nursing women).

Thus, the results of the assessment of risk associated with the permissible levels of content of *L. monocytogenes* in the separate groups of food products demonstrated that when exposed at the level of hygienic standards of the Customs Union countries, the standards of Codex Alimentarius and European Union before the release to the market by the manufacturer (absence of *L. monocytogenes* in 25 g of food products) the risk to health does not exceed the maximum permissible level of severe diseases ($1 \cdot 10^{-4}$) that ensures the safety to the health of population in the Russian Federation. The adoption of standards of Codex Alimentarius and European Union during the marketing of products (100 CFU *L. monocytogenes*/g) is unacceptable because it can result in the unacceptable risk of listeriosis both to the population of the Russian Federation in general (up to $6.93 \cdot 10^{-4}$) and for the most susceptible groups (up to $2.55 \cdot 10^{-3}$ in pregnant women and up to $2.86 \cdot 10^{-3}$ in nursing women).

Also within the study on the assessment of risk to the health of population associated with intake of *L. monocytogenes* with separate types of food products we conducted the assessment of the uncertainties of results which can be stipulated by the absent or incomplete information, gaps in the scientific theory required for forecast based on the causal relationships (uncertainties of model) and associated with parameters used for the exposure assessment and calculation of risks (uncertainty of parameters).

It is necessary also to take into account the uncertainties associated with the food products consumption. For example, the Russian Federation has the tendency to increase the share of meat and dairy products in the diet of population. The Federal Law No. 227-FZ dd. December 3, 2012 "On the consumer goods basket throughout the Russian Federation" provides the increase in the volume of consumption (in average per one person per year) of dairy and meat food products.

The uncertainties of models include also the limited number of these studies under the results of which the parameters of models were calculated. The values of these parameters can vary in the population, the inaccuracy in their determination can be defined by the use of summarized averaged data for the large populations. The use of standard values increases the uncertainties of the exposure and risk assessments the degree of which is characterized based on the parameters sensitivity analysis.

In addition, when assessing the uncertainty of results it should be noted that the listeriosis risk overestimation could be stipulated by the assumption that the quantity of *L. monocytogenes* in all the food products is at the upper limit of permissible content and that the vegetables and dairy products are consumed without preliminary heat treatment reducing the content of *L. monocytogenes* in them.

Both the overestimation and underestimation of risk could be stipulated by the use of models "exposure – response" developed for the separate products and extrapolation of dependences to the group of food products.

The underestimation of risk could be stipulated by the insufficiently accurate accounting of the listeriosis disease incidences, specially the absence of accounting of asymptomatic forms and light cases as well as the incomplete information about the probability of occurrence of listeriosis in a number of the most sensitive groups of population, for example, the persons with immune status disorder. It is necessary to take into attention the availability of information

about the occurrence of diseases when exposed to 10 CFU *L. monocytogenes*/g (European commission health & consumer protection directorate-general opinion of the scientific committee on veterinary measures relating to public health on Listeria monocytogenes).

Antibiotics of tetracycline group

Currently due to the entrance of Russia to WTO the actual is the harmonization of hygienic standards for the quality of products [Onishchenko G.G. et al., 2013]. One of the main requirements to the methodology for establishing the product safety standards is their justification under the health risk criteria. But the differences in their values can occur even at the observance of the risk assessment procedures during the justification of separate standards. In this case, every state, including the Russian Federation, is entitled to defend its positions confirming them by the results of conducted studies.

The justification of domestic hygienic standards for the residual quantities of antibiotics of tetracycline group in the food products can be used as an example of the defense of the Russian positions of justification. For the most adequate perception of existing situation it is more feasible to study the history of issue.

The standards for the permissible levels of tetracycline are the acceptable daily intake (ADI) and maximum permissible levels of content in the food products (MRL) - established in 1990 in the 36th report of joint expert committee on the food additives FAO/WHO (JECFA) [WHO, 1990].

Inactive daily dose of tetracycline (NOEL) is established at the level of 2 mg per day. It was based on the results of study of the tetracycline effect to people. The effect to the intestinal microflora (increase in the level of the coliforms resistance) was considered as the critical effect. The same study determined the minimum active dose – 20 mg per day. The changes in the intestinal microflora was studied as the key effect. The key effect selection is completely adequate and confirmed by the results of many studies not causing the doubts. The Russian scientific literature also contains the data on the main contribution of sub inhibitory concentrations of tetracyclines in the propagation of the most unfavorable transmissible type of resistance to antibiotics in microbes and the formation of new strains with changed properties and pathogenesis associated with it [Onishchenko G.G. et al., 2012].

The inactive daily dose established in the toxicological studies was 18 mg/day. When establishing the permissible daily dose (3 mg per 1 kg of body weight per day) the uncertainty factor 10 was taken due to he variability of intestinal flora in people. Herewith the conservative approach was used due to the absence of studies within the range of doses from 2 to 20 mg per day and it was noted that the real permissible daily dose can slightly exceed the established one. In the 40th report of the joint expert committee on the food additives FAO/WHO the permissible daily dose of tetracyclines was updated [Updating the Principles and Methods of Risk Assessment, 2006]. The updating was based on the results of *in vitro* experiment on the study of dosages equivalent to 0.025, 0.25 and 2.5 mg/kg of body weight. It was established that at the equivalent of dose to 2.5 mg/kg of body weight during 24 hours we can observe the increase in the share of resistant *E.coli* from less than 20 to more than 50%; this share decreased to 35% on the 6th day. In the control experiment without the use of tetracycline the share of resistant *E.coli* did not exceed 5%. At the equivalents of doses to 0.025 and 0.25 mg/kg of body weight no effect was observed. The committee based on the results of studies concluded that the variability among the individuals is small and the further use of uncertainty factor is not feasible, therefore, it is necessary to take 30 mkg per 1 kg of body weight per day as the permissible daily dose.

However such decision is unjustified under the following reasons:

1. The permissible daily dose is established for the conditions of consumption of products daily during the whole life and cannot be based on the data obtained during the short-term *in vitro* experiment without the corresponding analysis of uncertainty which takes into account the transfer of results obtained *in vitro* to human and data of the short-term study to the effect during the whole life [IPCS, 1987; WHO, 1996].

2. According to the formula (8.18) recommended by FAO/WHO [IPCHEM/WHO, 2000] we conducted the calculation of permissible daily doses for tetracycline and oxytetracycline for the different types of microorganisms.

$$ADI = \frac{MIC_{50}(\text{мкг/г}) \cdot \text{Масса кишечного содержимого (220 г)}}{\text{Биодоступная пероральная доза} \cdot \text{Фактор запаса} \cdot \text{Масса индивидуума (60 кг)}}. \quad (8.18)$$

The formula was developed based on the modal value MIC_{50} (MIC_{50} – is a minimum concentration of antibiotic inhibiting the growth of 50% of cultures for the certain microorganism), reserve factor to account the different types of variability, weight of intestinal content, weight of individual and bioavailability of the oral dose of antibiotic.

The values MIC_{50} of tetracycline and oxytetracycline for 10 different microorganisms were taken in accordance with WHO Food Additives Series 36 [Wouters M.F.A. et al., 1998], the reserve factor value – 1, share of bioavailable oral dose of tetracyclines – 0.6, eight of intestinal content – 220 g, average weight of individual – 60 kg.

The permissible daily doses for 10 different types of microorganisms obtained during the calculation in accordance with formula (8.18) varied from 0.37 mcg/kg of body weight in relation to *Clostridium spp.* to 195.6 mcg/kg of body weight for *Escherichia coli* and *Proteus spp.* (Table 8.27). Such high variability of results can mean the necessity to include into the calculation of the permissible daily dose the additional uncertainty factor for the most sensitive groups of population, for example, children and the health risk assessment conduction taking into account the peculiarities of these groups.

Table 8.27

Design permissible daily doses of antibiotics of tetracycline group for the different types of microorganisms

Microorganism	Permissible daily dose, mcg/kg
Escherichia coli	195.56
Bifidobacterium spp.	97.78
Bacteroides fragilis	24.44
Eubacterium spp.	12.22
Clostridium spp.	0.38
Streptococcus spp.	97.78
Fusobacterium spp.	0.76
Lactobacillus spp.	12.22
Proteus spp.	195.56
Peptostreptococcus spp.	12.22

3. The results of in vitro experiment [WHO, 1999] were used as the basis for refusal from the use of uncertainty factor during the establishment of ADI for tetracyclines. It was demonstrated that the concentrations equivalent to the inactive doses of 0,025, 0,25 and 2,5 mg/kg of body weight were studied and the conclusions of that the doses of 0,025, 0,25 and 2,5 mg/kg of body weight are inactive were proposed. Herewith it was impossible to establish how the assessment of the equivalence of doses to the levels of effect to microflora in the chemostat was performed. The assessment of proposed relation using the formula (8.18) demonstrated the lack of comparability in relation to the obtained results. This evidences the high uncertainty of data based on which it is proposed to refuse from the modifying factor 10 and permissible daily dose of 3 mcg/kg of body weight.

Due to the insufficient justification of the permissible daily dose for the residual quantities of antibiotics of tetracycline group in the food products it was necessary to develop the domestic standard using the health risk criteria.

During the justification of the content of residual quantities of antibiotics of tetracycline group under the health risk criteria at the hazard identification stage it was established that the drugs of tetracycline group are the bacteriostatic broad-spectrum antibiotics, the most common drugs used for the treatment and prevention of diseases of poultry and beef breeds [Zaitseva N.V. et al., 2012*b*]. The intestinal microflora balance violation is considered as the main response

from the side of health during the intake of residual quantities of tetracyclines with the food products [Van den Bogaard A.E., Stobberingh E.E., 1999; Van den Bogaard A.E. et al., 2000; Yvonne A. et al., 2002; Nowrouzian F. et al., 2003; Saarela M. et al., 2007; Lisbeth Elvira de Vries et al., 2009].

Table 8.28 presents the content of normal microflora and data of minimum inhibiting concentrations $Mic_{50,}$ Mic_{90} (concentration at which 50 and 90% of bacteria are inhibited) [Wouters M.F.A. et al., 1998; FAO/WHO, 1998].

Table 8.28

Values MIC_{50}, MIC_{90} for tetracycline in relation to the human intestinal microflora

Type of bacteria	Share in the normal intestinal microflora, %	$MIC_{50,}$ mkg/ml	$MIC_{90,}$ mkg/ml
Bifidobacterium *spp*.	85	16	32
Bacteroides *spp*.	4.99	1	32
Clostridia *spp*.	0.01	0.062	32
Fusobacterium *spp*.	2	0.125	–
Lactobacterium	4	2	2
Peptostreptococcus	2	2	32
E. coli (coliform bacterium)	1	32	64
Facultative flora	1	–	–

The model proposed by A. Fazil [Fazil A.M., 1996] and based on the Poisson beta-distribution is used for the calculation of intermediate values of the minimum inhibitory concentrations:

$$p_i = 1-(1+\alpha C)^{-\beta}, \tag{8.19}$$

where p_i – is a percent of inhibited bacteria of type *i*;

C – is an intestinal tetracycline concentration;

α, β – are the parameters of model.

The system of two equations was solved for each type of bacteria to assess the parameters α, β using the Matlab package:

$$\begin{cases} 0,5 = 1-(1+\alpha MIC_{50})^{-\beta}, \\ 0,9 = 1-(1+\alpha MIC_{90})^{-\beta}. \end{cases} \tag{8.20}$$

The results of calculation of parameters for each type of bacteria in the intestinal microflora are specified in Table 8.29.

Table 8.29

Parameters for the models of tetracycline concentration effect to the inhibition of bacteria in the intestinal microflora

Type of bacteria	α	β
E. coli (coliform bacterium)	0.00024	148.4
Bifidobacterium *spp*.	0.00048	148.4
Bacteroides *spp*.	3.09	0.5
Clostridia *spp*.	219.2	0.26
Fusobacterium *spp*.	0.68	14.27
Lactobacterium	0.0078	148.4
Peptostreptococcus	0.89	0.68

Fig. 8.19 shows the models for dependence of the percent of inhibition from the tetracycline concentration for different bacteria which demonstrate that there is a variability in the sensitivity of different bacteria contained in the intestinal tract to tetracycline.

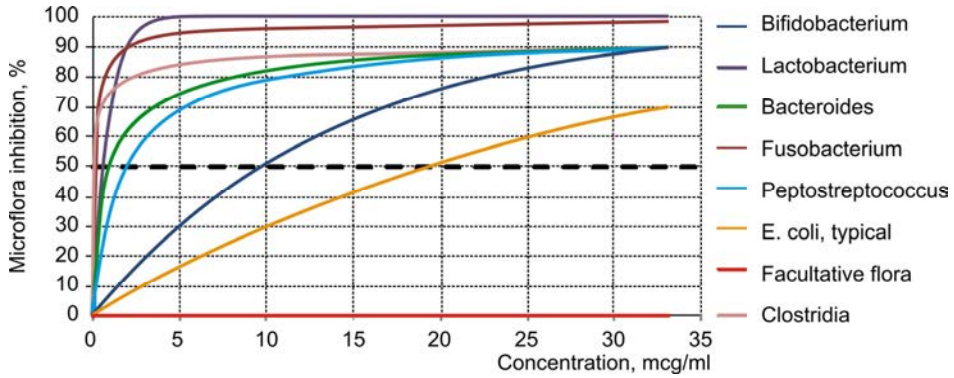

Fig. 8.19. The models for dependence of the percent of inhibition on the tetracycline concentration for different bacteria

Therefore, there are the reasons to argue that the increase in the intestinal tetracycline content results in the change of relation between the different types of bacteria. Herewith, according to the results of studies of D.E. Corpet (1993), M. Shuhaimi et al. (1999), J. Levy (2000), D.E. Corpet (2000), A. Perrin-Guyomard et al. (2001) which describe the growth of pathogenic microflora during the inhibition of the different types of microorganisms it is possible to perform the simulation of changes in the microflora composition under the influence of tetracycline based on the balance ratios.

The equation for the balance of microorganisms in the intestinal tract is presented as follows

$$\sum_i n_i = const = N, \tag{8.21}$$

where n_i – is a number of bacteria of type i;

N – is a total microflora number.

Since the inhibition of one bacteria results in the release of space for the growth of other the redistribution of percentage is performed. In other words, based on (8.22) it is possible to make the relation of integrity of the total number of bacteria in the form of

$$\sum_i \frac{n_i}{N} 100\,\% = \sum_i \lambda_i 100\,\% = 100\,\%, \tag{8.22}$$

where $\lambda_i = \frac{n_i}{N}$ – is a relative quantity of intestinal microflora of type i.

Based on the balance equation (8.21) and taking into account the influence of tetracycline on the inhibition of the different types of bacteria (8.22) we performed the calculation of the relative intestinal microflora composition depending on the tetracycline concentration under the ratio

$$\lambda_i(C) = \frac{\lambda_i(0)(1-p_i(C))}{\sum_i \lambda_i(0)(1-p_i(C))}. \tag{8.23}$$

The formation of disbalance in the microbial flora of intestinal tract under the data of in vitro studies can be illustrated by the results of mathematical simulation for the growth of facultative microflora on the background of the obligate flora inhibition, first of all of Bifidobacterium (Fig. 8.20).

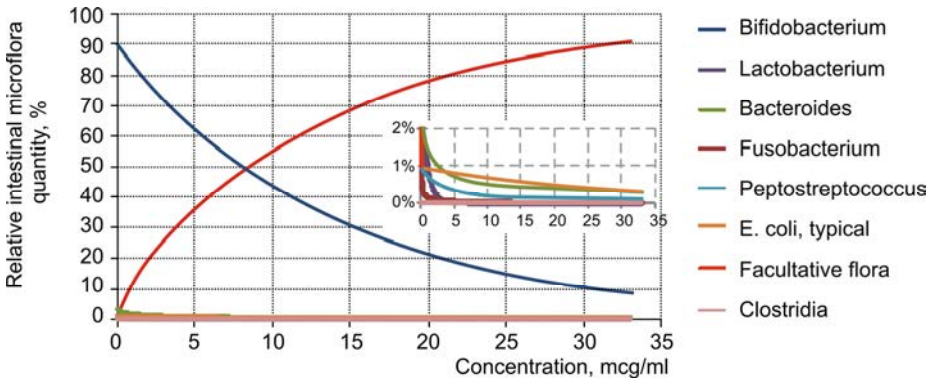

Fig. 8.20. Dependence of the relative quantity of intestinal microflora (%) on the tetracycline concentration

The results of simulation showed the regularities for the change in the microflora composition during the inhibition of the obligate bacteria growth: they are replaced by the facultative bacteria resistant to tetracycline. Thus, at the increase of tetracycline concentration the relative number of Bifidobacterium decreases achieving 9%. At that the facultative resistant to tetracycline flora is developed which at the increase of concentration can achieve 91% of the whole number of bacterial flora.

The charts for changes in the relative number of every type of microflora are presented in Fig. 8.21.

The intestinal microflora change frequency (k_i) is determined under the formula

$$k_i = n_i / n_i^{\text{норм}}, \tag{8.24}$$

where $n_i^{\text{норм}}$ – is a number of bacteria of type *i* in the normal microflora.

The change frequency calculation results are presented in Fig. 8.22.

The intestinal microflora is represented by the obligate (Peptostreptococcus, Lactobacterium, Bifidobacterium, Fusobacterium, Bacteroides, Clostridia, coliform bacterium) and facultative microflora (aerobic bacteria resistant to tetracycline). The charts for changes in the number of obligate and facultative intestinal microflora are presented in Fig. 8.23.

The share of facultative flora increases at the decrease of share of obligate microflora (Fig. 8.24).

The children in the age of 1–11 years with intestinal microflora sensitive to tetracycline and composing up to 70% of the whole children's population were selected as the risk group [Kamalova A.A., 2011].

The scientific studies dedicated to the study of pathogenetic processes in the intestinal tract [Gusakova E.V., 2003; Notice to applicants and notes for guidance, 2003; Ivanova T.N., 2008; Orlova N.A., 2010] present the materials on the frequency of violation of the balance of microorganisms with different degree at the different diseases among the children (table 8.30).

The violation of balance in the intestinal microflora at the specified diseases is established among the children's population: first category – from 2,0 o 74,0 %, second category – from 26,0 to 84,0 % an third category – from 0,0 to 39,1 %.

During the study for the children's population we developed the four exposure scenarios which took into account the data on the average daily consumption of food products of animal origin by the children's population of the Russian Federation and values of tetracycline MPL accepted in the Russian Federation (10 mcg/kg) (scenario 1), maximum residual levels (MRL) of tetracycline recommended by WHO (1990) (scenario 2), FAO/WHO (1998) (scenario 3) and accepted in the USA (scenario 4).

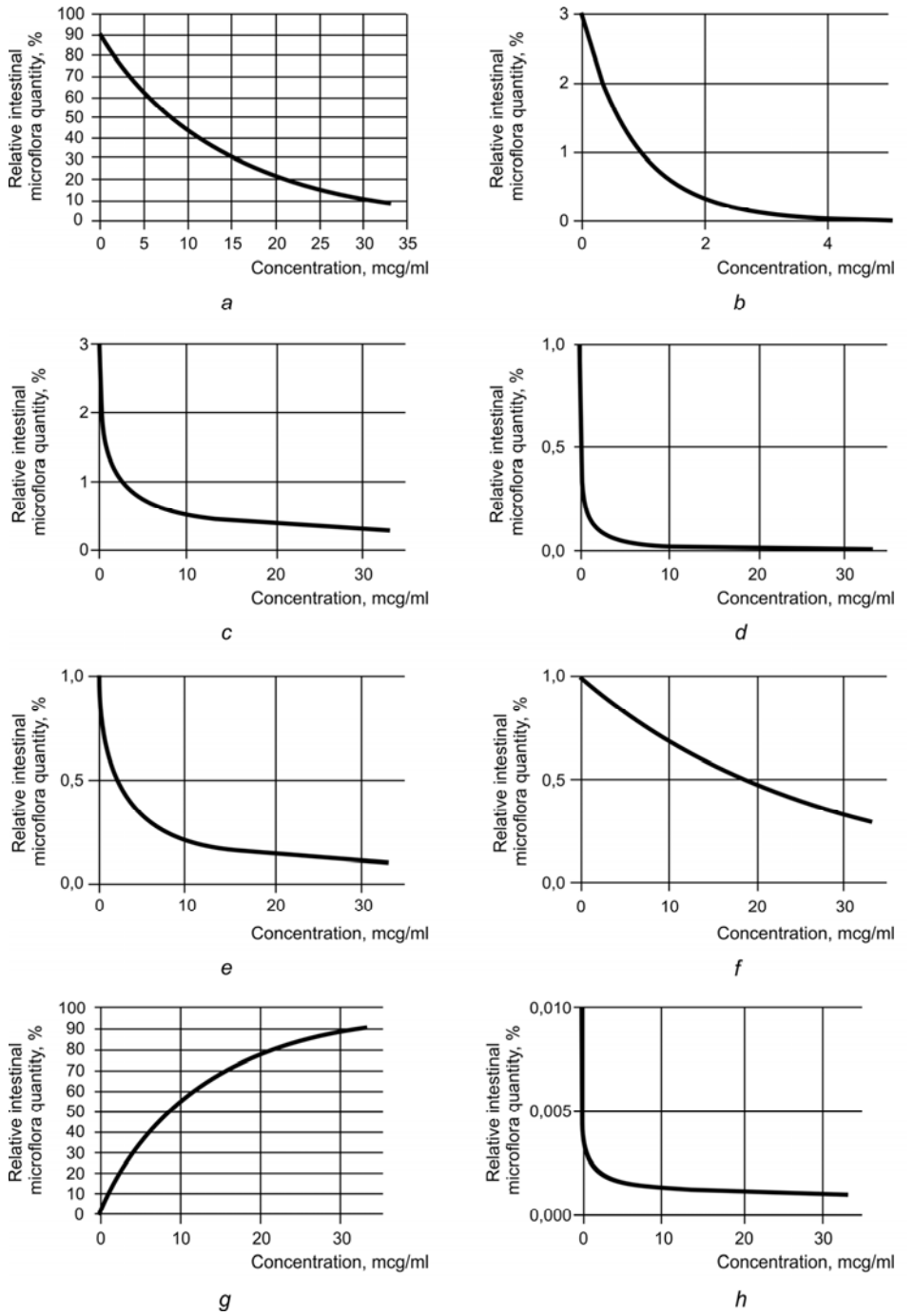

Fig. 8.21. Change in the microflora quantity under the influence of tetracycline:
a – Bifidobacterium; *b* – Lactobacterium; *c* – bacteroids; *d* – Fusobacterium;
e – Peptostreptococcus; *f* – *E. coli*; *g* – resitant; *h* – Clostridia

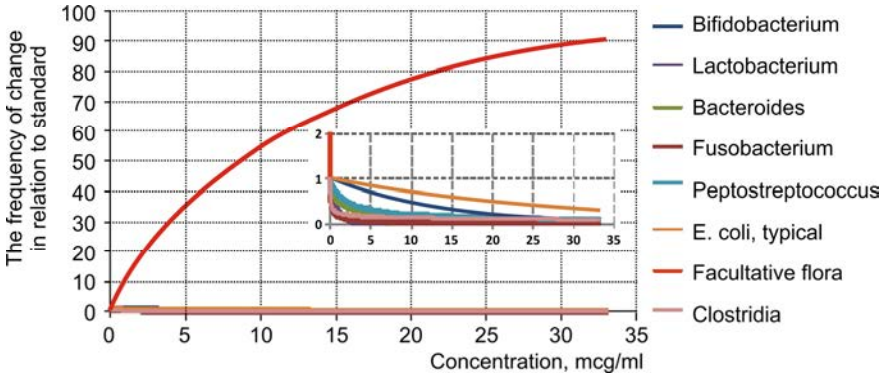

Fig. 8.22. The dependence of the frequency of the normal composition of intestinal microflora on the tetracycline concentration

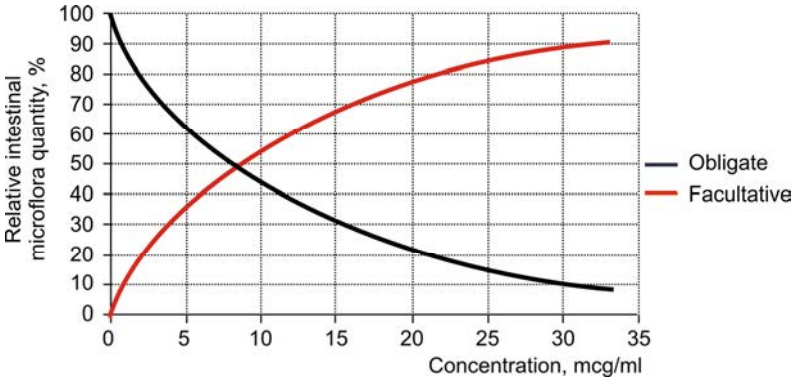

Fig. 8.23. Change in the balance of the relative quantity of intestinal microflora (%) on the tetracycline concentration

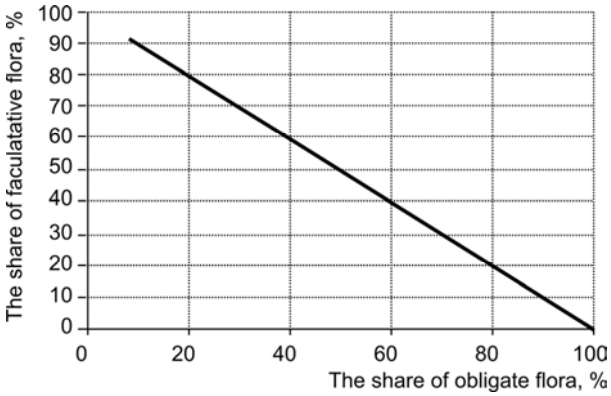

Fig. 8.24. Relation between the shares of facultative and obligate intestinal microflora for the different daily doses of tetracycline

Table 8.30

The frequency of the intestinal microflora violations at the different diseases (children), %

Group (code under MKB-10)	The violation of balance			
	Absence of violations	1st category	2nd category	3rd category
Irritable bowel syndrome with diarrhea (K58.0)	0	22.2	66.7	11.1
Coprostasia (K59.0)	0	74.0	26.0	0
Unspecified intestinal tract functional disturbance (K59.9)	0	15.0	84.0	1.0
Iron deficiency anemia (D50)	0	39.8	46.6	13.6
Other atopic dermatitis (L20.8)	0	40.6	37.2	22.2
Duodenitis (K29.8, K29.9)	26.7	31.5	33.7	8.1
Alimentary allergy (T78.0, T78.1, T78.4)	1.4	12.6	46.9	39.1
Total unspecified variable immune deficiency (D83.9)	0	2.0	80.0	18.0

The values of the maximum residual levels of tetracycline for the different types of animal tissues and the types of exposure are presented in table 8.31.

Table 8.31

***MRL* values for the different types of animal tissues and the types of exposure**

Food product	WHO, 1990	FAO/WHO, 1998	USA	Customs Union
Milk, mcg/kg	100	100	300	10
Muscular tissue, mcg/kg	100	200	2000	10
Fat tissue, mcg/kg	10		10	10
Eggs, mcg/kg	200	400	200	10
Liver, mcg/kg	300	600	300	10
Kidney, mcg/kg	600	1200	600	10

The indicators for the daily content of the products of animal origin in the nutrition of children's population of 3–7 years according to the guidelines of Moscow [Moscow Municipal Administration, 2007] are presented in Table 8.32.

Table 8.32

Daily norms for consumption of products of animal origin for the children's population in the Russian Federation

Food products	Daily consumption level, kg
Meat (muscular tissue)	0.074
Liver	0.007
Eggs	0.048
Milk	0.558

The obtained values of the maximum daily tetracycline consumption for the children's population in the conditions of the investigated exposure scenarios taking into account the average body weight (20 kg) are presented in Table 8.33.

The tetracycline concentrations in the gastrointestinal tract for the four options of exposure are calculated taking into account the average weight of content of intestinal tract in children (50 g) [Kamyshnikov V.S., 2007] (Table 8.34).

Thus, the tetracycline concentration in the gastrointestinal tract of the children's population for the four investigated exposure scenarios varied from 0,069 mcg/g (scenario 1) to 7,2 mcg/g (scenario 4).

Table 8.33

Values of maximum daily tetracycline intake for the investigated exposure scenarios

Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Maximum daily intake, mcg/kg	3.2	89.4	160.3	360.95

Table 8.34

Tetracycline concentrations in the gastrointestinal tract of children for the investigated exposure scenarios

Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Tetracycline concentrations in the gastrointestinal tract, mcg/kg	0.069	1.79	3.2	7.2

The assessment of risk for the development of the intestinal microflora balance violation and further increase in the risk of diseases in children associated with it taking into account the peculiarities of exposure for this group demonstrated that the risk for the development of the intestinal microflora balance violation under the influence of tetracycline for this group is absent only at the consumption of the food products with the residual quantities of antibiotics in the food products at the level of not more than 10 mcg/kg (scenario 1, Table 8.35).

Table 8.35

The intestinal microflora balance in children at the different scenarios of tetracycline intake with food products, % of the total number of bacteria

The type of bacteria	Scenario 7	Scenario 8	Scenario 9	Scenario 10
Bifidobacterium *spp*.	89.58	78.99	71.37	53.44
Bacteroides *spp*.	2.74	1.17	0.91	0.62
Clostridia *spp*.	0.006	0.002	0.002	0.002
Fusobacterium *spp*.	0.64	0.11	0.07	0.04
Lactobacterium	2.79	0.38	0.08	0.00
Peptostreptococcus	0.96	0.52	0.40	0.26
E. coli (coliform bacterium)	0.99	0.93	0.88	0.76
Facultative bacteria	2.29	17.9	26.28	44.87

Taking into account the frequency of different diseases associated with the intestinal microflora balance violations in children and morbidity of the children's population in the model region of the Russian Federation the individual risk of digestive organs diseases (K58.0, K59.0, K59.9, K29.8, K29.9) will be from 0,000081 to 0,001238. In addition, the intestinal microflora balance violation can stipulate the additional risk of anemia, dermatitis, allergy and immunodeficient conditions on children (Table 8.36).

Therefore, the children at the occurrence of the intestinal microflora disbalance including the disbalance stipulated by the residual tetracycline concentrations in the food products of more than the established risk-based standard (10 mcg/kg) have the increased risk of the digestive organs diseases to the level of 0,000461, dermatitis – up to 0,000725, alimentary allergy – up to 0,000149, blood diseases – up to 0,001372. The increase of the risk of morbidity for the children's population of the Russian Federation with the digestive system diseases can be up to 4% of cases, blood diseases – up to 8% of cases, dermal diseases – up to 0.9% of cases, allergic diseases – up to 0.1% of cases.

Table 8.36

The individual risk of additional morbidity for the different categories of the microflora balance violations (children)

Group (code under MKB-10)	1st category	2nd category	3rd category	Total
Irritable bowel syndrome with diarrhea (K58.0)	0.000016	0.000033	0.000032	0.000081
Coprostasia (K59.0)	0.000133	0.000032	0	0.000165
Unspecified intestinal tract functional disturbance (K59.9)	0.000025	0.000094	0.000007	0.000126
Iron deficiency anemia (D50)	0.001012	0.000796	0.001372	0.00318
Other atopic dermatitis (L20.8)	0.000334	0.000206	0.000725	0.001265
Duodenitis (K29.8, K29.9)	0.000452	0.000325	0.000461	0.001238
Alimentary allergy (T78.0, T78.1, T78.4)	0.000012	0.000030	0.000149	0.000191
Total unspecified variable immune deficiency (D83.9)	0	0.000010	0.000013	0.000023

Ractopamine

One more example for the hygienic standard establishment can be the justification of the maximum permissible level for the content of ractopamine in the food products. This drug is used as the feed additive stimulating the building-up of muscle bulk, reduction of fat tissue and efficacy of the use of feeds in pigs, cattle stock, turkeys, and the maximum permissible levels of content according to the decision of Codex Alimentarius were in the pork and beef – 0,01 mg/kg, liver – 0,04 mg/kg, kidney – 0,09 mg/kg and were based on the analysis of scientific data of the Joint FAO/WHO Committee on the Food Additives (JECFA) [FAO/WHO, 2012].

Currently the ractopamine is forbidden for use during the battening of agricultural animals in the 80 countries of the world, including the EU countries, but in 22 countries the use of ractopamine in the pig breeding is allowed [A Chronic Toxicity Study of Ractopamine…, 1987; Council Directive 96/22/EC of 29.04.1996; Scientific Opinion, 2009*a*].

When justifying the risk-based standard during the assessment of the risk to health associated with the intake of ractopamine with food products both the carcinogenic and noncarcinogenic effects to the public health were taken into account.

The information about the uterine leiomyoma development in the experiment with mice was used as the initial information for forming the model of dependence "exposure – effect" in order to calculate the carcinogenic risk level (Table 8.37) [WHO Food additives series: 53 ractopamine].

Table 8.37

The initial information for the simulation of carcinogenic risk associated with the consumption of residual quantities of ractopamine with the food products

Dose, mg/kg of weight per day	The number of mice in the trial	The number of response cases (uterine leiomyoma)	The probability of the uterine leiomyoma development	The additional risk of the uterine leiomyoma development
0	60	1	0.016667	–
35	60	5	0.083333	0.066667
175	60	8	0.133333	0.116667
1085	60	10	0.166667	0.15

This information corresponds to the dependence between the influencing dose of ractopamine and cases of uterine hyperplasia in rats described in the formula

$$R = aD, \tag{8.25}$$

where R – is a number of cases of uterine hyperplasia;

D – is the dose of ractopamine, mg/kg;

$a = 0{,}0011 \pm 0{,}000213$ – is a parameter of model.

In relation to the noncarcinogenic effect the simulation of dependence "exposure – effect" was conducted based on the information specified in the FAO/WHO reports [A Chronic Toxicity, 1987] of European experts [Scientific Opinion, 2009*a*]. The basic model was the evolution model for the accumulation of the risk of disorders in the function of cardiovascular system described in the guidelines "Quantitative assessment of noncarcinogenic risk when exposed to the chemical substances based on the building of evolution models" [MP 2.1.10.0062–12].

The recurrent relation for the accumulation of the risk of functional disorders for the cardiovascular system with the set initial value of risk R_0 is built in accordance with the specified document during the simulation:

$$R_{t+1} = R_t + (\alpha R_t + \beta D)C, \tag{8.26}$$

where R_{t+1} – is a risk of disorders in the moment of time *t+1*;

R_t – is a risk of disorders in the moment of time *t*;

$\alpha = 0{,}0835$ – is a risk evolution coefficient at the expense of natural causes;

β – is a ractopamine effect coefficient;

C – is a time empirical coefficient (for daily averaging C = 0,00274);

D – is a dose of ractopamine, mg/kg.

Based on the information on the ractopamine toxicokinetics (Elanco report № DO 4686, PO3086, and ABC-0330) its content in the body reduces during 1 day by 85% due to the elimination processes. The elimination processes description with the use of exponential dependence (Fig. 8.25) allowed making a conclusion that the effective dose increases by 17% at the daily intake, i.e. during the simulation, it is necessary to take into account the dose with coefficient of 1.17 that corresponds to the upper bound of the level of effect. When obtaining the assessments at the lower bound it is feasible to use the coefficient 1.17·0.15=0.176.

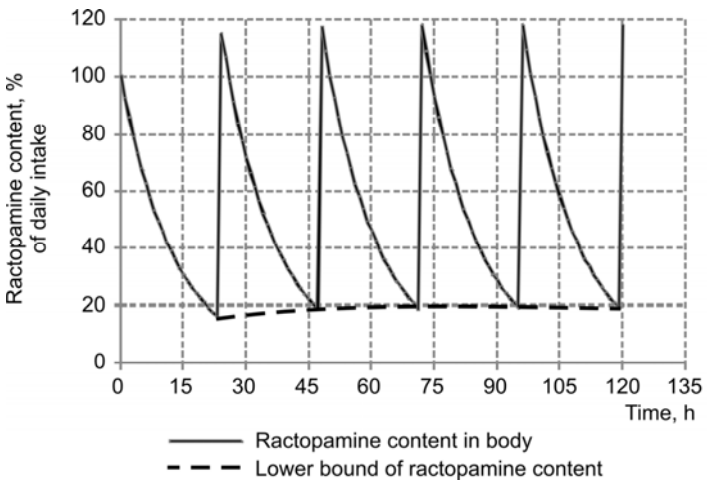

Fig. 8.25. Change of ractopamine content at the daily intake

When building the model for the accumulation of the risk of the cardiovascular system disorders stipulated by the effect of ractopamine the effect from this substance to the beta-adrenoceptors was taken into account. The adrenomimetic effect of ractopamine causes the cardiovascular system disorders the marker of which is a stable tachycardia. For parameterization of this effect presented by the coefficient β in the ratio (8.27) we used the results of experimental studies conducted in the USA on the assessment of ractopamine effect to the functional indicators of cardiovascular system [Scientific Opinion, 2009*a*]:

$$\Delta ЧСС = aD, \tag{8.27}$$

where $\Delta ЧСС$ – is a heart rate increment (strokes/min);

D – is a dose of ractopamine, mg/kg.

$a = 0{,}0871$ – is a parameter of model.

Under the specified data on the ractopamine effect to the change in the marker of effect (heart rate increment) we propose the model of dependence "dose – effect" presented in fig. 8.26.

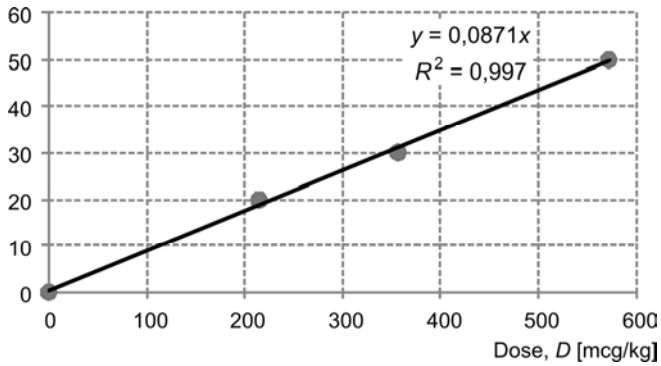

Fig. 8.26. The model of dependence between the ractopamine dose and change in the heart rate

The heart rate is one of the markers of disorders in the kinetic function of the cardiovascular system. In addition, the cardiovascular system disorders are combined with change of the whole complex of features. Taking into account the availability of stable cause-and-effect relationships between the set of parameters characterizing the condition of the cardiovascular system the assessment of dependence is performed

$$\Delta x_i = a_i \Delta ЧСС, \tag{8.28}$$

where Δx_i – is a change of parameter i characterizing the condition of the cardiovascular system;

a_i – are the relationship parameters (able 8.38).

Table 8.38

The parameters of relationship between the heart rate and the indicators of functional disorders of the cardiovascular system

Indicator	a_i
PQ segment	0.0001948
QRS complex	0.0000664
P tooth	0.0001819
Final diastolic volume	0.9405617

The accounting of changes in the set of indicators during the simulation for the accumulation of the risk of disorders in the function of cardiovascular system is performed according to the conversion described in the work of V.M. Chigvintsev, A.E Nosov (2012). Taking into account the relationships between the indicators the value of coefficient β in the model (8.29) is determined by the ratio

$$\beta = a\sum_i(\delta_i a_i)/0.00274, \tag{8.29}$$

where δ_i – is a weighted coefficient of indicator *i* for the cardiovascular system disorders (table 8.39).

Table 8.39

The weighted coefficients of indicators for the cardiovascular system disorders

The indicators of the cardiovascular system disorders	δ_i
PQ segment	0.00034
QRS complex	0.22800
P tooth	0.69000
Glucose in blood	0.22800
LDL cholesterol in blood	0.02295
Final diastolic volume	0.00051

Using the values of coefficients specified in Table 8.39 and 8.40 we obtained the value of coefficient β =0.191.

Therefore, the final form of the recurrent equation for the lower bound of the ractopamine effect to the cardiovascular system functions is presented by formula (8.30) with the initial condition R_0 = 0.001359:

$$R_{t+1} = R_t + (0.0835R_t + 0.191\cdot 1.17\cdot 0.15D)0.00274. \tag{8.30}$$

This recurrent equation is a basis for building the curve of the evolution of risk of the cardiovascular system disorders when exposed to dose D of ractopamine (design risk) and the adjacent curve without taking into account the ractopamine effect (*D*=0) (background risk). The additional risk (ΔR_t) is determined as the difference between the background and design risk curve.

The risk assessment is performed based on the calculation of the specified risk index:

$$\tilde{R}_t = \frac{\Delta R_t}{1 - R_t^{\Phi}} \tag{8.31}$$

The specified risk index was scaled under the ranges of values:

0–0.05 – negligible risk;

0.06–0.35 – moderate risk;

0.36–0.6 – high risk;

0.61–1 – very high risk.

The assessment of lifetime risk was performed for the time of ractopamine intake *t*=25550 hours that corresponds to 70 years.

The forest of additional cases of the cardiovascular system diseases in case of implementation of the design ractopamine effect risk (ΔZ) taking into account the age structure of population was performed under the ratio [Zaytseva N.V. et al., 2013*c*]:

$$\Delta Z = Z\frac{\sum_t \frac{\Delta R_t}{R_t^{\Phi}} N_t}{\sum_t N_t}, \tag{8.32}$$

where Z – is a number of cases of diseases registered during the year for the whole population.

The data on the food products consumption in the Russian Federation in 2011 were used for the assessment of ractopamine exposure for the population of the Russian Federation [Food products consumption in the households in 2011, 2012] (Table 8.40).

Table 8.40

The consumption of products of animal origin by the population of the Russian Federation

Food products	Daily consumption level, kg
Meat (muscular tissue)	0.221
Edible fats of animal origin	0.001

According to these data we established the maximum daily intake of ractopamine with the food products at the residual quantities of ractopamine proposed by Codex Alimentarius (for muscular tissue and edible fats – 10 mcg/kg, for liver – 40 mcg/kg, for kidney – 90 mcg/kg) which was 0,029 mcg/kg of weight per day. The standard human weight was taken according to the recommendations of the World Health Organization as 60 kg [P 2.1.10.1920–04].

Two exposure scenarios are considered: the first offers the consumption of food products with the residual content of ractopamine at the level recommended by Codex Alimentarius according to the consumption of products of animal origin for the population of the Russian Federation; the second considers the intake of ractopamine at the content in the food products at the level of lower bound of its quantitative determination in tissues (3–5 mcg/kg) [WHO Food additives series: 50 nitrate].

According to the results of the examination of households the average meat and meat products consumption by the population of the Russian Federation in 2011 was 80.9 kg or 0.2116 kg per day, the average consumption of edible fats of animal origin for the same period was 0.3 kg or about 0.001 kg. The information about the calculation of daily ractopamine doses under the selected scenario is presented in Table 8.41 and 8.42.

Table 8.41

The calculation of ractopamine dose at the consumption of food products with residual content at the level recommended by Codex Alimentarius

Product	Intake, kg	Content of ractopamine in product, mcg/kg	Intake of ractopamine, mcg	Dose, mcg/kg of body weight
Meat	0.2216	10	2.216	0.0369
Edible fats	0.0008	10	0.008	0.0001
Total	–	–	2.224	0.0371

Table 8.42

The calculation of ractopamine dose at the consumption of food products with residual content at the level of lower bound of its quantitative determination in tissues

Product	Intake, kg	The content of ractopamine in product, mcg/kg	The intake of ractopamine, mcg	Dose, mcg/kg of body weight
Meat	0.2216	3	0.664	0.011
Edible fats	0.0008	3	0.002	0.00004
Total	–	–	0.667	0.011

The average daily dose of ractopamine intake during the first scenario implementation will be 0.371 mcg/kg of body weight, the second scenario – 0.011 mcg/kg of body weight.

The calculation of carcinogenic risk associated with the consumption of ractopamine dose with the food products recommended by Codex Alimentarius (1 mcg/kg of body weight per day) demonstrated that the level of the upper 95% bound of carcinogenic risk will be $1.32 \cdot 10^{-6}$ that is classified as the level corresponding to the maximum acceptable risk.

The assessment of noncarcinogenic health risk at the ractopamine effect taken with the food products was performed for two scenarios proposed at the exposure assessment stage. The results of the calculation of the evolution of additional risk of the functional disorders of cardiovascular system for two scenarios are presented in Table 8.43.

Table 8.42

The evolution of the additional risk of the functional disorders of cardiovascular system

Age, years	Additional risk	
	Scenario 1	Scenario 2
5	0.000	0.000
10	0.001	0.000
15	0.002	0.001
20	0.003	0.001
25	0.005	0.001
30	0.008	0.002
35	0.013	0.004
40	0.020	0.006
45	0.030	0.009
50	0.046	0.014
55	0.071	0.021
60	0.108	0.032
65	0.164	0.049
70	0.249	0.075
75	0.287	0.114

The results of change in the specified risk index for two scenarios are presented in table 8.44.

Table 8.44

The results of change in the specified risk index

Age, years	Specified risk index	
	Scenario 1	Scenario 2
5	0.000	0.000
10	0.001	0.000
15	0.002	0.001
20	0.003	0.001
25	0.005	0.002
30	0.008	0.002
35	0.013	0.004
40	0.020	0.006
45	0.032	0.010
50	0.051	0.015
55	0.082	0.024
60	0.135	0.041
65	0.237	0.071
70	0.470	0.141
75	1.000	0.396

The assessment of change in the specified risk index for the cardiovascular system function disorders demonstrates that the unacceptable level of this risk will be formed in case of ractopamine intake at its content in the food products at the level of residual quantities recommended by Codex Alimentarius to the age of 25 years, at the level of maximum quantitative determination – to the age of 40 years.

As a result of the simulation of the cardiovascular system function disorders it was established that during the first scenario implementation (intake of food products containing ractopamine at the level of residual quantities proposed by Codex Alimentarius) the specified risk of the cardiovascular system function disorders will be 0.47 that according to MP 2.1.10.0062–12 is classified as the unacceptable risk. This level of risk can lead to the additional diseases of the cardiovascular system and reduction of the expected lifespan of population in the Russian Federation. The results of calculation for the specified scenarios are presented in Fig. 8.27–8.29.

When assessing the level of risk under the second scenario (intake of ractopamine at level of its maximum quantitative determination) the specified risk of the cardiovascular system function disorders will be 0.141 that according to MP 2.1.10.0062–12 is also classified as the unacceptable risk. This level of risk can also result in the reduction of the expected lifespan at the expense of the additional cases of diseases of cardiovascular system (diseases characterized by the increased blood pressure, atherosclerotic heart disease).

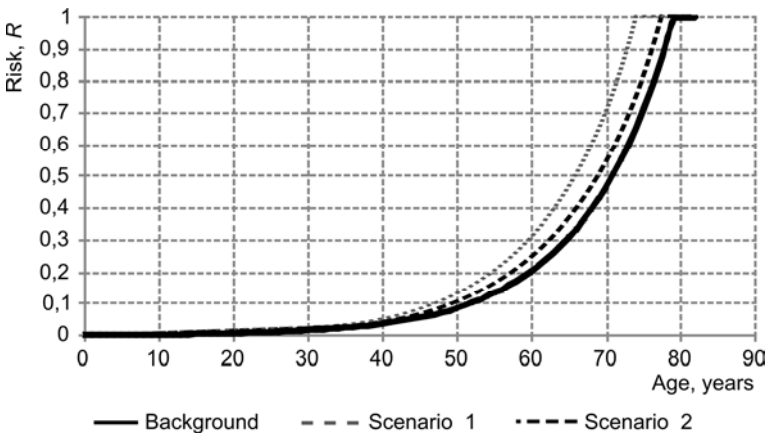

Fig. 8.27. Risk of the cardiovascular system function disorders

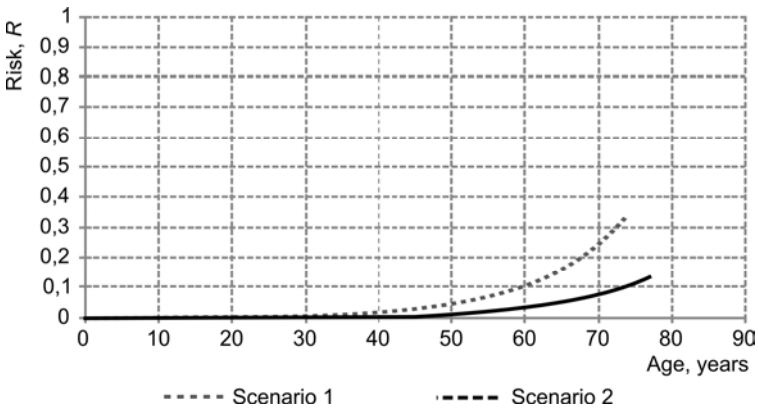

Fig. 8.28. The additional risk of the cardiovascular system function disorders

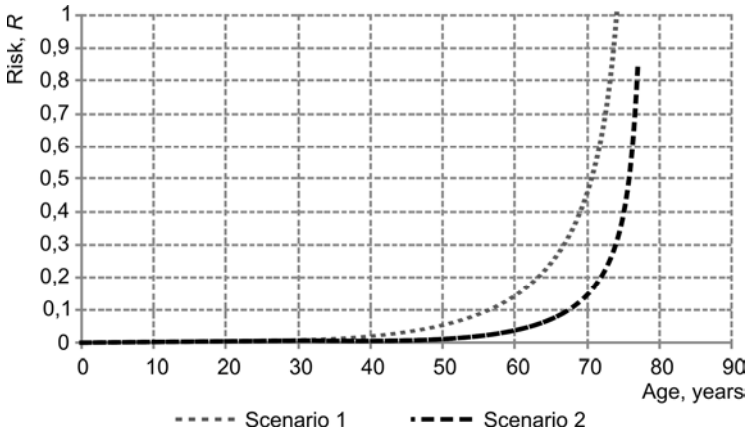

Fig. 8.29. The specified risk of the cardiovascular system function disorders

Thus, it was demonstrated that the ractopamine intake with food products at the level of residual quantities recommended by Codex Alimentarius, taking into account the level of consumption by the population of the Russian Federation of livestock products will lead to the unacceptable public health risk and will contribute to the growth of cases of diseases of cardiovascular system and the expected lifespan reduction. In this relation Russia defends the position against the acceptance of the maximum permissible level of ractopamine and considers its absence in the food products as the risk-based standard [Onishchenko G.G. et al., 2013*a*].

Nitrates

The differences between the domestic hygienic standards and food product safety standards and regulations of other countries exist not only for the residual quantities of veterinary drugs. In this relation the process for justifying the hygienic standards for the content of chemical substances in the food products is initiated. One of the most widely spread contaminants are the nitrates.

The main sources of the exogenic intake of nitrates are the vegetables (70%), water (20%) and other food products (6% – with meat and canned products); in addition, the nitrates are formed by endogenic way [Lundberg J.O. et al., 2004, 2008].

During the intake with food and water the nitrates are rapidly absorbed in the gastrointestinal tract [Spiegelhalder B. et al., 1976; Turek B. et al., 1980; Ellen G. et al., 1982; Bartholomew B., Hil M.J., 1984], herewith about 20% of nitrates contained in the blood plasm come to the salivary glands where they are concentrated and further eliminated with saliva. In the oral cavity under the influence of microorganisms the content of nitrates is reduced at the expense of their conversion to nitrites (about by 5–7%, according to certain data – by 7–9%) [Colbers E.P.H. et al., 1996; WHO Food additives series: 50 nitrate]. In stomach the nitrates under the influence of hydrochloric acid can participate in the synthesis of nitrosamines and other metabolites.

The toxic properties of nitrates/nitrites are the result of oxidation of the ions of iron Fe2+ in the molecule of dioxihemoglobin to Fe3+ with formation of methemoglobin which cannot be connected and cannot transport the oxygen. Depending on the share of methemoglobin it is necessary to distinguish the clinical manifestations of disease which include the cyanosis, heart rate disorder, organs and tissues blood supply disturbances, CNS disorders [ATSDR, 2007]. According to the data of T.T. Mensinga et al. (2003) the background level of methemoglobin content is 1–3%, at 10% the transport of oxygen by the blood sells is disturbed, at 20% it is possible to observe the development of cyanosis and hypoxia, the increase of methemoglobin content to 50–70% results in death [Fan A.M. et al., 1987; NRC, 1981; IPCS, 2006].

The acute effects from the action of nitrates are observed mainly in children that is associated with a number of factors including the higher levels of the liquid consumption per 1 kg of body weight, increased risk of the intestinal infections development, the higher tendency of hemoglobin in children than in adults to oxidation, the imperfections of the gastrointestinal tract resulting in the stomach pH increase, that in turn creates the favorable environment for the nitrate-restoring microflora and the restoring of nitrates to nitrites, in addition, the presence in the younger children of less active compared to the older children and adults methemoglobin reductase and therefor its ability to metabolize the excessive methemoglobin is also lower [Winton E. et al., 1971; NRC, 1981; Kross B.C. et al., 1992; Savino F. et al., 2006].

The other group suscetible due to the changes in the physical condition to the development of methemoglobin anemia includes the pregnant women, adults with reduced stomach acidity as well as the adults with low level of methemoglobin reductase [NRC, 1981].

The chronic exposure of nitrates is associated with the formation of nitroso compounds many of which have the carcinogenic potential [Public Health Goals, 1997].

The permissible levels for the content of nitrates in the Customs Union countries are established according to the Technical regulations of the Customs Union 021/2011 "On the food products safety" for 24 names of food products, including for the nutrition of pregnant and nursing women, young children, schoolchildren and preschool children [Technical regulations of the Customs Union 021/2011]. For EU countries the standards on the content of nitrates in the food products are established according to the Regulations of Commission (EC) No. 1881/2006 establishing the maximum levels of some contaminants in the food products, herewith the numerical values of the permissible levels for the content of nitrates are established only for spinach, some types of lettuce salad and infant food in general [EC, 2006]. According to the main document of Codex Alimentarius containing the requirements to the permissible levels of the content of contaminants in food – CODEX STAN 193–1995, the content of nitrates in the food products is not rated [Codex Stan 193–1995].

The permissible daily dose for nitrates 0–3.7 mg/kg of body weight was established in 1990 [EC, 1992], for nitrites – 0–0.06 mg/kg of body weight in 1997 (EC, 1997) [EC, 1997]. In 2002 the values of permissible daily doses were revised again and the level from 0 to 3.7 mg/kg of body weight was preserved for nitrates, and the level 0–0.07 mg/kg of body weight was established for nitrites [FAO/WHO, 2003].

The separate attention should be paid to the safety of nitrates for children during the first years of life. Thus, the European Food Safety Agency (EFSA) noted that during the consumption of nitrates with water by the children older than 3 months in the quantity not exceeding 15 mcg/kg of body weight per day the formation of methemoglobin does not occur. The recommended daily dose of the vegetables consumption for children is established at the level of 200 g/day. This value was established according to the body weight of child of 20 kg and nitrates consumption level from 2 to 12 mg/kg of body weight per day. During the conduction of calculations the factors reducing the content of nitrates in the food products were not taken into account. Therefore, the permissible daily consumption of nitrates for the children with body weight of 20 kg is 74 mg/child/day [Scientific opinion, 2010].

Within the justification of the risk-based standards for nitrates based on the published results of studies we built the exponential models of dependence between the occurrence of noncarcinogenic (8.33) (the development of methemoglobin anemia expressed in % of methemoglobin from the total volume of hemoglobin) [Shuval H.I., Gruener N.. 1972] and carcinogenic (8.34) [IARC, 2010] responses from the levels of nitrates intake with the food products of vegetable origin. When simulating the probability of the occurrence of methemoglobin anemia we took into account the conversion of 8% of nitrates taken with the food products to nitrites.

$$y = 1 - e^{0{,}000639x}, \tag{8.33}$$

$$y = 1 - e^{1{,}44\text{E-}07x}, \tag{8.34}$$

where y – is a percent of methemoglobin in blood;

x – is a quantity of nitrate taken to the human body (mg/person/day).

The exposure assessment was conducted based on the recommended and actual average daily intake of the food products of vegetable origin in the Russian Federation and the permissible levels of nitrates content in them used in the Customs Union countries.

The recommended and actual levels of the vegetable products and potato consumption by the different groups of population in the Russian Federation are presented in table 8.45.

Table 8.45

The levels of the consumption of vegetable products and potato by the different groups of population in the Russian Federation

Product	The recommended level of consumption, g/day	The actual level of consumption, g/day*			
		Age groups			
		from 1 to 11 years	from 11 to 18 years	from 18 to 60 years	older than 60 years
Watermelons	54.8**	2.85	6.24	6.20	9.02
Melons	54.8**	0.09	0.68	0.85	0.71
Potato (including the frozen)	211	111.40	153.70	179.35	167.03
White and red cabbage	87.7–137	16.64	26.23	31.94	28.92
Cabbage of salad types	8.2–13.7	0.53	0.61	0.96	0.79
Carrot	16.4–27.4	10.78	13.95	16.49	15.57
Beetroot	13.7–27.4	6.44	10.41	13.39	12.97
Tomatoes	68.5–87.7	8.82	17.44	26.52	26.87
Cucumbers	27.4–35.6	1.91	1.47	3.35	2.64
Bulb onion	16.4–27.5	13.16	20.56	24.72	20.68
Green onion		0.37	0.98	1.24	0.96
Sweet pepper	2.7–8.2	1.04	3.01	4.58	2.98
Marrows, scalloped squash	5.5–8.2	0.90	1.07	3.05	8.46
Eggplants	5.5–8.3	0.08	0.25	0.51	1.28
Garlic		0.07	0.12	0.25	0.28
Corn	13.7–21.9***	0.38	0.14	0.03	0.00
Salads	–	0.29	0.21	0.46	0.58
Radish	–	0.02	0.00	0.07	0.27
Leaf vegetables (dill, parsley, celery, cilantro, etc.)	–	0.19	0.24	0.43	0.23
Brined, marinated and pickled vegetables	–	7.65	13.77	16.37	14.64
Other edible roots (please, specify)	–	0.78	1.34	1.80	1.99
Canned vegetables	–	1.53	1.46	3.28	1.78
Vegetable juices	–	2.01	4.50	3.18	2.11

Note: * – the results of the epidemiologic studies of the individual consumption of food products by the different groups of population obtained by FSBI "Research Nutrition Institute" affiliated to the Russian Academy of Medical Sciences at the representative Russian sampling of more than 10 000 of persons;

** – the total consumption of watermelons and melons;

*** – the total consumption of corn and green peas.

The permissible values of the nitrates intake with different food products of vegetable origin in the Customs Union country are presented in Table 8.46.

During the exposure assessment we formed 5 scenarios accounting the intake of nitrates with the products of vegetable origin at the recommended level of intake for the vegetables and potato (the maximum values of range) (scenario 1), at the average actual level of consumption by the population in the age from 1 to 11 years (scenario 2), in the age from 11 to 18 years (scenario 3), in the age from 18 to 60 years (scenario 4), in the age older than 60 years (scenario 5) and the permissible levels for the content of nitrates in the vegetables and potato accepted in the Customs Union countries.

Table 8.46

The permissible values of the nitrates intake with different food products of vegetable origin [Technical Regulations of the Customs Union 021/2011]

The group of products	The permissible levels of nitrates (the Russian Federation), mg/kg
1	2
Potato	250
Early white cabbage (before September 1)	900
Late white cabbage	500
Early carrots (before September 1)	400
Late carrots	250
Tomatoes	150
	300 (protected soil)
Cucumbers	150
	400 (protected soil)
Red beet	1400
Bulb onion	80
Green onion	600
	800 (protected soil)
Leaf vegetables (salads, spinach, sorrel, cabbage of salad types, parsley, celery, cilantro, dill, etc.)	2000
Sweet pepper	200
	400 (protected soil)
Marrows	400
Watermelons	60
Melons	90
Fresh lettuce salad – grown in the protected soil from October 1 to March 31	4500
– grown in the unprotected soil from October 1 to March 31	4000
– grown in the protected soil from April 1 to September 30	3500
– grown in the unprotected soil from April 1 to September 30	2500
Iceberg lettuce salad – grown in the protected soil	2000
– grown in the unprotected soil	2500
Meat and cereal canned products with vegetables	200
Dietary supplements on the basis of algae	1000
Products for the nutrition of pregnant and nursing women: products on the fruit and vegetable basis (fruit and vegetable juices, nectars and drinks, fruit infusions); – on the vegetable and fruit-vegetable basis	200
– on the fruit basis	50
Products for the nutrition of young children: products on the fruit and vegetable basis, fruit and vegetable canned products (fruit, vegetable and fruit-vegetable juices, nectars and drinks, fruit infusions, pureed products on the fruit and (or) vegetable basis, fruit-milk and fruit-grain puree): – on the fruit basis (except for the products containing bananas and strawberry)	50
– on the vegetable and fruit-vegetable basis, as well as the products containing bananas and strawberry	200
Products for the nutrition of young children: meat and cereal canned products (cereal and meat canned products); fish and cereal canned products	150

End of Table 8.46

1	2
Products for the nutrition of preschool children and schoolchildren: – ready-to-serve fish and non-fish foods; for the products containing vegetables	150
Fruit and vegetable canned products (juices, nectars, drinks, fruit infusions, purred products on the fruit and (or) vegetable basis, fruit-milk and fruit-grain puree, combined products) – on the fruit basis	50
– on the vegetable and fruit-vegetable basis, as well as for the products containing bananas and strawberry	200
Main raw materials and components used during the manufactures of the infant food products:	
a) fresh fruit and vegetables, semi-finished puree – beetroot	600
– cabbage	400
– vegetables, bananas, strawberry	200
– fruit	50
b) fruit concentrated juices of aseptic canning or quick-frozen	100

The possible daily intake of nitrates with vegetables and potato was calculated for the developed scenario (Table 8.47).

Table 8.47

The possible daily intake of nitrates with vegetables and potato

Parameter	Scenario				
	1	2	3	4	5
The intake of nitrates, mg/day	202.2	47.9	70.5	87.5	84.0

The calculation of nitrates dose for the developed scenarios was carried out using the standard values of the average body weight for children (22.6 kg), teenagers (53 kg) and adults (60 kg). The obtained values for the daily doses of nitrates taken with the products of vegetable origin are presented in Table 8.48.

Table 8.48

The doses of nitrates taken with the products of vegetable origin

Parameter	Scenario				
	1	2	3	4	5
Dose of nitrates, mg/kg/day	3.4	2.1	1.3	1.5	1.4

The probable levels of the methemoglobin content for the 5 considered levels of exposure were obtained under the results of simulation of dependence "dose – response" (Table 8.49).

The levels of methemoglobin content for all the investigated scenario are located within the range from 0.24% (scenario 2) to 1.03% (scenario 1).

Taking into account the background level of methemoglobin is from 1 to 3% and the health disorders are observed at the levels of more than 10%, the results of the health risk assessment in relation to the permissible levels of nitrates content in the crop products demonstrated the absence of risk of development of noncarcinogenic effects (methemoglobin anemia) associated with the intake of nitrates with the products of vegetable origin.

Table 8.49

The probable levels of the methemoglobin content for the different conditions of exposure to nitrates

Scenario	The intake of nitrates with the food products of vegetable origin, mg/day	The level of methemoglobin, %
1	202.2	1.03
2	47.9	0.24
3	70.5	0.36
4	87.5	0.45
5	84.0	0.43

The results of simulation for the probability of carcinogenic effects development at the intake of nitrates with vegetables and potato are presented in Table 8.50.

Table 8.50

The levels of carcinogenic risk for the different conditions of exposure to nitrates

Scenario	The intake of nitrates with the food products of vegetable origin, mg/day	Carcinogenic risk level
1	202.2	2.92^{-05}
2	47.9	6.92^{-06}
3	70.5	1.02^{-05}
4	87.5	1.26^{-05}
5	84.0	1.21^{-05}

The level of carcinogenic risk for all the exposure scenarios is at the maximum permissible level ($1 \cdot 10^{-6} – 1 \cdot 10^{-4}$), herewith the maximum level of carcinogenic risk was obtained for scenario 1, taking into account the recommended standards for the consumption of food products of vegetable origin and the permissible values of nitrates content in these products ($2.92 \cdot 10^{-5}$).

The maximum values for changes characterizing the noncarcinogenic effects associated with the intake of nitrates with the food products of vegetable origin as well as the maximum level of carcinogenic risk were observed at the exposure scenario taking into account the recommended norms of daily consumption of vegetables and potato and permissible values for the content of nitrates in the crop products. It was established that the increase in the methemoglobin level will be 1.03% and the carcinogenic risk level – $2.92 \cdot 10^{-5}$, these changes are considered as acceptable.

Thus, the assessment of hygienic standards for the content of nitrates in the crop products for the Customs Union countries under the risk criteria demonstrated that the exposure both at the recommended and real levels of the consumption of the products of vegetable origin will not result in the unacceptable health risk and will ensure the safety for the health of population in the Russian Federation. Therefore, it is feasible to consider as the risk-based standards the maximum permissible levels of nitrates content in the food products of vegetable origin established in the Technical Regulations of the Customs Union TP TC 021/2011 "On the food products safety".

Risks associated with the use of non-food products

The risk evolution assessment methodology was also used for the non-food products safety assessment. The evolution simulation was applied to the assessment of the risk of the occurrence of respiratory disorders in the consumers when exposed to formaldehyde migrating from the furniture products.

To assess the risk, we selected the standard exposure scenario – the contact of consumer with furniture made of laminated wood chip board (LWCB) used in the office premises at the room temperature. The volume of office premise, average size of workplace, and the premise mircoclimate parameters were determined in accordance

with normative requirements. The exposure was simulated for the conditions of office premises filled with furniture on the basis of 1 workplace per 6 m^2. The average size of office premise designed for 4 workplaces was accepted as equal to 24 m^2, with volume V=24·3=72 m^3. The workplace consisted of writing table and pedestal with total surface area of 10 m^2. Total furniture surface area S=4·10=40 m^2. Rated air exchange velocity with external environment for premises was taken as equal to v =1 $hour^{-1}$. For the selected exposure scenario we used the average statistical value of consumer contact with products - an eight-hour shift during the whole life. The formaldehyde emission level from LWCB was taken as equal to 0.005 mg/m^2h. The formaldehyde source capacity in the premise was M=40·0.005=0.2 mg/h. The following calculation were performed to assess the change of formaldehyde concentration with time inside the premise. According to the mass balance equations of the following type (8.35):

$$\frac{dC_i}{dt} = v\left(C_0 - C_i\right) + \frac{M}{V}, \tag{8.35}$$

where C_i – is an internal concentration (mg/m^3);

v – is an air exchange velocity (1/h);

C_0 – is a concentration outside the premise (mg/m^3);

M – is the speed of the source of contamination in premise (mg/h);

V – is the volume of premise (m^3).

The differential equation solution in general view (8.36):

$$C_i\left(t\right) = \left(1 - e^{-vt}\right)\left(\frac{vC_0V + M}{vV}\right), \tag{8.36}$$

where C_i – is an internal concentration (mg/m^3);

v – is an air exchange velocity (1/h);

C_0 – is a concentration outside the premise (mg/m^3);

M – is a speed of the source of contamination in premise (mg/h);

V – is a volume of premise (m^3).

Fig. 8.30 shows the change of concentration inside the premise at the selected conditions.

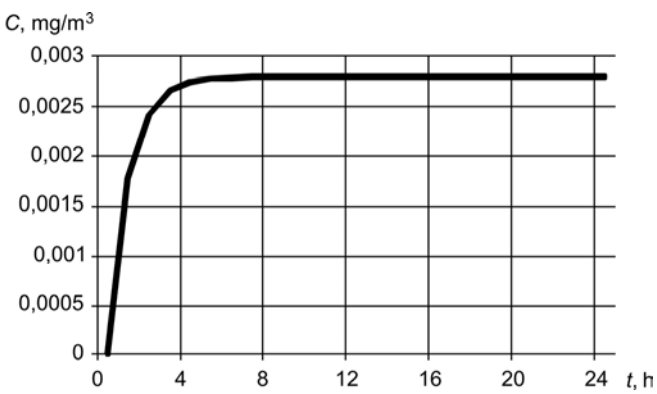

Fig. 8.30. The dependence of formaldehyde concentration in premise on time

The equilibrium condition inside the premise will be created at the concentration equal to 0,0028 mg/m^3, according to the used parameters. This equilibrium condition will be created 6 hours after the beginning of formaldehyde evaporation from furniture.

The mode for the use of such type of products corresponds to the eight-hour shift during the whole life (Fig. 8.31).

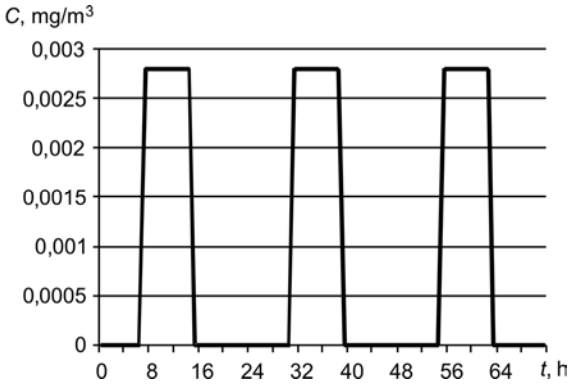

Fig. 8.31. Setting the formaldehyde exposure in accordance with time

The equation (8.37) was used for the evolution of the risk of respiratory system disorders in consumers [Report about research activity, 2011]:

$$R_{t+1}^{D} = R_{t}^{D} + \left(0{,}0245 R_{t}^{D} + 0{,}013 \left\langle \frac{1}{1+e^{-(-0{,}072+150{,}6 X^{F})}} - \frac{1}{1+e^{-(-0{,}072+150{,}6 \cdot 0{,}0013)}} \right\rangle \right) 0{,}000114, \quad (8.37)$$

where R_{t+1}^{D} – is the risk of respiratory system disorders for the next time step;

R_{t}^{D} – is the risk of respiratory system disorders at the initial (established) moment of time t;

X^{F} – is the concentration of formaldehyde in the air (mg/m^3);

$\langle\ \rangle$ – are the Kelly brackets accepting the values $\langle x \rangle = 0$ at $x < 0$ and $\langle x \rangle = x$ at $x \geq 0$.

The background evolution of the risk of respiratory system with time and the evolution of risk in the exposure conditions are shown graphically in Fig. 8.32.

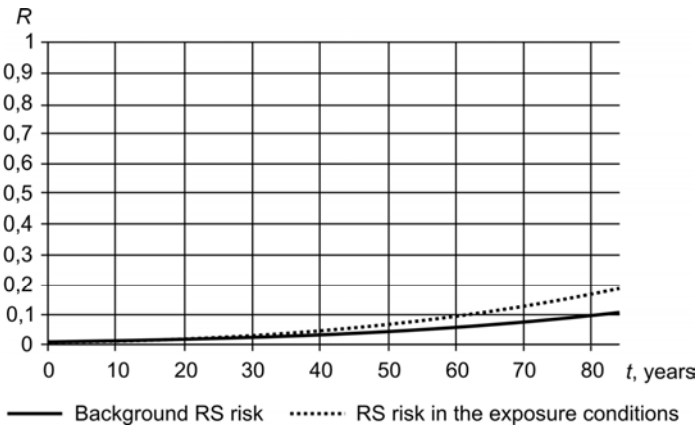

Fig. 8.32. The dependence of the risk of respiratory system disorders on time

Based on the evolution simulation it was obtained that at the risk of respiratory system disorders at the initial moment of time equal to 0,014177 the risk in 50 years under exposure will be 0,069, the risk without exposure – 0,048.

The additional risk and specified risk index are shown in Fig. 8.33.

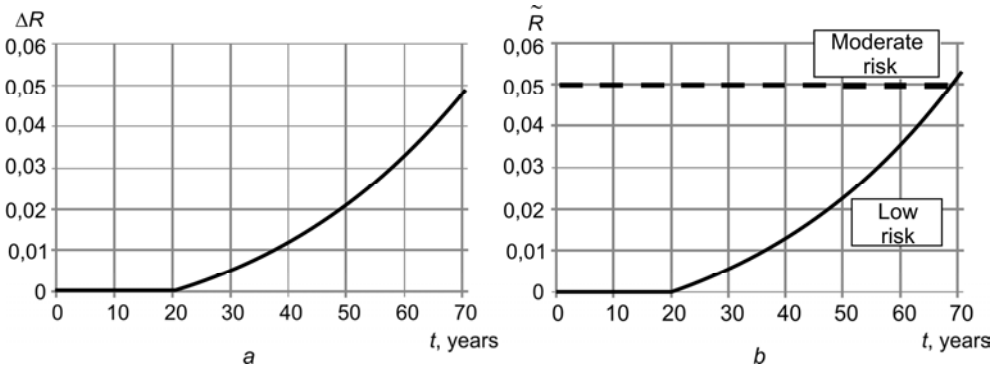

Fig. 8.33. The dependence of additional risk (*a*) specified index of risk (*b*) for the respiratory system disorders on time

The value of specified integral risk index is transferred from negligible to moderate in the age of 68 years.

The obtained materials were used during the establishment of the permissible levels of formaldehyde migration from the furniture products.

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9. THE INTEGRATION OF HEALTH RISK ANALYSIS IN THE SOLUTION OF THE STRATEGIC PROBLEMS OF STATE SOCIAL AND ECONOMIC DEVELOPMENT

9.1. The improvement of policies to minimize the health risks and the development of the legal framework

Health risks minimization government policy, as a general guide for action and decision-making, which contributes to the achievement of objectives in this area, defines the relationships with other subjects of political interests (states, corporations, etc.). In this section it is traditionally distinguished in two aspects: external and internal.

It is feasible to single out the vector of the harmonization of national principles and the methodology of health risk assessment and management with analogues used in international practice on the one hand, and the pursuance of the recognition of the positions of the Russian Federation in this area by the international community allowing defending the interests of the state in the field of safety for life and health of citizens on the other as main foreign policy directions in the field of risk analysis.

Main domestic trends in the health risk analysis methodology can be described as an extension of its implementation as a tool to validate state, corporate and public governance decisions for the minimization of probable losses associated with public health disorders.

It is advisable to coordinate the main directions of state policy in the field of health risks minimization with the objectives of the basic documents that define the political strategy of the Russian Federation:

- "The concept of the long-term socio-economic development of the Russian Federation for the period until 2020" [The concept of long-term socio-economic development of the Russian Federation for the period until 2020, 2008].
- "Fundamentals of the state policy in the field of chemical and biological safety of the Russian Federation for the period until 2025 and further perspective" [Fundamentals of the state policy in the field of chemical and biological safety of the Russian Federation for the period until 2025 and further perspective, 2013].
- "Environmental Doctrine of the Russian Federation" [Environmental Doctrine of the Russian Federation, 2002].
- Presidential Decree No. 598 dated 07.05.2012 "On the national health policy improvement" [On the national health policy improvement, 2012].

Policies to minimize health risks should include primarily the definition of strategic target risk levels, the achievement of which will minimize the state losses associated with citizens health risk. Of course, the implementation of such levels requires enormous resources, the allocation of which is fully impossible now. In this regard, it is advisable to determine the intermediate (stage) levels of health risk, consistent achievement of which may be regarded as tactical objectives of risks minimization policy together with objective levels. These levels of risk may be regarded as a benchmark for the declaration of the acceptable levels of health risk for a certain time period. Naturally, the political statements of this kind

should be based on a detailed analysis of the socio-economic and sanitary-epidemiological situation, taking into account the long-term forecasts of its development. The determination of optimal balance between losses associated with health risks, and minimum costs for its prevention in real time are the main difficulty at intermediate risk levels determining.

In this regard, the development of tools for health risk analysis based on te improvement of legislation in this area should be one of the priorities of health risk minimization policy.

The development of the concept of the improvement of the legislation of the Russian Federation in the field of sanitary and epidemiological safety of the population based on the analysis of new threats and hazards to the health of citizens of the Russian Federation, including in the context of new threats associated with markets opening, human resources flows intensification, introduction of modern materials and technologies is appropriate for the systematic improvement of the system of sanitary and ecological legislation of the Russian Federation in respect of health risk analysis.

This concept should make provision for the aspects of the harmonization of legal and international norms and supplementation of the existing legal framework with provisions that take into account the current situation in the field of sanitary-hygienic safety.

At the harmonization of the provisions relating to health risks analysis, the legislation focuses on legislative recognition of this methodology as a tool providing for the clarification of specific document targets and criterial base of legal norms compliance. Harmonization may affect legal acts in relation to the analysis of health risk associated with various factors: professional, living environment, production.

Amending the Federal Law "On the sanitary-epidemiological welfare of the population" is the most important for the harmonization of general concepts in the field of risk analysis and the provisions relating to the risk associated with living environment factors. First of all, these amendments should relate to the definition of the public health risk as the probability of adverse changes in the health of citizens with regard to their severity and hygienic safety as a condition in which there is no unacceptable risk associated with harm to citizens life or health caused by living environment factors. In the same law it is reasonable to define the concept of hygienic standard as permissible quantitative value that ensures the safety of living environment factors for human as the absence of an unacceptable health risk. Legislative consolidation of these concepts will require amending the number of other provisions of this legislative act.

The amendments are needed in the Federal Law No. 7-FZ dated 10.01.2002 "On Environmental Protection", which is currently not focused on living environment safety for human health. These amendments should affect the application of health risk criteria in the validation of environmental regulations, environmental impact assessment, ecological expertise. It is reasonable to make similar amendments in the Federal Law No. 96-FZ dated 04.05.1999, "On Ambient Air Protection", the Water Code of the Russian Federation, Law "On Production and Consumption Waste".

It is necessary to consider the preparation of the Federal Law "On the chemical safety of the population" with the obligatory inclusion of health risk assessment as safety criteria, which provides for the development of national chemical profile of the Russian Federation with the health risk assessment.

The support of economic fundamentals of health risk management can be optimized by the establishment of legislative framework system for the development of insurance against human health risks associated with breach of sanitary legislation. Of course, it is necessary to review the volumes of the economic responsibility of objects – the sources of hazard or negative impact on the human living environment once again at the establishment of the system.

It is reasonable to complete the ratification of a number of international agreements, especially ILO Convention 161 "On occupational Health Services" as part of the prerequisites for the harmonization of the legislation of the Russian Federation and the Customs Union in the field of occupational health risk analysis. This will allow revising a number of provisions of labor legislation and focusing it not only on the prevention of occupational diseases and injuries, but also on the prevention of all diseases associated with work.

It is necessary to make amendments to "The agreement on coordinated policy in the field of technical regulations, sanitary and phytosanitary measures" dated 28.01.2008, that

establish an obligation of technical regulation drafters to prove the safety of products as an absence of unacceptable risk to the health and providing for products risk monitoring as well as obligation to conduct control and surveillance activities, taking into account the results of life and health risk assessment in order to harmonize the legislation of the Russian Federation and the Customs Union in the field of analysis of products risk for health. The development of technical regulations "On general product safety", harmonized with the Directive of the European Parliament and the Council 2001/95/EC dated 03.12.2001, "On general product safety", that defines harmonized principles for products risk assessment for health could be an important step in this area. Standards (norms) that are included in the technical regulations, validated in accordance with these principles will also make a significant contribution to the harmonization of national legislation with international standards.

The option of a road map can be offered as a model for the development of the regulatory framework (Table 9.1). It involves the simultaneous solution of problems of health risk assessment position strengthening in the system of technical regulation of the Customs Union and preparation of the grounds for the integration of health risk assessment in sanitary and ecological legislation of the Russian Federation.

Table 9.1

"Road Map" of the improvement of the legislation of the Russian Federation and the Eurasian Economic Commission in a part of the strengthening of the position of health risk assessment methodology in the problems of technical regulation and the maintenance of sanitary and epidemiological welfare of the population

Year	Actions to improve legislation
2014	The strengthening of the position of health risk assessment in the system of technical regulation of the Customs Union and Eurasian Economic Commission. Preparation of proposals for amendments to the "Agreement on coordinated policy in the field of technical regulations, sanitary and phytosanitary measures" and other documents of the Customs Union with regard to: – the inclusion of the risk assessment procedure determination in the text of the agreement on sanitary measures; – the definition of the responsibilities of manufacturers, suppliers, conformity assessment authorities and regulatory authorities on risk assessment issues; – the determination of a list of priority products that require health risk assessment.
	The preparation of the recommendations of the Eurasian Economic Commission (EEC) on the methodology of assessment of products (goods) risk for health. The preparation of proposals to improve the system of the establishing of mandatory requirements for products according to health risk criteria. The preparation of proposals for the establishment and functioning of authorities and organizations responsible for products risk assessment and development of a database for its performance
	The preparation of reasons for health risk assessment aspects inclusion in sanitary and ecological legislation of the Russian Federation. The development of the project "The concept of the development of the Russian Federation legislation in the field of sanitary and epidemiological welfare of the population"
2015	The strengthening of the position of health risk assessment in the system of technical regulation of the Customs Union and Eurasian Economic Commission. The approbation of ECE recommendations on the priority types of products. The preparation of proposals for the harmonization of technical regulations in a part of products risk assessment for health. The determination of the list of priority Technical regulations for the harmonization of products risk assessment for health. The development of methodologies to establish ECE risk-based norms for products. The preparation of a list of regulatory, information and methodological documents that are required for the implementation of the risk assessment of products and/or additions required to be made in the existing guidance documents

Continuation of Table 9.1

Year	Actions to improve legislation
	The preparation of reasons for health risk assessment aspects inclusion in sanitary and ecological legislation of the Russian Federation. The discussion of the "Concept of the development of the Russian Federation legislation in the field of sanitary and epidemiological welfare of the population" with all interested parties. The preparation of explanatory note and specific proposals for amendments to the Federal Law "On the sanitary-epidemiological welfare of the population." The development of methodologies to establish ECE risk-based norms of the Russian Federation for the quality of living environment objects
2016	The strengthening of the position of health risk assessment in the system of technical regulation of the Customs Union and Eurasian Economic Commission. The preparation of proposals for amendments to the technical regulations in a part of food risk assessment for health (TR CU on grain, meat and meat products, juice products, etc.). Technical regulations as defined by the Customs Union. The preparation of terms of reference for the development of priority sub-statutory guidance documents for the assessment of products risk. The preparation of proposals to improve the hygienic standardization system in terms of inclusion of risk assessment stage in the establishment of the basic requirements of technical regulations. The preparation of proposals to improve the hygienic standardization system in terms of inclusion of risk assessment stage in the system of establishment of the basic requirements of technical regulations
	The preparation of reasons for health risk assessment aspects inclusion in sanitary and ecological legislation of the Russian Federation. The direction of the "Concept of development of the legislation of the Russian Federation in the field of sanitary and epidemiological welfare of the population," in the Council for The codification and Enhancement of Civil Legislation under the President of the Russian Federation. The preparation of the draft Law "On Chemical Safety of the population"

9.2. Health risk analysis in the solution of the strategic objectives of the state social and economic development

The strategic objectives of the state socio-economic development both currently and in the near term are defined in the "Concept of long-term socio-economic development of the Russian Federation for the period up to 2020" (hereinafter – the Concept). The objective of the development of this concept was to determine the ways and means of ensuring long-term sustainable well-being of Russian citizens, national safety, dynamic economic development, strengthening of Russia's position in the world community. The basic trends in long-term socio-economic development of the country, target indicators, priorities and main tasks of long-term state policy in the social sphere, in the field of science and technology and other provisions concerning the foundations of long-term development of the state were formulated in the Concept in accordance with this objective.

It is reasonable to use health risk analysis methodology as an adequate tool in a solution of the major part of tasks of the state socio-economic development. As main tasks in which the use of decision analysis methodology of health risk can be most effective, special attention shall be paid to:

- the enhancement of the efficacy of human capital;
- the assurance of the high standards of human well-being;
- the development of the National Security Organization;
- the improvement of goods competitiveness at the global level;
- ensure a balanced spatial development.

It is necessary to improve the legislative framework aimed at the minimization of health risks and the creation of preconditions for the systemic transfer of the Russian economy in the mode of innovation development for the integration of health risk analysis in the solution of strategic tasks of the state socio-economic development.

The enhancement of the efficacy of human capital

Human capital is an intensive productive factor of economic development, which includes the generated part of the labor forces, knowledge, the tools of intellectual and management labor, living and labor activity environment that ensure its effective and efficient functioning as a productive factor of development [Korchagin Yu. A., 2009]. Human capital is considered as a major factor in the formation and development of innovative economy and knowledge economy as the next higher stage of development. One of the main conditions of its formation is the availability of labor resources i.e., the part of the population, which is able to engage in socially useful activities according to the physical development, acquired education, professional and qualification level.

Since the current stage of development of Russia is characterized by reduction in labor supply due to the declining of working age population, sharpening of a shortage of professional staff, there is a pressing need for the adoption of legislative acts governing the conservation and rational use of available labor forces.

The most promising direction in the development of national legislation is its improvement based on accepted international instruments, especially the World Health Organization and the International Labour Organization.

The World Health Organization adopted the "Global Plan of Action on Health at Work for 2008–2017." [the Global Plan of Action on Health at Work for 2008–2017, 2007], which provides for improvement of assessment and management of health risks in the workplace through measures for the prevention and control of mechanical, physical, chemical, biological and psychosocial risks associated with working conditions, capacity building for the primary prevention of occupational risk factors and diseases, including strengthening of human, methodological and technological resources. Also, the Global Plan provides for the establishment of systems of epidemiology surveillance for workers health to accurately identify and control occupational risks. This includes the development of national information systems, building of capability of the assessment of occupational diseases burden, creation of registries of exposure to major risk factors and so on. This document clearly states that "priority should be given to primary prevention of occupational health risks." That is why there was significant focus on the problems of occupational risk assessment.

The Russian Federation has ratified a number of Conventions of the International Labour Organization (ILO). Among them, ILO Convention 187 "On the Promotional Frameworks for Occupational Safety and Health" [Convention on the Promotional Frameworks for Occupational Safety and Health, 2006], the Convention 148 "On the protection of workers against occupational risk caused by air pollution, noise and vibration on the shopfloor" [International Labour Organization Convention No. 148 on the protection of workers against occupational risk caused by air pollution, noise and vibration on the shopfloor, 1977] and others. General agreement between the All-Russia associations of trade unions, employers and the Government of the Russian Federation for 2011–2013 provides for the ratification of a number of ILO conventions. Among them the Convention 161, "On Occupational Health Services" (in the English original "On occupational medicine services") [ILO Convention No.161, "On Occupational Health Services," 2014].

According to the estimates of E.I. Denisov, based on a comparative analysis of the current policy, legislation and practice in the Russian Federation and requirements of the Convention 161 [Denisov E.I., 2013] the degree of compliance of Russian legislation with the Convention 161 is not high enough: 15% of the regulations correspond to the Convention, 50% correspond partially, 35% does not correspond.

It is necessary to complete the process of ratification of ILO Convention 161 and supplement domestic legislation with relevant rules as soon as possible for the tasks of retention

of the existing labor forces. One has to agree with N.F. Izmerov (2012) that a regulatory framework for an assessment and management of occupational risk with a shift of focus from labor safety to workers health care is needed for hygiene support of innovative technologies. This framework should include a regulation setting out the policy, systems and programs that protect workers health. The creation of such a framework will be fully consistent with the provisions of the "Global Plan of Action on Health at Work for 2008–2017." [Global Plan of Action on Health at Work for 2008–2017, 2007], which identifies the need of development of national policy frameworks for the protection of workers' health taking into account relevant international labor conventions. It should include: the enactment of legislation; the establishment of the mechanisms of the intersectoral coordination of activities; the funding and mobilization of resources for the protection and promotion of workers' health; the integration of objectives and actions for workers' health into national health care strategies. The presence of such a framework is a condition of the guarantee of socio-economic development of the country with the systemic translation of the Russian economy to innovation development.

The health of workers is determined not only by the risks that are present in the workplace, but also by social and individual factors. The key risk factors are lifestyle factors. Not accidentally the distribution of healthy lifestyle standards is defined as one of the main priorities of social and economic policy in the field of human development in the second stage. Already, a number of legislative acts aimed at "coercion" to a healthy lifestyle [No. 15-FZ "On protection of public health against exposure to tobacco smoke and consequences of tobacco consumption", 2013; No.171-FZ "On state regulation of production and turnover of ethyl alcohol and alcohol products and on limitation of alcohol products consumption (drinking)", 1995; No. 38-FZ "On Advertising", 2006]. The task of health risk analysis as a methodology is an assessment of the efficacy of decisions made and determination of further actions in this area.

A healthy diet factor plays an essential role in the formation of the lifestyle-associated risk. This issue has two main aspects: balanced nutrition and food safety.

The results of the analysis of per capita consumption of food by the population of the Russian Federation according to the sample survey of household budgets for the period 2008–2012 showed a positive trend of the consumption of dairy products, eggs, vegetables and meat products. Compared to 2008, their number increased by 21 liters, 17 and 11 kg, respectively.

However, this rate of the improvement of food patterns of the population, especially employable is insufficient. The excess of fat by 15.7%, carbohydrates - by 15.2%, as well as a slight deficiency of the protein – by 0.5% in the diets were revealed according to the analysis of the macronutrient diets of the population of the Russian Federation, compared with the average recommended consumption rates. The level of the consumption of macronutrients by the population of the Russian Federation bears the evidence of unbalanced diet with a tendency of the expansion of the consumption of foods containing saturated fats, and the reduction of the consumption of complex carbohydrates, which leads to the risk of metabolic disorders, increased cardiovascular diseases, neoplasms, endocrine disorders, including diabetes [State report "On the sanitary and epidemiological welfare of the population in the Russian Federation in 2013," 2014].

In this regard, it is reasonable to consider measures, including legislation to reduce the risk. The development of products for dietary, therapeutic and preventive nutrition is a priority for the purpose of implementation of the state policy foundations in the field of healthy diet. The concept of a specialized food product includes not only food, but also determines the obligatory presence of proven therapeutic effect of a particular specialized food product used in dietotherapy [Tutelian V.A., 2014]. In addition, preventive nutrition foods, as well as all other foods should be safe for health.

In the context of the anticipated increase in the demographic load the value of the economically active period of human life and as a consequence the cost of losses associated with health risks shall be increased significantly. Solution of the problem of the achievement of stable demographic indices and the increase of life expectancy implies minimization of the health risk associated with the maximum number of living environmental factors. This concerns not only the health of the working population, but also the health of children as contingent, which has the potential ability to work.

An important aspect of a healthy child population is to reduce the risks to the reproductive health of the population. Phased closure of work places with conditions that are harmful or hazardous to reproductive health and that cause an unacceptably high risk of reproductive function disorders in both women and men could be identified as a prerequisite for this process.

A sufficiently large number of hazards that have a negative effect on the reproductive system is recorded in the living environment. The development of information support and the methodological basis of analysis of risk associated with these factors will enable timely identification of priorities in this area and by means of appropriate measures for those risks reduction to ensure the stability of the labor potential of human capital in the subsequent stages of socio-economic development of Russia.

Thus, it is necessary to focus the use of health risks analysis methodology on the assessment and management of risks that pose a threat of the enhancement of the destabilization of demographic situation and labor shortages in a solution of the strategic objective of socio-economic development of the country, increase of the efficacy of human capital. These risks include the risk of premature mortality and diseases related to work. At that the most attention at the current stage of socio-economic development of the Russian Federation should be paid to the minimization of the risk of health problems, which determine the reduction in the period of economic activity of the working population. Poor working conditions make quintessential contribution to the deterioration of this indicator, so first of all it is reasonable to focus efforts on the reduction of the risk of workplace-related diseases, but not occupational ones in the field of the improvement of professional risk management.

To ensure the stability of the labor force in the next stages of socio-economic development of the state, it is necessary to forecast and prevent the probable deficiency of labor forces due to demographic losses, including due to the negative impact of production and living environment factors. The use of the methodology of risk analysis as a tool for the solution of such problems is fully justified. In this case, the analysis of reproductive risks and risks with a large time lag implementation will be the priority. Risks of this kind are usually caused by chronic exposure to hazards.

Thus, at the solution of the problem of improving the efficacy of human capital the main area of the application of health risks analysis is to ensure the stabilization and, in the future, increase of labor forces. To do this, the minimization of the risks of health problems associated with the operation and management of risks associated with environmental and occupational factors that determine the negative consequences in the long term for working ability for present and future generations of Russian citizens is primarily suitable at the current stage of socio-economic development.

The assurance of the high standards of human well-being

The high standards of human well-being include the quality of life, which is determined by a number of indicators, including GDP per capita (a general indicator of the standard of living), life expectancy, the proportion of the population living in areas with adverse environmental conditions, and so forth. It is expected that these figures should be significantly changed for the better to 2020: GDP per capita will represent an increase of by almost 2.5 times; life expectancy will increase to 72–75 years, the proportion of the population living in areas with adverse environmental conditions, will drop more than 3-fold [the Concept of long-term socio-economic development of the Russian Federation for the period up to 2020, 2008].

The achievement of these targets will require considerable labor and financial costs. The methodology of health risk analysis can play a significant role in their optimization. The problems of increasing the efficacy of human capital – one of the main factors of GDP growth – were discussed in the previous section. We would like to emphasize the dual effect of reduction of the risk to the health of citizens in the formation of GDP and the state budget. On the one hand, the reduction of health risks and its implementation leads to the reduction of the losses of the period of economic activity and, consequently, an increase in GDP and, accordingly, the revenue side of the budget. On the other hand, the same risk reduction leads to a reduction in government

spending on medical and social assistance associated with health problems. These funds may be regarded as an additional investment to the economic development of the country, which will also contribute to the growth of GDP.

There are already a number of mechanisms to ensure the high standards of human well-being, including the use of a methodology for health risk analysis.

First of all, these include technical regulations designed to ensure protection against unacceptable risks to the life and health of citizens. The regulations aimed at the prevention of the risk of products for the population health are actively developed under this system. These include the technical regulations on food products, which must ensure protection against unacceptable risks to the life and health of consumers. It is approved and practically implemented the Federal Law No. 88-FZ dated June 12, 2008 "Technical regulations on milk and dairy products." Documents such as Federal Law No. 90FZ dated June 24, 2008 "Technical regulations for fat-and-oil products," Federal Law No. 178-FZ dated October 27, 2008 "Technical regulations for juice products made of fruits and vegetables ", etc. came into practice following the issuance of these regulations. However, not all product requirements in these documents are based on the criteria of acceptable risk. There was a need to organize bringing the requirements of technical regulations in compliance with the Law No. 184-FZ "On Technical Regulation" – provide for regulations provision with risk-based standards.

As technical regulations of the Customs Union recently being developed, it is necessary to pay considerable attention to the harmonization of legislation and legislative and regulatory compliance practices with the EurAsEC countries. This pertains, inter alia, to regulatory and methodological framework of health risks assessment. Thus, the use of methodologies for assessing the risk of the goods that were agreed by member-states of the Eurasian Economic Community will ensure not only the competitiveness of the products of these countries, but the safe for health. This, in turn, will contribute to the implementation of a policy for the preservation and enhancement of the labor potential of common economic space, can increase the attractiveness of the membership in this economic union, which will lead to the strengthening of external positions of Russia.

The governments of the Russian Federation, Belarus and Kazakhstan in the customs territory of the Customs Union apply "Uniform sanitary and epidemiological and hygienic requirements for goods subject to sanitary and epidemiological supervision (control)" under the Customs Union (CU) Agreement on sanitary measures. Uniform sanitary requirements are binding upon the executive authorities of the member-states of the Customs Union, local authorities, legal entities of any organizational legal forms, individual entrepreneurs, individuals. Currently, 31 Regulations out of 47 priority technical regulations planned to be adopted were adopted by the Customs Union, including the regulations on safety of rolling stocks, perfumery and cosmetic products, toys, products for children and adolescents, food, grain, and furniture, etc.[1] The creation of a valid system of technical regulations that ensure protection against unacceptable health risks, should contribute to an increase in life expectancy and be a guarantee of its stabilization at levels that are consistent with high standards of human well-being.

Of course, "... current situation requires a change in priorities in planning strategies for health promotion, namely the shift from clinical approach to the prevention programs ..." [National Healthcare Development Program of the Russian Federation until 2020, 2012].

At the same time current reduction in the life expectancy of Russian citizens is determined for modern generations by living conditions in which they are at present, and the accumulated burden of diseases. The risk contingents that are in the danger zone need the delivery of health care even now. Since the mechanisms and manifestations of health disorders under the adverse effects of living environment factors, may differ from the traditional, it is necessary to use specific methods for such disorders correction.

Risk management methodology includes a component, which is represented by the technologies that make it possible to reduce this risk even in conditions of the continuing impact of health hazards of ambient and occupational environment [Zaitseva N. V. et al.,

[1] Onishchenko G.G. On the Rospotrebnadzor's implementation of uniform principles and rules of technical regulation within the Customs Union Agreement Hygiene and sanitation. 2013. No. 4. P. 4–8.

2013; Zaitseva N. V. et al., 2009; Zaitseva N. V. et al., 2010; Zaitseva N. V. et al., 2009; Ustinova O. Yu., 2010].

"... the formation of targeted research programs on development and implementation of the new efficient technologies of the early diagnosis, prevention and treatment of socially significant diseases, the rehabilitation of patients; the maintenance of health and healthy lifestyle ..." is critical for further improvement of the technologies of this kind [The strategy of development of medical science in the Russian Federation until 2025, 2012].

Living in areas with favorable ecological and sanitary-hygienic environment is the principle of the high standards of human well-being. In this regard, the provision of sanitary and epidemiological welfare of the population of the Russian Federation, particularly hygienic safety of the places of residence, should be considered as one of the key factors in the formation of high standards of human welfare. Currently, according to the results of the analysis of living environment and its impact on the health of the population of the Russian Federation, made on a range of indicators (113 indicators used), the most important are chemical, biological and physical factors (the estimated share of the most exposed population is 72.9%). These factors include: the contamination of food, drinking water, ambient air and soil; physical factors; the conditions of the learning and education of children and adolescents in organized groups; working conditions and production factors in industrial enterprises. At outlined stabilization of the population exposed to chemical load complex, the population exposed to physical factors is reduced.

In 2013, according to the results of social-hygienic monitoring (SHM) and risk assessment 2512 great management decisions were made, among them 1058 – in the framework of regional targeted programs for the prevention of mass non-communicable diseases due to exposure to living environment factors [On the state of sanitary and epidemiological welfare of the population of the Russian Federation in 2013, 2014]. This confirms the thesis that the health risk assessment methodology is in demand at the formulation of programs for the safe development at regional and municipal levels [Onishchenko G.G., 2013], but its introduction to the work of not only the competent authorities that are responsible for ensuring the sanitary-epidemiological welfare, but the government as a whole could be more supportive of the approximation to the high standards of human well-being.

The high standards of human well-being are formed with the participation of the citizens themselves. A role of the individual in the management of risks associated with unhealthy lifestyle is especially significant. Lifestyle factors that have a negative impact on the health of the population, namely: low-quality and unbalanced nutrition, the consumption of alcoholic beverages and beer, tobacco are characteristic for almost all subjects of the Russian Federation [On the state sanitary and epidemiological welfare of the population in the Russian Federation in 2013, 2014].

Risks associated with lifestyle factors, can be a significant cause of the loss of human potential [Zaitseva N.V. et al., 2011].

The anagement of these risks has three main components: the creation of macro-social conditions for the implementation of healthy lifestyle (the sphere of primary responsibility of state administration bodies), information on the health risks from lifestyle, and measures to minimize them (the sphere of primary responsibility of the competent authorities), the implementation of the principles of a healthy lifestyle and recommendations on risks minimization (the scope of primary responsibility of citizens).

In the management of these risks the importance of such a component of risk analysis, as information about them is extremely high. The key task of information is in the provision of accurate and scientifically based information on the factors that may have a harmful effect on human health, health risk levels, the necessary preventive measures, as well as the ways and means of the individual prevention of health disorders to the representatives of different social groups that are, in particular, the risk contingents. The solution to this problem requires a clear awareness that the risk is not only exclusively objective and knowable fact, it is always moderated by social and cultural stereotypes and processes. Understanding the perception of health risks by different social groups, recording of the types of perception in the construction of a system of risk communication will improve the efficacy of regional policy in the field of risk management, minimize the losses of human capital [Zaitseva N.V. et al., 2010].

Thus, health risk analysis methodology can make the most significant contribution to the high standards of human well-being in terms of the reduction of the number of people living in areas with adverse environmental conditions, the increase of life expectancy and, as a result, the prevention of GDP losses.

The development of the National Security Organization

In the past 15 years, the concept of safety has largely evolved, meanwhile its main emphasis has shifted from the military and political aspects at the national level to the safety of every person and of society as a whole [Vladimirov V.A., 2002]. In terms of the principle of sustainable development ecological safety takes a special place in the new concept. A human and natural ecosystems are the central objects in its assessment, and risk analysis is one of the main assessment tools.

Recent years are characterized by the development of existing chemical threats associated with:

- development and introduction into the production of the fundamentally new classes of substances with insufficiently studied effects on human health (nanomaterials) and an increase in the use of chemicals with high toxicity;
- an increased hazard of harmful substances into the environment;
- an increase of accidental risk in enterprises due to the increasing deterioration of the equipment and declining of personnel qualifications;
- the accumulation of hazardous persistent compounds in the environment, including banned toxic chemicals;
- the globalization of trade, including in the framework of Russia's joining the WTO and, consequently, the increased risk of the importation of agricultural products obtained using different plant protection products and agrochemicals.

The main sign of the chemical threat of the object is the presence of production, processing, use, transportation, treatment, the storage or disposal of hazardous (harmful) chemicals, as well as the use of technologies with the implementation of chemical processes. In addition to traditional anthropogenic processes (the sources of chemical threat), such as the emissions and discharges of industrial enterprises to the environment as a result of their activities, or in emergency situations, at the present stage chemical threat may result from the political and economic conditions (the increase of the risk of terrorist attacks using chemicals, the market entry of products that do not always correspond to the domestic regulations in connection with Russia's joining the WTO).

The sources of chemical threat should be considered as the sources of the risk of chemical hazards impact. Due to the fact that safety is interpreted as a lack of unacceptable risk, the issues of risk assessment, including risks for human life and health, determination of its tolerability and the development of the risk management system become an extremely topical.

The main tasks for the prevention and minimization of the risks of chemical factors impact on human health and living environment are the following: the development and introduction of the modern methods and means of population and living environment protection against the adverse effects of hazardous chemicals; the validation and implementation of preventive measures among risk groups; the implementation of fundamental and applied scientific researches on the development of new chemical technologies that reduce the risk of negative impacts to an acceptable level; the replacement of worn-out equipment and off-market technologies with more modern ones; the provision of personal protective equipment to population and the personnel of chemically hazardous facilities [Onishchenko G.G., 2014].

An important task is the categorization and ranking of the levels of facilities and territories danger in accordance with international legal and economic requirements and the transformation of chemical threats in the field of the management of chemical substances and mixtures. The validation of common criteria and methods for categorizing and ranking of facilities and territories in terms of chemical threats, the creation of science-based guidance documents for the classification of facilities and territories based on categorization and the ranking of the levels of chemical threats play an important role in its decision. The levels of

individual and population health risk and environmental risk are one of the criteria for the categorization of facilities and territories.

The widespread use of population health risk assessment methodology as a method that combines complex approaches to the assessment of sources, the routes of intake, probable effects to public health is appropriate for the categorization and ranking of facilities and territories in terms of chemical threats based on the properties of chemicals with a number of negative effects.

In today's presentation of the international community, there are a narrow and a broad interpretation of biological safety. The meaning narrow understanding is defined by the presence of international requirements at work (diagnostic, industrial, experimental) with pathogenic biological agents in accordance with the regulated levels of biohazard and safety. The broad interpretation of biological safety has no conceptual, terminological and definitive bases. The results of the surveys helped establish that the biosafety conceptually covers the whole field of sanitary and epidemiological welfare, the related areas of veterinary-sanitary, phytosanitary provision, environmental safety, living environment (production, socio-economic, geopolitical infrastructure, ecological system) and shall be carried for the purpose of prevention and management of biological emergencies. It is shown that the difference between this emergency situation from ones in the field of public health care of international importance as defined in the International Medical and Sanitary Regulations (2005), is, as a rule, high socio-economic and geopolitical significance of the negative impact on human activity, that is comparable with the threat to national and international safety. The conceptual foundations of biological safety, which require legal (legislative), normative (substatutory), methodical consolidation in the Russian Federation have been developed [Onishchenko G.G. et al., 2013].

Conceptual, terminological and definitional framework is created in accordance with the developed conceptual framework of modern (broad) format of biological safety and the requirements of the International Medical and Sanitary Regulations dated 2005. The key concept is the biological safety, which is defined as the state of protection of the population (individual, society and state) from the direct and/or indirect impact of hazardous biological factors through the living environment (industrial, socio-economic, geo-political field, ecological system). The ultimate purpose of biosafety consists in the prevention and mitigation of the biological emergencies of natural and artificial (man-made) origin, arising from the direct and indirect effects of hazardous biological factors on human health on a scale that is commensurate with the threat to national and international safety [Onishchenko G.G. et al., 2013].

Biological hazard is associated with the risk of dangerous and especially dangerous infections, including natural focal, spontaneous and re-emerging ones, as well as their distribution among the population, the emergence of various biological disasters (due to pandemics, accidents at biologically dangerous facilities, as well as uncontrolled technological activities, including the breeding and selection of antibiotic-resistant pathogenic strains of microorganisms, and natural disasters, which lead to the outbreaks of infectious diseases). In addition, taking into account a number of specific properties, biological agents can be used for terrorist attacks.

The main sign of the biological threat of a facility or a specific territory in terms of the risk of occurrence and the spread of infectious diseases is the presence of natural (including virus carriers) or artificial reservoirs of pathogens (anthracic animal burial sites, biothermal pits, collections of museum culture strains in research institutions, laboratories, and biofactories).

Certain risks are also associated with the current active use of genetic engineering technologies, which were the most widely used in the construction of new crop varieties that impose special requirements to food safety. The objective sources of the presence of actual or potential biological risks of genetically modified (GM) foods are: the unpredictability of the introduction of foreign DNA paragraph into the plant genome; the insufficient knowledge of the mechanisms of the regulation and functioning of the genes of higher plants; the presence of the pleiotropic effect of secreted transgene; the violation of genome stability and the change of its functioning due to the transformation process; the violation of the stability of foreign DNA fragment that is secreted in the genome; the presence of "technological waste" inserted DNA fragment, including antibiotic resistant genes and viral promoters; allergic and toxic effects of a foreign protein.

In general, the significance of biological threats can not be overestimated, since infections are the second leading cause of mortality and the first cause of premature mortality in the world according to the recognition of the World Health Organization. At the same time the following occurrences pose the greatest biological threat:

- the microorganisms' overcoming of interspecific barriers (anthropozoonosis, infections of remote biological species);
- re-emerging, controlled by vaccination infection, those which become active after a period of epidemiological well-being due to the closure of population immunization programs;
- infections that occur in new areas (the delivery of rare or previously encountered infections);
- new infections caused by previously unknown pathogens;
- the increase of the epidemiological significance of opportunistic pathogens and the increase of the incidence of opportunistic infections (infections that appear in people with compromised immune systems of any nature);
- the spread of hospital infections;
- the biological terrorism of all forms.

The growing importance of the above risk factors caused the formation of the Russia's National System of chemical and biological safety.

The "National Security Strategy of the Russian Federation until 2020" notes that the strategic objectives of national security in the health care and health of the nation are the increase of life expectancy, the decrease of disability and mortality. The Russian Federation determines the enhancement of preventative health care, focus on the preservation of human health as main areas of national security in the health care and health of the nation in the medium term. The national system of the protection of human rights, including in the field of the prevention of violations of sanitary and epidemiological and (or) sanitary standards of consumed by the population of the country drinking water, the provision of continued access of all categories of citizens to foods that are necessary for a healthy lifestyle, the enhancement of the protection of the population against natural and man-made emergency situations will be improved to counter threats to national security in the field of improvement of the quality of life of Russian citizens.

The "Principles of State Policy in the field of chemical and biological safety of the Russian Federation for the period up to 2025 and further," state that the document was prepared in connection with the need to improve the government regulation of the activities for the gradual reduction of the risk of the negative impacts of hazardous chemical and biological factors on people and the environment in the territory of the Russian Federation to an acceptable level. In this context, the identification, analysis, forecasting, introduction of uniform criteria for assessment and ranking of the risks associated with the adverse effects of chemical and biological factors, and the implementation of a complex of measures on the neutralization of chemical and biological threats, the prevention and minimization of risks, the improvement of security of the population and the environment, as well as the assessment of the efficacy of these measures is currently assigned to the priority areas of the state policy in the field of safety of the Russian Federation.

Increased global competition, an expected new wave of technological changes, the growing role of human capital as the main factor in the development of the country, the exhaustion of the potential of the model of economics based on the export of raw materials pose the safety issues of territory and population of the Russian Federation in a number of priority.

The shift from measures on respond to the situation and mitigation of harmful effects ("culture of reaction") to the prediction and prevention of hazards ("culture of prevention") is assigned to the priorities of public policy on the safety of the population and territories. Such changes place new demands on the development of methods, tools, techniques and criteria for the identification, forecasting, classification and ranking of external and internal risks to the vital interests of security objects. However, the scientific and methodological support of modern forms of state supervision, inspection, expertises and monitoring of ambient and working environment hazards continue to be relevant.

It is is advisable to choose the objects and territories for state supervision and monitoring based on their categorization.

The methodology for objects categorization will allow the justification of the classification characteristics of the different categories of objects of supervision attributed to the different activities, and the justification of the main content and scope of supervisory actions on objects of different categories of hazards and risks to health.

The continued inclusion of new chemicals in circulation and the increase of the requirements of the international community to their accounting and control, the emergence of new infectious agents and the increase of the probability of the spread of epidemics in the intensification of displacement, including migration processes on the one hand, and the burden of chemical and biological contamination of the environment that has been built up over many years on the other hand, require the sprawling of scientific and methodological base, primarily in the area of health risk analysis. The purpose is to rise scientific researches to the level of the world achievements, including recent advances in biotechnology, computer science, nanotechnology, health and other areas.

Priority development is assumed with respect to the objects that provide scientific and scientific-production activities in the field of chemical and biological safety, as well as organizations under the jurisdiction of the federal executive authorities with the powers to exercise control (supervision) and monitoring of hazardous production facilities and the population living environment. Need to support organizations that are focused on the development and introduction of modern medical-preventive technologies, which are designed for both persons who work in hazardous chemical and biological facilities, and the population of the territories with risk of adverse effects. The objectives of basic public documents in the preservation of human, including the labor capacity of the country require innovations in the field of risk minimization and the prevention of diseases.

Upon reaching a number of positive results in chemical and biological safety of the territories and population the situation is characterized by a complex of disturbing indicators and trends that will continue in the absence of the prospect of an interconnected system of program activities on the minimization of the risks to public health.

The problem may be solved by several ways. The first way consists in the support of the existing safety system at achieved level, which ensures the absence of the deterioration of the situation in the conditions of the emergence of new risks at the impact of the most dangerous chemical and biological factors on the population, technosphere and environmental systems. The second way is the development of the existing system as a strategically oriented national system that is aimed at the reduction of the risk of exposure to hazardous chemical and biological factors on the population to an acceptable level with the integration into the international safety systems.

The first way makes provision for the implementation of activities, which include:

- the coordination of interaction and information exchange of federal executive authorities, executive authorities of subjects of the Russian Federation, local governments and organizations in determination of priorities for the development and implementation of the system of chemical and biological safety of the population at the federal, regional, local and site level;
- the drafting of information and guidance documents, as well as the validation of proposals for cooperation with other countries in the field of chemical and biological safety;
- comprehensive studies aimed at assessment and management of risks to public health and the functioning of the key objects of the technosphere, including in critical and emergency situations;
- development of proposals for improvement of reliability of functioning of the objects of chemical and biological hazards, modernization of systems of control and management of emergency risks and mitigation;
- the development of innovative technologies for prevention of risks and damages under the existing complex of chemical and biological contamination as a result of economic activity;

♦ development of principles, guidelines and mechanisms for the legal and economic responsibility for unacceptable levels of risk and insurance of the responsibility for the problems of improvement of the legal framework of the Russian Federation;

♦ coordination and intensification of fundamental and applied researches on creation and identification of hazards of new facilities and technologies, improvement of existing and development of new methods for hazard identification, health risk assessment and functioning of economic entities, prevention and indemnification of damage in the implementation of this risk;

♦ development of methodological, hardware, and information and analytical and other support of the effective functioning of the system of professional development for federal executive authorities, executive authorities of subjects of the Russian Federation, local authorities and organizations in the field of chemical and biological safety risk assessment and management;

♦ the creation of information system of federal executive authorities, executive authorities of subjects of the Russian Federation, local authorities and the public about the health risks, ways to reduce them, measures aimed at protection against hazards based on federal and regional governance structures resources.

This solution to the problem is focused on the adjustment of the current unfavorable situation, especially in areas of high risk. At this way, the priorities are the development of foundations for a stable security system in the Russian Federation and the elimination of unacceptable levels of risk to the health of the majority of citizens.

Waiver of these activities can lead to incoordination of efforts of federal executive authorities, executive authorities of subjects of the Russian Federation, local governments and businesses in the field of safety. This would result in the risk of unnecessarily high costs, which is formed on the one hand, by the need for compensation due to the influence of negative factors of damage when not taking timely actions to prevent it, and lack of coordination of safety on the other can lead to unnecessary at this stage, economically inefficient expenditure of manpower and financial resources, including through the duplication of individual activities.

The second way provides for implementation of additional activities other than those provided in the first way. They include:

♦ coordination of interaction and information exchange of federal executive authorities in the implementation of domestic and foreign policy of the Russian Federation in the field of chemical and biological safety;

♦ serving the national interests in the field of chemical and biological safety in the conditions of Russia's integration into the world community;

♦ the inter-regional coordination of information exchange and interaction at risk of the transboundary impact of hazardous chemical and biological objects;

♦ the introduction of mechanisms for legal and economic responsibility for the unacceptable levels of risk and insurance of this liability;

♦ the creation of a nationwide organizational and the functional structure of safety for public health, including the center of risk management, information and control structures of vertical and horizontal interaction;

♦ the development of a range of stimulation measures to achieve the minimum levels of health risk, the increase of the period of the economic activity of the population;

♦ the development of the intelligent tools of forecasting and assessment of new manufacturing processes and facilities risks;

♦ the formation of the bank of risk management innovative technologies.

The advantage of this way is that it would create a comprehensive system of validation of management decisions in the field of chemical and biological safety, industrial base, the biosphere and ecological systems, including through regional cooperation.

However, it is more expedient to give preference to the first way in the current economic situation because the implementation of the expanded way of the program is associated with a high risk of extreme loads on the economy and slowing down of the socio-economic development of the country. In this case, the prerequisites for the formation of a stable system of chemical and biological safety will be generated along with the

implementation of the basic measures on reduction of the risk of impact of hazardous factors on the population of the country.

For the development of a national system of chemical and biological safety, that would consistently provide a decrease to an acceptable level of the risk of the population exposure to hazardous factors as a condition for sustainable socio-economic development of the country, it is necessary to solve the following **problems**:

- the detection, forecasting, criterial provision and ranking of external and internal risks to the vital interests of security objects;
- the improvement of state regulation in the field of chemical and biological safety with the development of model elements for integration into supranational, interstate and international systems;
- the optimization of multi-level inter-agency organizational and functional interaction and coordination in the system of chemical and biological safety;
- the development of the resource potential of the territorial and functional elements of the national system of chemical and biological safety;
- the implementation and assessment of the efficacy of a complex of operational, tactical and strategic measures on neutralization of threats and hazards, prevention and minimization of risks, improvement of protection of the population, ecological systems and the technosphere.

The priority areas of this system are determined by the current socio-economic situation in the country and political vectors that were defined by the basic state documents in recent years.

It is necessary to implement measures as priority areas for the implementation of these tasks in the area of environmental safety for the health of citizens in such priority areas as:

1) the detection, forecasting, criterial provision and ranking of external and internal risks to vital interests of security objects;

2) the improvement of national administration in the field of chemical and biological, sanitary-epidemiological safety with the development of model elements for integration into supranational, interstate and international systems and optimization of multi-level inter-agency organizational and functional interaction and coordination in this area;

3) the development of the resource potential of the functional elements of the national safety system at all levels, including the strengthening of the material-technical base of the institutions under the jurisdiction of the federal executive authorities with regard to the powers and functions of the implementation of the control (supervision) and monitoring in the area of public safety of the Russian Federation population and its information on the risks to health;

4) the implementation and assessment of the efficacy of a complex of operational, tactical and strategic measures on the neutralization of threats and hazards, prevention and minimization of risks, improvement of protection of the population.

It is advisable to carry out a series of activities for each priority.

The first priority should include the following activities:

- the comprehensive analysis of the situation, the identification and assessment of new chemical and biological threats and hazards;
- the scientific, information-analytical, criterial and methodical support of an assessment of risks that are formed by priority sources of hazard;
- the scientific and methodological support of the assessment of harm, damage and insurance against risks that are associated with the activities of objects – the sources of hazard;
- the development of methods for the indication and identification of biological agents and chemical substances in the environment and biological media;
- methodological support to state supervision, inspection, verification and monitoring of hazards in ambient and working environment;
- the scientific and methodological validation of the response measures at all levels of control and interaction in the field of sanitary-epidemiological safety based on situation and simulation modeling of parameters in terms of legislative, structural-functional and other changes in Russian Federation;

♦ development and harmonization with the international standards of hygienic regulations, the content of chemical and biological agents in living environment and human biological medium, including risk criteria.

It is necessary to make provision for the following activities on the second priority area based on a comprehensive analysis of the current situation in the Russian Federation:

♦ the development of the mechanisms of the improvement of the state regulation and control of safety at all levels of legislative and executive authorities;

♦ the scientific validation of the ways and means of improving the structural-functional model of risk management at federal, federal subjects and municipal entities and businesses with regard to legislative and structural and institutional reforms in the country;

♦ the scientific information support of the development of the legal framework that supports the integration of Russia into the WTO, the OECD, the international community and other measures on implementation of the obligations of the Russian Federation under international treaties (conventions) in the field of chemical and biological safety;

♦ the development of international cooperation in the field of safety for the life and health of citizens, which promotes economic development and integration of the Russian Federation within the frameworks of the Customs Union, the Eurasian Economic Community, the WTO and the OECD.

The third priority should include the following activities

♦ the development of the scientific and industrial and material-technical base of organizations under the jurisdiction of the federal executive authorities with regard to the powers and functions of the implementation of control (supervision) and monitoring in the field of chemical and biological safety of the Russian Federation, the objects of industry, science, utility and other industries of economic activity, the functioning of which is aimed at safety;

♦ the development of scientific and methodological basis of the objects of industry, science, utility and other industries of economic activity, the functioning of which is aimed at safety;

♦ the development of medical-preventive technologies of the diagnostics, treatment and prevention of health disorders related hazards;

♦ the improvement of personnel training in the field of safety;

The fourth priority should include the following activities:

♦ organizational and technical, technological and planning measures on the identification and neutralization of threats and the minimization of risk inherent in hazards;

♦ the implementation of a complex of medical and preventive measures against individuals at risk of the negative impact of factors on dangerous facilities and in areas of influence.

The target indicators of the implementation of measures on the safety of life and health of citizens of the Russian Federation could include:

♦ the number of the standards of risk factors in environment objects and production developed and harmonized with international requirements;

♦ the number of new methods of indication of hazardous chemicals and biological agents;

♦ the number of reconstructed and constructed facilities, which are equipped with means of control for safety, under the jurisdiction of the federal executive authorities with powers and functions for the implementation of control (supervision) and monitoring under the authority of competent supervision (control) authorities;

♦ the proportion of population that lives in an unacceptable level of the risk of exposure to hazardous chemical and biological agents for which the risk is reduced to an acceptable;

♦ the number of developed modern medical technologies for prevention, diagnosis, treatment and rehabilitation of population that lives in the conditions of hazardous chemical and biological impacts;

♦ prevented environmental, life and health, industrial facilities damage as a result of the implementation of risk management measures.

A separate safety issue is food safety of the Russian Federation i.e., the state of the economy, which shall ensure food sovereignty, guarantee the physical and economic availability of food, which correspond to the requirements of the legislation of the Russian Federation on

technical regulation, in amounts that are not less than the rational norms of food consumption, which is necessary for an active and healthy lifestyle.

Food safety involves risks that could significantly weaken it. The risks associated with differences in the requirements for food safety and the organization of their compliance control system are one of the most significant ones;

The control of compliance with the legislation of the Russian Federation in the field of agricultural, fishery and food products, including imported, at all stages of production, storage, transport, processing and marketing is necessary for food safety. It is necessary to eliminate the uncontrolled distribution of food products that were derived from genetically modified plants, with the use of genetically modified micro-organisms that have genetically modified equivalents. The harmonization with the international standards of food safety indicators is to be continued based on fundamental research in the field of nutritional science [On approval of the Food Safety Doctrine of the Russian Federation, 2010].

The development of national standards based on internationally recognized principles of health risk assessment is necessary for full harmonization. However, the adoption of foreign standards without peer review by national experts in the field of health risk assessment is absolutely unacceptable in the frameworks of food safety.

Thus, the development of the national safety system in regard to the provision of the absence of unacceptable risk to human life and health is one of the key areas of the application of risk analysis methodology in the solution of the strategic tasks of the state socio-economic development.

The improvement of goods competitiveness at the global level

The competitiveness of goods is defined as the product's ability to be attractive in comparison with the other products of similar type and purpose through the better compliance of the characteristics with the requirements of the market and consumer evaluations.

The competitiveness of goods and services is the main factor of the quality of life. According to the UNESCO Commission on Human Population and Quality of Life [Korsunskaya M. P., 1999], the concept of "quality of life" includes the following:

1) health;
2) education;
3) sensible (adequate) nutrition;
4) stable, clean environment, including habitation;
5) safety;
6) health care;
7) participation in society, the creation of the necessary services for its development;
8) equity;
9) gender equality.

The fulfillment of the first seven conditions is directly dependent on the competitiveness of goods and services [Lifits I.M., 2009].

The indicators that characterize good competitiveness, usually divided into two groups (the so-called "price – quality"):

1) indicators that characterize the consumer properties of goods (the quality), which make up its beneficial effect. They represent a set of "hard" and "soft" indicators;

2) economic indicators that characterize the economic properties of the goods (the so-called price).

However, as reasonably believed an American scientist Deming, the basis of products competitiveness is its quality.

"Hard" quality indicators provide physical ability to use product for its intended purpose and are divided into the following groups:

1) technical i.e., intended use indicators (the properties and functions of the goods, which determine its scope), ergonomics (which is characterized by product conformity to the properties of the human body), technical indicators (technological solutions, reliability, safety);

2) the regulations i.e., indicators of compliance with the requirements of international and national standards, regulations, which operate in a market where this product is supposed to sell.

The difficulty is that consumer at the assessment of the quality of goods is largely oriented to own tastes and ideas about the commodity rather than to the quality indicators that are regulated by the normative documents. At that sometimes many consumers have very superficial ideas of the product, mainly at organoleptic characteristics, which are not always adequately and objectively characterize the utility of goods to consumers. For example, the reduction of nitrate added to cooked sausages, would increase their safety, but worsen the color that gets the gray shades. However, most consumers prefer sausage with a strong pink color, unaware of its nature (the pink color is the result of the interaction of nitrates with myoglobin of meat, resulting in nitrosomyoglobin, which in high doses is unsafe for humans). Another example. Many food additives (synthetic colorants, acidifiers, foaming agents, etc.) improve the organoleptic properties of food, and preservatives extend shelf life, that provides them with consumer preferences. However, the utility of such food is lower than natural ones.

Thus, we can talk about the consumer assessment of the level of quality that is set as the ratio of actually determined values of organoleptic quality indicators to prospective customers values of the same indicators.

At the same time, the use of the objective criteria of food utility in combination with the appropriate level of assessment of its safety for human health will contribute to the ability of consumers to correctly identify the quality of the food and to assess its real competitiveness.

The criteria of "quality level" (quality) and "consumer price" (price) without exaggeration can be considered as priority, as a pair of "quality – price" is mainly used in the assessment of the competitiveness in commercial practice.

Food safety for health is considered as one of the components of the product quality. The Law of the Russian Federation No. 2300-1 dated 07.02.1992 "On Protection of Consumers' Rights (hereinafter - the Law on Consumer Protection), No. 29-FZ dated 02.01.2000 "On Food Quality and Safety" (hereinafter - the Federal Law on Food Quality), No. 184-FZ dated 27.12.2002 "On Technical Regulation" and other legislative acts are the legal basis of mandatory requirements for quality. Technical regulations are also the main carriers of the mandatory requirements for product quality at the present stage. Domestic technical regulations are accepted in the form of federal laws. Technical regulations of the Customs Union also have effect in the territory of the Russian Federation.

The national standards (GOST) and standards organizations are the regulatory framework of quality requirements. If the main purpose of technical regulations is to protect the life and health of citizens and protect property and the environment, the use of standards is primarily aimed at products competitive recovery.

The Concept of long-term socio-economic development of the Russian Federation assumes the accelerated development of technical regulation as an important tool to stimulate innovation development by:

- the modernization of outdated regulations and standards, which are barriers to the expansion of innovation activities of enterprises;
- the consistent and long-term predictable strengthening of requirements for the efficient use of natural resources, products (services) safety for the environment and public health, the reduction of energy and materials, the determination of the appropriate system of incentives and sanctions;
- the harmonization of Russian and international standards, especially in the areas with prospects for the expansion of innovative products export.

The stringency of the requirements of the technical regulations, standards, contracts, specifications, terms of reference for product development, against which it will be checked, determines the level of product quality. Leading producers or producers that aim to become a leader put very strict quality and safety requirements in their company standards.

According to analysts, recently it is appropriate to consider the ratio "price – quality – safety" (Fig. 9.1) in the assessment of the competitiveness of goods. This is due to the fact that more and more consumers associate product quality with its safety for health, i.e., the absence of unacceptable risk.

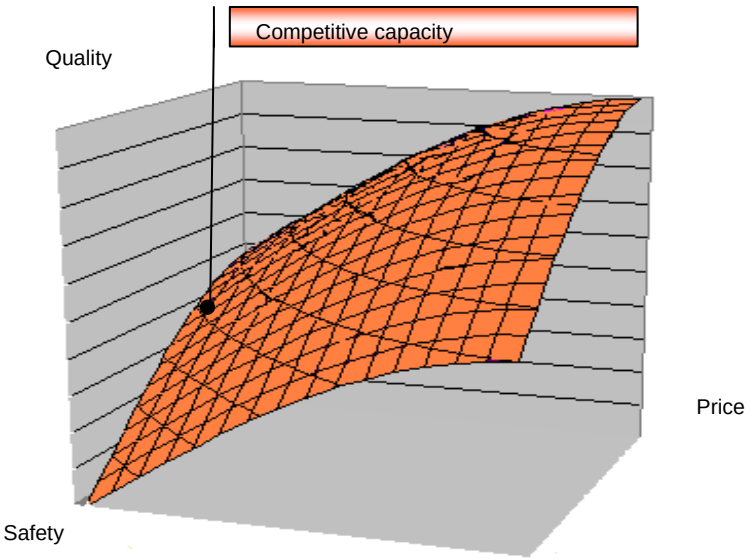

Fig. 9.1. "Price – quality – safety" ratio
in product competitiveness assessment

The recognition of this fact is reflected in the principles of the development of the norms of products harmful effects on health, which are justified by criteria of acceptable health risk (risk-based).

Chapter 2 sets out the methodological approaches and experience of Russia in the validation of standards in accordance with internationally recognized principles. Intensive work on the validation of the requirements of technical regulations and common sanitary rules that define the safety of the goods, using the criteria of health risk is currently being taken both in the Russian Federation and in the countries of the Customs Union. The use of the most modern approaches to products risk assessment for health ensures the greater safety of domestic products and thus increases its competitiveness.

The carrying-out of requirements for product safety, which are based on the criteria of acceptable risk, stimulate domestic producers to introduce innovations that can give benefits under equal conditions of competition in foreign markets. At the same time the rejection of the principle of zero risk, which was used during the hygienic standardization, reduces barriers to market entry in the form of unnecessarily stringent quality standards of products, providing a complete lack of impact of health hazards.

It should be noted that products safety assessment based on the criteria of risk to health is one of the key conditions for the harmonization of requirements for goods. This primarily refers to the Eurasian Economic Area of Participatory Development. Harmonized requirements and methods of their validation will create the equal conditions of competition within the Eurasian Economic Space and other markets with similar requirements. In addition, the harmonization of the methods of risk analysis and products safety requirements that were developed with their use, will contribute to the development of sustainable production cooperative ties with countries – technology leaders, including for the implementation of the joint projects of global markets entering, which can significantly improve the competitiveness of domestic products.

Thus, the methodology for health risk analysis can be considered as a tool that contribute to growth of competitiveness of goods produced in the country, both domestically and globally.

The provision of a balanced spatial development

Significant economic, social and political changes taking place in the last 15 years in Russia, lead to the formation of a new national geo-economic space that will soon be integrated into the world. The continued deepening of integration processes in the country, as well as the systemic transformation of economic processes only reinforce the need for new management models to address the regional socio-economic issues and the sustainable development of the economy of territorial systems [Dvortsov V.I., 2008].

Balanced spatial development is considered as one of the aspects of the sustainable development of the state. Using the experience of the European Union, namely the provisions, which are presented in the most important document (along with the "Guiding Principles for Sustainable Spatial Development of the European Continent") in the context of European spatial development through the European Union – European Spatial Development Perspective [On balanced and sustainable development of the EU – European Spatial Development Perspective - ESDP, 1999].

ESDP at the sequential achievement of balanced supra-regional spatial development of the territory has three main goals:

1) the strengthening of economic and social cohesion;

2) the conservation of natural resources and cultural heritage;

3) ensuring a balanced competitiveness of the territory.

This suggests a more decentralized development and determines the choice of appropriate policies, which may include:

- the strengthening of the polycentric and balanced system of metropolitan regions and urban networks;
- the development of the strategic role of metropolitan regions and gateway cities (e.g., ports, cities with international airports, international financial centers);
- the improvement of coordination between spatial development policy, and transport and telecommunication planning and so forth.

The need for a balanced spatial development of our state is dictated by the uniqueness of the size of the Russian Federation and the extreme heterogeneity of its territory by natural and climatic conditions, density and demographic characteristics of the population, economic development, financial saturation, investment attractiveness and so forth.

The spatial imbalance of labor resources is the most significant in Russia. Herewith, there is a concentration in the areas of developed industrial potential, which is accompanied by a negative impact on the environment objects that causes a health hazard. On the one hand, a large proportion of the labor force is in the areas with the highest risk to human health and the maximum probability of their losses. On the other hand, the implementation of a balanced spatial development in compliance with the principle of the polycentricity of balanced territorial system implies the creation of new centers, which assume the concentration of production and economic potential, and consequently the working-age population.

It is necessary to develop tools for the management of risks that arise at projected situations for the prevention of the losses of the labor potential of the spatially balanced distribution of resources.

For example, in terms of existing industrial and residential agglomerations, the environment is polluted by a large number of harmful chemicals that even at the compliance with existing hygienic standards an unacceptable risk to public health is created. In these cases, it may be appropriate to introduce more stringent regional hygienic standards, which shall be prepared with regard to the risk of combined, integrated and associated impact. In this case, air, water, soil and other environment objects quality standards will correspond at least a safe level of their impact on human health. In either case, the reduction of losses associated with health disorders, which leads to the increased production of gross domestic product and employment will be achieved. The increase of investment and demographic attractiveness of the area may be an additional effect of such measures.

As environmental regulations are currently being determined using the results of hygienic standardization, this measure can lead either to reduction of the health risk due to the

reduction of anthropogenic load, or to the formation due to charging for excess emissions and discharges of the economic base for medical and preventive measures on risk reduction.

The imperative establishment of permissible anthropogenic load standards for these areas would set quantitative and qualitative targets for the development of programs to minimize health risk and the gradual decrease of the negative impact of the economic actors.

At the formation of new centers of economic and social development, which bears on the development of energy and transport infrastructure and the creation of a network of territorial and industrial clusters, which realize the competitive potential of the areas, for the provision of sanitary-epidemiological and ecological safety of the population must initially use the existing experience as health risk controls based on spatial analysis, including those described in Chapter 3. To take full advantage of this experience and its development, the preparation and adoption of territorial planning and urban development zoning documents shall be completed, as provided for under "Concept of long-term socio-economic development of the Russian Federation for the period until 2020". In order to ensure full consideration and balanced plans of spatial development, it is reasonable to involve experts in health risk analysis to assessing the reasonableness of the spatial urban planning decisions both at the level of the country as a whole, and at the local level.

"The Concept of long-term socio-economic development of the Russian Federation for the period until 2020" notes that the poles of ecological trouble has been formed for many decades in Russia (and not only in the European part), which negatively affects the quality of people's life, their health and lifetime.

The identification of areas where the situation is classified as "dangerous" that endangers health and life of the resident population should be one aspect of the application of the methodology employed to analyze health risks associated with the quality of the environment. It is important to note not only existing or planned sources of hazard to be placed, but also the accumulated environmental damage and the risk to public health. The identification of such areas is extremely important, since at their further development planning, it will be necessary to provide a set of measures on the improvement of the sanitary-epidemiological and ecological situation, the redistribution of industrial, transport, residential and other areas to reduce health hazards.

Health risk values can be offered as a component of the index of regions attractiveness for development. These values also demonstrate the efficacy of government and can be part of the index of socio-economic development of territories. Of course, in this case it is necessary to take into account the risks, which can be reduced at the performance of certain functions by the authorities within their competencies.

In general, with a corresponding improvement of the legal framework, which is aimed at the minimization of health risks, the use of health risk analysis methodology as a tool to improve the efficacy of human capital, the provision of high standards of human well-being and the development of the national safety system, improve goods competitiveness at the global level, balanced spatial development, creates the preconditions for the transfer of the Russian economy in the mode of innovation development.

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