# PREVENTIVE MEDICINE: URGENT ASPECTS OF HEALTH RISK ANALYSIS

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## ACTUAL PROBLEMS OF ENVIRONMENTAL FACTORS RISK ASSESSMENT ON HUMAN HEALTH AND WAYS TO IMPROVE IT

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*The article provides an analysis of global trends and new areas of assessment and analysis methodology for helath risk caused by exposure to chemicals, environmental pollutants as well as the contemporary issues of national assessment methodology. Most details are considered: risk assessment evidence base, modern methods and problems of carcinogenic risk assessment, hygienic regulation based on risk assessment, the economic aspects of the methodology. Particular attention is paid to reasons of recent years perceived gaps in the Russian methodological basis of the best foreign samples. The urgent measures to improve the national risk assessment methodology are proposed, the main of which are: legislative consolidation of the basic concepts of risk assessment, a further update of the methodology and the practice of hygienic regulation on the basis of risk assessment, improving the valuation of damage to human health, the tightening of the requirements to the developed regulatory guidance documents on risk assessment, as well as to the training and retraining of personnel in the risk assessment.*

***Key words:*** *evidence-based risk assessment, risk analysis, carcinogenic effects, hygienic regulation*

The analysis and assessement of risk to the health of population from the impact of the different environmental factors is one of the most rapidly developing and interdisciplinary directions in the modern science and practice [1, 2, 4, 6, 7, 11]. The major significance during the development of these directions is attributed to the quality and conclusiveness of the risk assessments, scientific justifiability and real efficiency of managerial decisions taken on the basis of it [8].

In the context of crisis in the field of toxicology, epidemiology and risk assessment occurred in XXI century stipulated by the low compliance and insufficient appropriateness of existing scientific tools and accepted practice, for the last 10 years the risk analysis and assessment methodology made the qualitative and quantitative burst in the activity of practically all the international organizations and their subdivisions, as well as the agencies of the leading countries (the Ministry of Health and Environment of Canada, U.S. Environmental Protection Agency, EU, New Zealand, Australia, etc.). The occurred changes are based on the transition to the methodologies based on the evidence-based medicine [13] the scientific directions of which include such sections as the evidence-based toxicology and evidence-based health risk assessment.

The evidence-based toxicology (EBT) is a process of transparent, sequential and objective assessment of available scientific evidence when searching for the answers to the problems of modern toxicology.

The evidence-based health risk assessment (EBHRA) is based on studying the mechanisms of toxic action, biostatistics and validization. The basic directions of this section of medicine include the meta-analysis, detection of the causality of harmful effects, clinical and epidemiological studies.

The EBHRA is based on such new types of the evidence-based medicine as the evidence-based epidemiology (EBE), modern principles of good laboratory practice (GLP), the best risk assessment practices and tools completely complying with scientific evidence which, in a number of cases, shall not conflict with precautionary principle, regardless of the existing differences between these approaches. Thus, the measures for control of smoking never had been



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applied, if only the strict scientific arguments and the existing incomplete evidence on the impact of tobacco smoke on the human body would be used.

It is evident that the proper balance between the scientific proving of causality and the necessity to take the protective measures, even if the final and complete evidence and proof are absent, is required. Anyhow, it is necessary to have the clear understanding of that, where the reasoned final scientific evidence is, and, by contrast, when the society can act without them.

Already in 1931 the Austrian logician, mathematic and philosopher of mathematics Kurt Gödel in his "incompleteness theorem" proved that "the absence of evidence does not prove their absence. There will be always more true events than it can be proved at this moment" [17].

That is why, nonrandomly, a number of countries performed the large-scale epidemiological studies of the impact of chemicals on the tens of thousands of people using the biomonitoring methods with determination in the biosubstrates of about 1900 chemicals and their metabolites that allowed for highly reliable assessment of risk to the health of population.

Currently, the following is the underlying principles of the health risk assessment recognized at the international level.

• Transparency – the characterization of completeness and apparent openennes of methods, initial assumptions, logic, explanations, extrapolations, uncertainties and full force (conclusiveness) of each stage of assessment.

• Clarity – the risk assessment results shall be easily available for understanding of readers – both for the risk assessment participants and the third persons; the documents shall be complete, short, free from jargon and contain the understandable tables, charts and required equations.

• Sequence – the risk assessment shall be carried out according to the requirements of the state (federal) manuals and shall comply with the common policy of the nature protection organizations, taking into account the specific character of the regional features.

• Rationality – the risk assessment shall be based on the apparent statements, methods and assumptions corresponding to the current state-of-the-science and covered on the basis of completeness, balance and informational content.

• The scientific validity, taking into account the risk assessment principles and criteria based on the evidence.

The basic principles of modern toxicology and risk assessment based on the strict scientific evidence were formed on the basis of these international principles:

– the sequential use of the transparent and systemic approach to achieve the reliable and significant conclusions;

– ensuring the transparency and systemity of the testing and assessment processes, the readiness to their continuous improvement;

– the readiness to audit on the basis of provisions on which the current toxicological practice and risk assessment is based;

– the inclusion of all the aspects and branches of toxicology as well as all the types of evidence to the process of the hazard identification, risk assessment and retrospective analysis;

– the generation and use of all the best scientific evidence;

– the recognition of demand for new and verified tools to acknowledge the necessity of effective training and development of professionals;

– high requirements to new and improved scientific tools for their critical assessmen and integration with the existing scientific tools;

– covering all the aspects of toxicological practice and all the types of evidence use for the risk assessment and characterization as well as the retrospective analysis of causality;

– the critical assessment and quantitative integration of scientific evidence;

– combining all the branches of toxicological science: human health assessment, quality of environment, ecotoxicology and clinical toxicology.

None of the listed principles is used to the complete extent in the risk assessment and hygienic standardization methodologies existing in Russia.

The performed information studies revealed the significant retardation of the considered branches of domestic science from the global trends (Table 1).

Even of the field of the human health risk assessment the number of the Russian publications hardly increases the one third of percent.

Table 1

Number of Publications in the World According to the Requests in the Computer System of the USA National Library of Medicine (USA NLM)

| Key words | Number of publications in the world |
|---|---|
| Regulatory toxicology based on the evidence | 123 |

| | |
|---|---|
| Risk for children and elderly | 316 224 |
| The best practices in the human health risk assessment | 80 201 |
| Human health risk assessment | Total – 277 769;<br>USA – 81 268,<br>Russia – 928 (0.33%) |
| Evidence-based health risk assessment | 8 064 (Russia – 0) |
| Evidence-based epidemiology | 4 498 (Russia – 0) |
| Evidence-based toxicology | 307 (Russia – 0) |

Recently, a lot of manuals, monographs and recommendations on the different aspects of chemical safety and risk assessment methodology, among which the following shall be considered [15, 16, 19, 20, 21, 22], have been issued abroad.

New international standards in the field of risk analysis and assessment were entered into force [14, 18, etc.]. Russia in 2011 adopted the National Standard "Risk Management. Risk Assessment Methods" similar to the international standard ISO/IEC 31010:2009 "Risk Management. Risk Assessment Methods" [18].

Unfortunately, during the last 8 years the domestic methodology and practice of the assessment of risk to the health of population suffered from the apparent crisis events. In many ways, they are stipulated by the following negative trends.

· The harmonization of principles and mehods of the hygienic standardization is slow, especially in the field of the harmful action criteria establishment and the meathods of their measurement, methods and principles for the uncertainty factors establishment (reserve coefficients, calculation factors).

· The probabilistic threshold (reference) doses (BMD5, BMD10) are not applied, though there are the available computer programs allowing for calculation of these values and their confidence boundaries by the dozen of models.

· The issue of the annual updating of the list of the reference concentrations of chemicals for the assessment of risk and attributing of legitimate status to this procedure is not solved.

· The approved guidelines and study guides for the higher educational institutions contain the egregious blunders which completely discredit this interdisciplinary section.

· Such underlying principles as the weight-of-evidence assessment, good laboratory practice and the similar sections: good epidemiological, toxicological practice and risk assessment are practically not introduced into the risk assessment.

· The quality, scientific value and practical significance of a number of methodical documents approved after 2010 decreased rapidly. These documents do not contain the scientific and practical validity of the introduced mathematical expressions and mix the risks different by their nature. They contradict the human health risk assessment methodology adopted in the international organizations and in Russia.

· The unified approach to the economic assessment of damages to the health of population is absent. Currently, not less than 10 guidelines which differ both by the concepts and cost characteristics are applicable in Russia.

· The development of principles and methods for the assessment of natural and cost damages to the health and their use for the scientific justification of the proposed managerial decisions is the most acute problem in this field.

Table 2 contains some examples of the existing in the world systems for assessment of the so-called epidemiological risks on the basis of E-R dependencies "exposure – response". As the latter these systems use such parameters as the indicators of mortality, number of diseases, symptoms and material damages, number of additional outcomes, attributive share, background number of outcomes, etc.

Table 2

Global systems for assessing the damages based on the E-R functions "exposure – response"

| System | Country, region | Intended use of system |
|---|---|---|
| EAHEAP, COMEAP | UK | Assessing the damages to health from the impact of atmospheric air |
| ECOSENSE | Germany | Integrated tool for analyzing the damage to the human health and environment |
| AirPack | France, EU | Forecasting the impact of atmospheric air on health |
| FERET | USA | Calculating the natural and cost damages to the health |

| | | |
|---|---|---|
| APHEIS 1,2,3 | EU | Contamination of atmospheric air in the large cities, collection of demographical data, information about the heath condition, forecasting the probable damages to the health |
| IEHIA | EU | System for the health damages assessment |
| AQVM | Canada | Assessing the damages to the health and economic losses from the contamination of atmospheric air for different age groups |
| EPA | U.S. EPA | Reports on the risk/benefir ratios from the use of the clear air law |
| AirQ (ver. 1.0 – 2.3) | WHO | Assessing the mortality, morbidity, frequency of symptoms, number of non-lived years from the atmospheric air contamination |
| TERA2.5 (EpidRisk Module) | Russia | Assessing the damages from the atmospheric air contamination. Contains the results of 162 epidemiological studies, relative risks for each 10 mg/m$^3$ for 10 XB and 182 effects at the different duration of exposure |

The models and systems specified in Table 2 are based on the principles and methods commonly recognized in the world and recommended by WHO, European Union and agencies of the leading countries of the world, same as in the Russian manual R 2.1.10.1920-04 [9].

As it is known, the most important feature of the prognostic model is the accuracy of reflection of the specific features of the studied process. As a rule, the purely empirical formulas are not very reliable [5, 12].

In this respect, the assessment of reliability of methods for the accelerated determination of the toxicometry and risk parameters shall always be started from checing the logic of the selected model.

Recently, the requirements to the analyzed samples became more severe. In addition to the separate analysis of the training and control samples with further assessment of the accuracy and reliability of forecast using the special methods (cross-validation, PRESS-criterion, etc.) it is commonly supposed that for the best reliability there shall be 20-30 observations per each parameter of the recommended model.

Some scientific publications and even methodical documents appeared recently which contain different prognostic methods in the field of toxicology and risk assessment, as a rule, do not include the results of the described above procedure for the audit of mathematical dependencies recommended by the authors which provides the basis for the doubts in relation to their self-consistency, accuracy and reliability.

Unfortunately, it is possible to constate the apparent crisis phenomena in the domestic methodology and practice for the population health risk assessment.

The issues of training and re-education of staff are the most acute problem. Only for the last 10 years in Rospotrebnadzor the number of doctors in the state medical service subdivisions decreased almost by 4 times (from 1319 in 2005 to 352 – in 2013). The number of the state medical service subdivisions also decreased by 4 times – from 808 to 202, respectively.

Works on the state medical service optimization on the basis of risk assessment became exotic, the major part of studies are performed by the private companies which are predominanely oriented to justifying the sufficiency of sizes of the sanitary protection zones of enterprises of the 1 and 2 classes of hazard.

To our opinion, the following is the priority concerns on the overcoming of crisis in the field of the population health risk assessment:

– justification and establishment of the quantitative values for the levels of “acceptable risk” – nationwide notion introduced by “The basics of the state policy in the field of ensuring the chemical and biological safety of the Russian Federation for the period before 2025 and further perspective” which shall be differentiated under the types of risk, its objects and subjects;

– inclusion of notions “acceptable risk”, “acceptable level”, procedure and methods for their establishment to the developed project of the federal law “On the chemical safety” and as the amendements to the federal laws No. 52-FZ “On the sanitary and epidemiological well-being of population”

dd. March 30, 1999, No. 96-FZ “On the atmospheric air protection” dd. May 4, 1999, etc.;

– radical renovation of the methodology and practice of domestic hygienic standardization based on the risk assessment and deep critical analysis of the foreign experience which includes the system for establishing of DNEL (Derived No-Effect Level) and DMEL (Derived Minimal Effect Levels) adopted in the international system REACH (Registration, Evaluation and Authori-zation of Chemicals);

– deep comparative analysis of all the extrapolation methods used for the establishment of hygienic standards: safety factors (uncertainty factors), interspecific and intraspecific (toxico-dynamic and toxico-kinetic) differences, calculation from one way of intake to the other, calcula-

tion from the less durable impact to the life-long exposure;

– bringing the structure of hygienic standards to the best foreign examples. The main in this direction is the review of the hygienic standards in the atmospheric air of a number of substances differentied depending on the time intervals of averaging (short-term exposure limit, maximum permissible mean daily concentration, and maximum permissible mean year concentration). Such work was performed at the Federal State Budget Institution "A.N. Sysin Research Institute of Human Ecology and Environmental Health" within the performance of the state task in 2012-2014. To date the list containing the maximum permissible concentrations of 102 substances is prepared;

– in favor of the risk assessment and the chemical safety principles globalization it is necessary to approve legislatively in Russia the Globally Harmonised System of Classification and Labelling of Chemicals – GHS which came into force in EU in 2009;

– all the lists of maximum permissible concentrations shall indicate the belonging of substance to the reliable or suspended human carcinogene, that corresponds to the 1 and 2 groups of this classification;

– together with authoritative economists (in particular, from Lomonosov State Moscow University, Nuclear Safety Institute of the Russian Academy of Sciences, Kurchatov Institute, EMERCOM of Russia) it is necessary to develop the methodical document on the cost assessment of damages to human health based on the unified scientific principles.

In conclusion, it should be noted that currently the manual R 2.1.10.1920-04 still remains in Russia the single document which to the complete extent reflects the classical risk assessment methodology adopted by the international scientific society.

The "Health risk assessment manual" updated in accordance with modern international trends, developed by the work group and transferred for approval to Rospotrebnadzor in 2010 according to the established procedure focuses on the modern exposure factors, weightness of the scientific basis for the risk assessment methodology based on the evidence-based epidemiology and toxicology [10]. Only the quantitative risk criteria specified in the annexes shall be clarified.

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