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METHODOLOGICAL APPROACHES TO THE DEVELOPMENT OR HYGIENIC STANDARDS USING HEALTH RISK CRITERIA AND THEIR APPLICATION IN THE CASE OF AMBIENT AIR MANGANESE

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Abstract. Results of ambient air manganese hygienic standard development using health risk assessment approaches harmonized with international ones are presented. According to health risk level evolutionary modeling results as annual average ambient air manganese standard 0.00005 mg/m^3 was offered, as relevant critical effects – hypersensitivity reactions.
Key words: health risk assessment, evolutionary modelling, manganese, benchmark level.

The Russian Federation's participation in the WTO and the Customs Union within the Eurasian economic community makes optimizing the sanitary law, particularly, bringing the sanitary-hygienic standards of the environmental quality in accordance with the international standards, one of the top priorities.

Risk assessment today is the key element in setting up the environmental safety standards. It must be conducted based on a structured approach that includes hazard identification, exposition assessment, dose-response relationship evaluation and risk analysis [6, 8, 13].

According to Canadian Environmental Quality Guidance, Canadian Council of Ministers of the Environment [8], the air quality standards are developed based on the following principles: the standards set for air pollutants shall not create public hazard; the standards shall be developed

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for a believable exposure scenario; a critical effect for health shall be determined with the account for the most sensitive population groups; the standards shall be credible and feasible.

In the Russian Federation, the maximal one-time and daily average maximum permissible concentrations are used as they hygienic standards for the pollutants in the air. Those standards do not fully represent the inhalation effects from the chemicals throughout one's life and thus may not be used for the purposes of health risk assessment which in its turn requires the use of the quantities that take into account the safety of life-long exposure. Specific standards for the Russian Federation that may be used in risk assessment can be obtained after setting-up risk-based standards with annual averaging.

In accordance with an internationally acknowledged risk assessment methodology at the state of hazard identification with the use of a set of criteria, a priority pollutant is selected which is later used to determine a risk-based standard for the air pollutant concentrations. The developed criteria for the determination of the priority air pollutants under chronic inhalation exposure include the differences between the standard values in the Russian Federation and in other countries; the data about the toxic and hazard levels of chemical components including cancer potential; being included in the international and national lists of priority pollutants; the data about the abundance in the environment [7].

At the stage of exposure assessment, the agent enters the body with the air in a determined quantity in real-life conditions [6, 13]. The next stage of the risk assessment procedure is evaluation of the 'exposure-response relationship which includes empirical determination of the relationship between the exposure of the chemical under study and organ/system dysfunction, with the account for its intensity [6, 13].

When assessing non-cancer health risks under chemical exposure, it is possible to use various paired-comparison mathematical models included in the guidelines and recommendations of the leading international organizations (WHO, OECD, etc.) or in the published research papers (EPA, ATSDR etc.). If no 'exposure-response' model is available, it is possible to use the results of specialized epidemiological studies.

When modelling 'exposure-response' relationships for non-cancer risk assessment purposes, a liminality principle is used according to which negative health effects are displayed starting from the reference level. In the course of the study, we had several hypotheses about the relationship between the exposition of different levels and the development of health disorders; at that, the population group under the exposure below the level under study was considered the control group, and above the level under study – the experimental group. For each of the hypotheses, we tested the relationship in terms of odd ratio; its value served as a basis for the

mathematical relationship model of the 'chemical concentration in the air – odd ratio'. For the reference level of the air pollutant, we used a value that corresponded with the 95% confidence limit of the built model.

Additionally, in order to evaluate the 'exposure-response' relationship, it is also possible to use multiple evolutionary models that reflect the impact of chemicals on the incidence of health disorders depending on the age and length of exposure and taking into account the accumulation of functional disorders due to natural causes. Determination of the risk-based standard value for the air chemical is conducted based on the reference level and the uncertainty factor (UF). The value of the uncertainty factor is determined with the account for a possible impact on the reliability of evaluation of a number of factors. When selecting the values of the uncertainty factor components, the following is recommended to be accounted for: intraspecific extrapolation; propagation of the data obtained in the conditions of relatively short-term exposure to longer exposure; effect on the growing organism; extrapolation from one route of entry to another, transfer from a minimum database to a full database, etc. [5, 13].

At the stage of risk description, we conducted the assessment of risk acceptability to health using the atmospheric air quality standards. When developing risk-based atmospheric air quality standards in the Russian Federation in accordance with the internationally approved risk assessment procedure at the stage of hazard identification based on the ab chemical ove selection criteria, manganese was included in the list of priority chemicals for the risk-based air quality standardization.

The choice of manganese for the development of risk-based standards is explained by significant differences in the values of manganese regulation for the atmospheric air under chronic exposure in the Russian Federation and abroad. Analysis of the current hygienic standards of the air levels of manganese used in Russia and abroad showed the differences both in the methodology of their determination and the values of those indicators. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) recommends that the MRL of manganese (Minimal Risk Level) equal – 0.00004 mg/m3[14].

According to the WHO (1999) [9], the recommended air level of manganese is 0.00015 mg/m3. Additionally, a group of researchers including M. Egyed and G.C. Wood (1996) [11] recommend that the normative air level of manganese equal 0.0001 mg/m3. The U.S. Environmental Protection Agency sets the recommended air level of manganese and its compounds at 0.00005 mg/m3 [10]. As for REL (Reference Exposure Level), the Office of Environmental Health Hazard Assessment recommends that the value equal 0.0002 mg/m3.

According to GN 2.1.6.1338–03 [1], the value of Threshold Allowable Concentration TACcc, set for the developed effects, manganese and its compounds in the RF, equal 0.001 mg/m3.

Additionally, manganese is included in the International ATSDR list of hazardous substances and the sampling plan within the socio-hygienic monitoring system of a number of the RF subjects. To assess exposure, we used the estimated data on air pollution in an industrial town in the points of residence of each child approximated based on the results of instrumental research [2]. The range of levels of manganese in ambient air in the area of residence of the group under study totaled from 0.000014 to 0.00022 mg/m3.

The reference levels of manganese in ambient air were determined based on a cross-sectional epidemiological study that included 382 children aged 3-7 residing in an industrial town. The level of health in that group was assessed based on a multi-year data on medical referrals.

We reviewed nosological activities as responses when modelling the 'manganese level in ambient air – chance ratio' relationship, including representatives of the three classes of diseases by MKB-10 (V - mental and behavioral disorders; VI – diseases of the nervous system; X – diseases of the respiratory system), corresponding to the critical organs and systems for the conditions of chronic inhalation exposure to manganese [6]. Moreover, since manganese is a proved allergy-causing agent, we took into account the respective health effects, including nosological, when modelling the 'manganese level in ambient air – chance ratio' relationship [12, 14].

In the process of mathematical modelling, we developed and evaluated 29 models of 'manganese level in the ambient air – chance ratio' relationships. As most appropriate for the objectives of the study, the following models and values of the reference levels were selected: for sleep disorders (G 47) – 0.00009 mg/m3; atopic dermatitis (L 28.0) – 0,00008 mg/m3; increase in the absolute number of eosinocytes – 0,0002 mg/m3, increase in the number of general IgE – 0,00004 mg/m3. By criteria of the limiting indicator, the reference level of manganese in ambient air may be equal 0.00004 mg/m3.

However, uncertainties related to the presence in the ambient air (in the area under study) of a number of pollutants that have synergetic effect with manganese have a considerable impact in the reliability of results of epidemiological studies used to determine the reference levels. In order to minimize the uncertainties when determining the values of risk-based standards of the levels of manganese in ambient air, we created a risk evolution model, which is considered one of the most adequate methods used to predict and assess potential environmental impact on public health [3].

Within this study, the health risk evolution model was built with the use of a linear non-threshold model, calculation of a coefficient that reflects the impact of the factors on the intensity of risk accumulation, and determination of the levels of manganese in ambient air corresponding to the risk magnitude below 0.05 which is considered small to negligible (acceptable, permissible), not different from the regular everyday risk [4].

Based on the results of the mathematical modelling of risk evolution for atopic dermatitis as a specific response for manganese in the conditions of chronic inhalation exposure, the level at which the health risk is small to negligible totaled 0.00005 mg/m3. The level of 0.00005 mg/m3 for manganese in ambient air may be considered inactive and used for the subsequent determination of risk-based standard of the ambient air quality. Calculation of the final value of risk-based standard of ambient air quality for manganese is conducted with the use of the inactive level determined on the basis of evolutionary modelling and cumulative uncertainty coefficient [5].

For this type of study, we reviewed the following uncertainty factors:

– uncertainty factor that accounts for the cross-species extrapolation – 1, as we used an inactive level obtained in the result of the epidemiological study;

– uncertainty factor that accounts for the intraspecific extrapolation – 1, as we studied the impact on a sensitive group (children aged 3-7);

– uncertainty factor associated with the transition of the study results from the high levels of exposure to the low levels – 1, as the study was conducted in the conditions of real-time exposure.

Consequently, the value of the quality standard of ambient air determined on the basis of the health risk assessment totals 0.00005 mg/m3; the critical effect for manganese – allergic reactions. The obtained results correspond with the ones of the US EPA.

Therefore, the principle activities aimed at bringing together the sanitary-hygienic standards of environmental quality in the RF with the international standards include the development of risk-based standards that take into account the annual averaging period with the use of epidemiological research methods.

These new approaches were tested when determining the risk-based standards of the level of manganese in ambient air. The approaches will be widely used to improve the hygienic standards in the Russian Federation.

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