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METHODOLOGICAL APPROACHES TO HEALTH RISK ASSESSMENT UNDER EXPOSURE TO CHEMICAL, PHYSICAL AND BIOLOGICAL FACTORS TO DETERMINE PRODUCT (GOODS) SAFETY INDICATORS

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Abstract. The publication focuses on the principle algorithm and methods to assess consumer products safety in terms of public health. The methodology is based on a standard risk assessment procedure including the following stages: hazard identification, exposure assessment, dose-response assessment, and risk characterization. The key feature of the developed approaches is the use of mathematical modeling to describe risk development based on the adjustment of paired 'factor (exposure) – response" relationships obtained in the course of epidemiological studies for the purposes of risk escalation assessment. A dynamic model of functional disorders associated with product safety is a mathematical description of the process of change in the state of health of consumers under long-term exposure to product-related hazardous factors combined with natural ageing.

The publication describes approaches to the assessment of cumulative risk associated with various product factors, suggests risk structuring techniques and an internationally harmonized risk assessment scale. The methodology is universal, aimed for a wide range of objectives, and serves the purposes of the Customs Union.

The methodology was tested when validating food product safety criteria in assessing the risks associated with such long-use products as furniture, construction and finishing materials.

Keywords: consumer products, health risk, risk development.

In pursuance of the Agreement of the Customs Union for a coordinated policy in technical regulations, sanitary and phytosanitary measures which determines food safety as 'absence of unacceptable risk' (Article 3), and the Decision of the Customs Union Commission on equivalence of sanitary, veterinary or phytosanitary measures and conduct of risk assessment, where health risk is regarded as a criteria for an adequate level of public sanitary and phytosanitary protection (Article 6), we developed and tested the methodological approaches to consumer health risk assessment.

The approaches take into account and further develop international methodological tools presented in the global standards, CODEX Alimentarius Commission, EU guidelines, etc. [1, 6, 7, 10-13]. In addition to the methods recommended by the international organizations, the suggested approaches take into account development (evolution) which is important in the context of long-term consumption of the same product (e.g. furniture) or systematic repeated use

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of one-type product (e.g. same brand milk and flour, same brand cleaning products, etc.).

Methodological approaches may be used for assessing and preventing potential damage (harm) to consumer health; marking the products as 'risk-bearing'; determining requirements to product marking; making decisions regarding recall or withdrawal of products; making other management decisions to minimize product-related risks.

The target of risk assessment is any product including products included or planned to be included in the Product Classifier for Foreign Economic Activities of the Customs Union subject to the Customs Union technical regulations and Common Sanitary, Epidemiological, and Hygienic Requirements to Goods.

The methodology described below expands the scope of the current approaches and allows assessing health risks under simultaneous exposure to heterogeneous product-related factors (chemical, biological, and physical), determining the risk structure, and identifying time and age periods when a risk level may undergo and qualitative change (grow from low to moderate, from moderate to high, etc.). It also takes into account multiple responses and accumulation of health disorders over time. The algorithm underlying the suggested methodology is fully harmonized with the common equivalent, and regardless of kind and type of product, health assessment for all the product types follows the standard stages: exposure assessment, dose-response assessment, and risk characterization (Figure 1).

Hazard identification for a specific type of products is conducted in accordance with the technical regulation requirements, based on the technical documents on the products, test protocols and/or special measurements, studies, tests, information about the product risk factors that can be found in the internationally acknowledged databases, reports, and relevant sources of scientific literature. Expert evaluation of the sources of information and data by the criteria of accuracy, completeness and relevance to the study tasks is mandatory.

When identifying the consumer group, it is necessary to be guided by the associated documents, scientific reports and sociological study results. Vulnerable population groups require special attention (Table 1).

Exposure scenarios, routes of entry and points of contact of the consumer and the product-related health risk factors are formed on the basis on the analysis of the full range of most possible exposure route and those that have the shortest path to injury. A scenario-forming path in terms of health risk assessment for the product category "Toys" is presented in Figure 2.

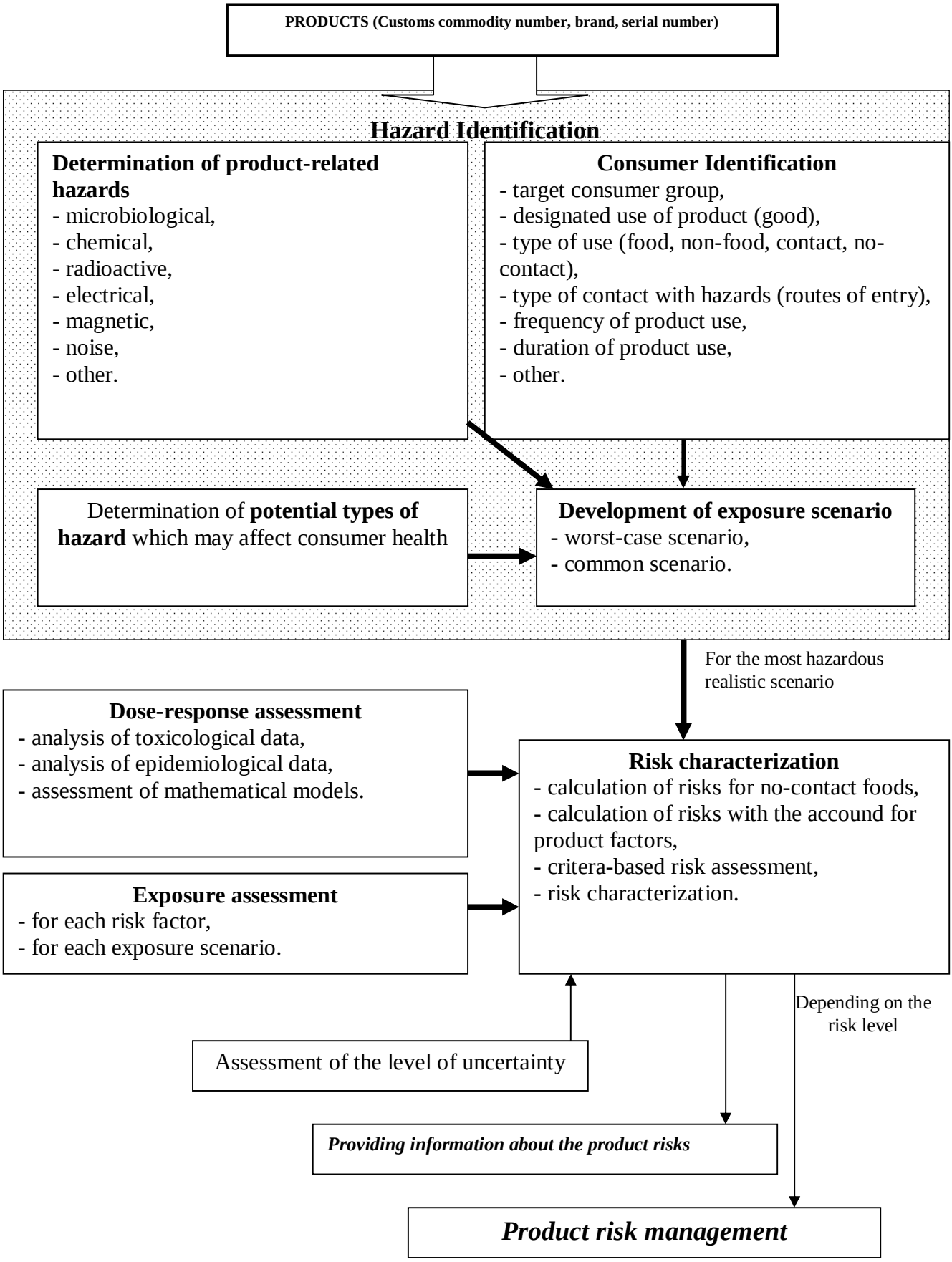

Figure 1. General health assessment scheme for product-related risks

Table 1

Consumer Groups

Consumer groups	Description
Very vulnerable consumer groups	Small children (aged 0-3) Disabled people with 1-2 class disabilities Pregnant and nursing women
Vulnerable groups	Children aged 3-14 Physically or mentally disabled persons People with a weak immune system Adults aged 65 and up People with no product experience
Other consumers	Consumers that do not fall under the first two categories

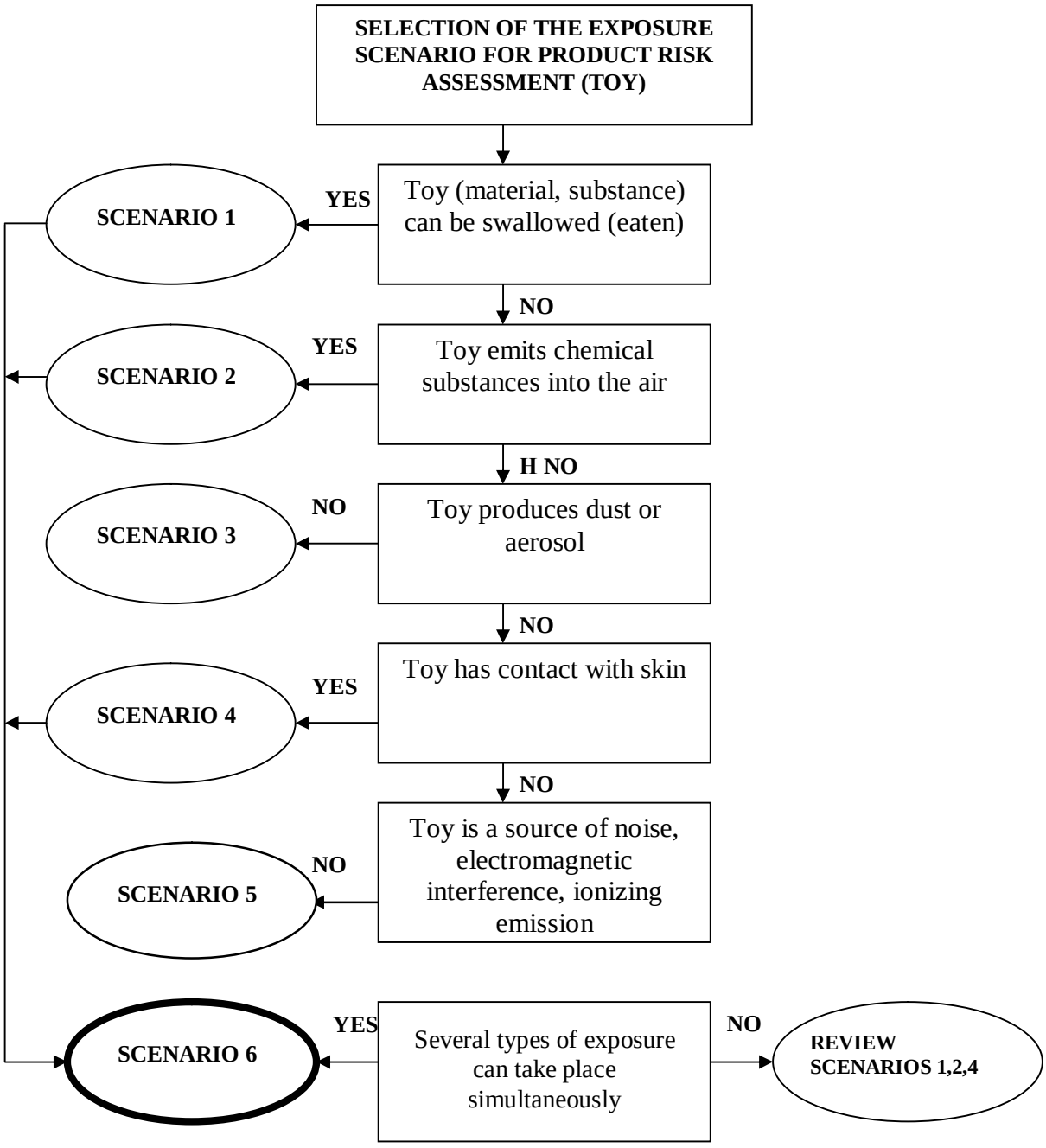

Figure 2. Selecting exposure scenarios when assessing product-related risks (toy)

For each of the identified chemical, biological and physical hazard factor, it is necessary to establish possible health disorders which may be caused by the product. At this stage, the method suggests that all the available relevant information be used about the "exposure-response (effect)" relationships in the form of adequate mathematical models and product safety criteria. It is suggested that the results of the toxicological studies be used on animals, in clinical and epidemiological studies (the latter are a bigger priority) reflected in the recognized databases including ATSDR, IRIS, monographs and scientific reports by the international organizations ((WHO, IPCS, EFSA, Codex Alimentarius Commission); publications and scientific peer-reviewed magazines, etc.

The evolutionary model of health risk accumulation (evolution of risk of functional and system disorders) when using the product is a mathematical description of the process of change in the state of consumer health under exposure to hazardous product-related factors in the course of an extended period of time.

The evolution of functional and system disorders in people is caused by the following mechanisms: natural disorders related to cell damage in organs, and risk accumulation due to non-standard exposure to product-related factors.

The estimated form of an evolutionary model is a system of recurrent relations registered for each type of response (health effect) [2, 4]. The general recurrent relation is presented below (1):

$$R_{t+1}^{i} = R_{t}^{i} + (a_{i} R_{t}^{i} + \sum_{j} \Delta R_{t}^{ij}) C, \qquad (1)$$

where

R_{t+1}^{i} – health disorder risk for the i-th response at the moment of time t+1;

R_{t}^{i} – health disorder risk for the i-th response at the moment of time t;

a_{i} – coefficient that takes into account risk evolution caused by natural reasons; ,

ΔR_{t}^{ij} – health disorder risk growth for the i-th response, created by the j-th factor in the period of 1 year from the time moment t;

C – time empirical factor.

The time empirical factor can be used when running the calculations with the time interval of less than 1 year. The factor values for different time intervals range from 0,000114 for the interval 1 hour to 1.0 for the interval 1 year

Health disorder risk growth caused by product-related factors is calculated using the following paired relations (2) [4]:

$$\Delta R_t^{ij} = b_{ij} f^{ij}(X_t^j), \qquad (2)$$

where

ΔR_t^{ij} – health disorder risk growth for the i-th response caused by the j-th factor during 1 year from the time moment t;

b_{ij} – coefficient that reflects the power of impact of the j-th factor that is typical of the product on the risk growth rate of the i-th effect (response);

$f^{ij}(X_t^j)$ – function that reflects the relation between the exposure to the j-th factor (X_t^j) and health disorder risk for the i-th effect (response);

X_t^j – exposure to the j-th factor at the moment of time t.

The evolutionary model of consumer health risk growth is built with the use of couple relations identified during 'dose-response' assessment. A specific shape of function $f^{ij}(X_t^j)$ and the values of the factors b_{ij} may be different for each 'factor – effect (response)' pair due to differences in action mechanisms and model building methods.

To build a recurrent equation, it is necessary to use established paired models of the 'dose–effect' relation identified during 'dose-response' assessment. To do that, equation (1) for the pair 'factor-effect (response)', omitting i, j, can be written in the form of a differential equation (3):

$$\frac{dR(t)}{dt} = a \times R(t) + b \times f(X), \qquad (3)$$

where

$R(t)$ – relation between the health effect (response) risk and time t;

a – coefficient that accounts for risk evolution due to natural causes;

b – coefficient that reflects the power of impact typical of the product on risk growth rate;

$f(X)$ – function that describes the law of impact of the factor typical of the product on risk growth rate;

X – level of the factor typical of the product.

The adapt the formalized "factor-effect (response)" relation, the standard form of which is presented by the function, $f(X)$, it is necessary to define a multiplier b that brings the results of evolutionary modelling to the relations obtained in the course of the studies.

The algorithm for finding unknown coefficient b is based on the following statement: health disorder risk growth under exposure to a factor of the level X defined by the function $f(X)$ is formed in the period of time $[t_1, t_2]$, corresponding to the factor exposure time. Then the equation (7.1) will have an analytical solution, with the help of which the expression that defines coefficient b can be presented in the following form (4):

$$b = \frac{\left(\frac{f(X)}{f(X_0)} - 1\right) \times R(t_0) \times \left(e^{a \times t_2} - e^{a \times t_1}\right)}{e^{a \times t_0}} \Big/ f(X) \times \left(\frac{\left(e^{a \times t_2} - e^{a \times t_1}\right)}{e^{a \times t_0} \times a} - (t_2 - t_1)\right), \quad (4)$$

where

b – coefficient that reflects the power of impact of the factor typical of the product on risk growth rate.

$f(X)$ – function that describes the law of impact of the factor typical of the product on risk growth rate

X – level of the factor typical of the product;

X_0 – background or standardized level of the factor in relation to which risk growth is calculated in the given data;

$R(t_0)$ – health disorder risk at the starting moment of time;

t_0 – starting moment of time;

a – coefficient that takes into account risk evolution due to natural causes;

t_2 – ending time of factor exposure;

t_1 – starting time of factor exposure.

Function (4) is universal and oriented at arbitrary functions. Special cases of functions have singularities when conducting the adaptation procedure. In publications, dose-response

assessment is most often conducted on the basis of linear models including threshold and non-threshold.

Examples of adaptation of paired models to the tasks of evolutionary modelling are presented in Table 2.

The coefficients that take into account risk evolution due to natural causes (αi) are defined based on the background indicators of disease incidence and death rate for the disease classes (in the event of non-cancer risk) and individual nosologies (when assessing carcinogenic effects) that reflect functional disorders of critical organs and systems.

Identification of the parameters of the models of disorder risk growth due to natural processes in a human body is conducted on the basis of statistical data on the disease incidence with the account for the severity of the disease and the death rate among adults.

Application of risk evolution modelling provides an opportunity at later stages to conduct an integral assessment of health risks and characterize the product as a source of various risk factors, also – to evaluate risk growth during the use of the product including for various consumer groups.

It is noteworthy that the assessment of microbiological risk stands alone when using the described method. For the microbiological hazard factor, “dose-response” assessment is included in the hazard identification stage. When assessing “exposure-response” relations for the biological factors, it is important to analyze susceptibility of the population groups to the negative biological factors of the hazardous product, ensure the necessity of assessment(when using the results of laboratory tests) of the sources and methods of preparation of the material that comprises pathogens; take into account the changeability and virulence of the agent in the course of interaction with a susceptible organism and the environment; estimate the probability of impact of the biological agent on people with different immune systems; estimate the opportunity to preserve the microorganisms in the source, factors of the infectious agent transfer; use statistical models that show the relations between the dose, virulence and manifestations (type, severity) of the responses among susceptible population groups, with the account for routes of entry.

In practice, researchers use models based on non-threshold assessment of a case of infection (provided that even one microorganism can cause an infection) and models with an established threshold – criteria of minimal infecting doses of microorganisms that can cause a disease in a susceptible organism.

Poisson-Weibull distribution models are considered the most effective in the analysis of the “dose-response” relation when assessing microbiological risks.

Table 2

Examples of paired mathematical models that meet the above requirements and adapted dependency models for recurrent ratios

Model	Base model	Source	Dependency model for the recurrent ratios
Non-cancer risk of cardiovascular disorders from noise exposure	Development of non-specific effects: $R = \frac{1}{\sqrt{2\pi}} \times \int_{-\infty}^{P} e^{\frac{y}{2}} dy$, where $P = -4,551 + 0,0853x_0$	[22]	$\Delta R = 0,015 \times \left\langle \frac{X}{58,5} - 1 \right\rangle$
Non-cancer risk of respiratory disorders from nitrogen dioxide in the air	$\Delta R_{\text{ñëó÷àéâ}} = -\left[9,33E - 6 \times \left(e^{-0,00318 \times \Delta NO_2} - 1\right)\right]$	[8]	$\Delta R = 0,36 \times \left\langle e^{-0,000151} - e^{-0,00378 \times X} \right\rangle$
Non-cancer risk of respiratory disorders from ozone in the air	$\Delta R_{\text{ñëó÷àéâ}} = -\left[2,58E - 5 \times \left(e^{-0,00498 \times \Delta O_3} - 1\right)\right]$	[8]	$\Delta R = 0,36 \times \left\langle e^{-0,000149} - e^{-0,00498 \times X} \right\rangle$
Non-cancer risk of cardiovascular disorders from lead, received perorally	$\left[1/\left(1 - e^{2,744 - 0,793 \times \ln(Pb)}\right) - 1/\left(1 - e^{2,744 - 0,793 \times \ln(0,03)}\right)\right]$	[9,19]	$\Delta R = 0,004367 \times \left(\frac{1}{1 + \exp^{2,744 - 0,793 \times \ln\left(5,6 + 2,62 \times \sqrt[3]{X}\right)}} - \frac{1}{1 + \exp^{2,744 - 0,793 \times \ln\left(5,6 + 2,62 \times \sqrt[3]{0,03}\right)}} \right)$
Non-cancer risk of cardiovascular disorders from arsenic, received perorally	Disease risk is 2.51 times higher under exposure to arsenic in water at the concentration of 0.025 mg/l.	[17]	$\Delta R = 0,00037334 \times \left\langle \frac{X}{0,0003} - 1 \right\rangle$
Risk of gastric cancer under exposure to strontium at the level-90, received perorally	Under one-time exposure to the dose 0.1 Sv – life-long risk totals 81 additional cases of gastric cancer (per 100 thous.)	[21]	$\Delta R = 2,8 \times 10^{-8} \times 0,71 \times 10^{-4} \times X$
Risk of bladder cancer under exposure to cesium at the level-137, received perorally	Under one-time exposure to the dose 0.1 Sv – life-long risk totals 81 48 additional cases of bladder cancer(per 100 thous.)	[21]	$\Delta R = 1,3 \times 10^{-8} \times 0,55 \times 10^{-4} \times X$

Model	Base model	Source	Dependency model for the recurrent ratios
Risk of salmonellosis under exposure to Salmonella Typhi, received with food products	Equation – Poisson distribution $P = 1 - \left(1 + \frac{x \times \left(2^{\frac{1}{b_1}} - 1\right)}{b_2}\right)^{-b_1}$, where P – probability of disease; x – received dose of bacteria; Parameters of the equation: $b_2 = 1110000$; $b_1 = 0{,}175$.	[15], [20]	No risk accumulation, risk in the event of daily exposure: $R = 1 - \left(1 + \frac{X \times \left(2^{\frac{1}{0{,}175}} - 1\right)}{1110000}\right)^{-0{,}175}$
Risk of listeriosis under exposure to Listeria monocytogenes, received with food products	Equation – exponential model $P = 1 - e^{-b_1 \times x}$, where P – probability of disease; x – received dose of bacteria. Parameters of the equation: $b_1 = 5{,}6 \times 10^{-10}$.	[11]	No risk accumulation, risk in the event of daily exposure: $R = 1 - e^{-5{,}6 \times 10^{-10} X}$
Risk of nephrolithiasis under exposure to melamine, received perorally	Disease risk increases by 10% with a melamine dose of 0.74 mg/kg per mass unit	[13]	$DR = 6{,}19 \times 10^{-8} \times \left\langle \frac{X}{0{,}2} - 1 \right\rangle$

Undoubtedly, accurate exposure assessment is a very important stage of risk assessment; it helps to define the measure of contact of an organism with a hazardous product factor, i.e. determine the measured of calculated amount of the agent in contact with the borderline organs (lungs, digestive tract, skin, etc.).

The data on the intensity of the factor is obtained in the course of targeted instrumental measurements, calculations, when analyzing technical documents on the product, scientific reviews, reports, reference books, with no data.

The frequency of impact and possible duration of the use of a specific type of product are assessed based on the results of specialized studies or literature, statistical material, results of sociological surveys, information about the product characteristics, its operating life, standards of consumption, etc. For example, the data on children's contact with the toys provide information that can be used to develop various scenarios of impact and validate the parameters for health risk assessment (Table 3).

Table 3

Examples of data on the duration (and frequency) of the products in use (toys) [8]

Children's age (months)	Product	Duration of peroral 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 teethers, rattles	0,19	0,44	1,69	4,4
	Teethers, toys 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, teethers, rattles	0,02	0,1	0,2	1,0
	Игрушки, teethers, rattles made of hard plastic	0,56	1,8	5,6	18
24 - 36	Soft plastic	0,07	0,21	0,7	2,1
	Soft plastic, teethers, rattles	0,02	0,01	0,2	0,4
	Toys, teethers, rattles made of hard plastic	0,21	0,94	2,1	9,4

It is noteworthy that in Russia, the studies that provide similar data are rather rare and thus are very on demand, especially in the sphere of non-food products.

The procedure of health risk assessment related to product use based on evolutionary models suggests that the calculation results be compared with risk under zero exposure to the active factors (or with their values equal to the reference level) – background risk. Risk evolution is calculated separately for each of the groups of responses (non-cancer, carcinogenic, microbiological). Here health risks obtained for each of the responses are summed up (integrated) using the following formula (4):

$$R_t^{Int} = 1 - \prod_{i=1}^{r} \left(1 - R_t^i\right), \quad (4)$$

where

R_t^{Int} – value of the integrated risk for each of the effect (response) groups at the moment of time t;

r – number of individual effects (responses) in each group caused by the factors related to the product use;

R_t^i – health disorder risk for the i-th response at the moment of time t.

Additional health risk associated with the product factors is calculated for individual effects (responses) (5):

$$\Delta R_t^i = R_t^i - R_t^{i/\hat{o}}, \quad (5)$$

where

ΔR_t^i – additional risk for the i-th effect (response) at the moment of time t;

R_t^i – health disorder risk for the i-th response at the moment of time t;

$R_t^{i/\hat{o}}$ – background health disorder risk for the i-th response at the moment of time t.

Additional integrated risk for each of the effect (response) groups is calculated based on the following formula (6):

$$\Delta R_t^{Int} = 1 - \prod_{i=1}^{r} \left(1 - \Delta R_t^i\right), \quad (6)$$

where

ΔR_t^{Int} – additional integrated risk at the moment of time t;

r – number of individual effects (responses) in each of the groups caused by the product-related factors;

ΔR_t^i – additional risk for the i-th effect (response) at the moment of time t.

To assess the level of non-cancer risk, it is necessary to calculate the reduced health risk index associated with the factor impact - for each of the modelled time intervals, for each effect (response) (7):

$$\%R_t^i = \frac{\Delta R_t^i}{1 - R_t^{i/\hat{o}}}, \quad (7)$$

where

R_t^i – reduced health risk index for the i-th effect (response) at the moment of time t;

ΔR_t^i – additional risk for the i-th effect at the moment of time t;

$R_t^{i/0}$ – background health disorder risk for the i-th response at the moment of time t.

To assess the integrated non-cancer risk, it is necessary to calculate the integrated reduced health risk index using the following formula (8):

$$R_t^{Int} = \frac{\Delta R_t^{Int}}{1 - R_t^{Int/0}}, \quad (8)$$

where

R_t^{Int} – integrated reduced health risk index at the moment of time t;

ΔR_t^{Int} – additional integrated risk at the moment of time t;

$R_t^{Int/0}$ – integrated health disorder risk under zero exposure to product factors (or with the factor values at the no-effect level), obtained using the following formula (4): $R_t^{Int/0} = 1 - \prod_{i=1}^{x} \left(1 - R_t^{i/0}\right)$.

Reduced risk index describes the probability of a health disorder under exposure to the product-related factors with the account for the total health risk accumulation under growing duration of exposure. The risk levels are categorized based on the assessment scale for reduced indices

R_t^i, R_t^{Int}, which serves as a basis for developing guidelines for managing product-related health risks (Figure 3).

At the level of less than 0.05, the risk is considered low to negligible with little effect on consumer health. This risk level does not require mitigation measures. There are no restrictions on the product in terms of health risk criteria.

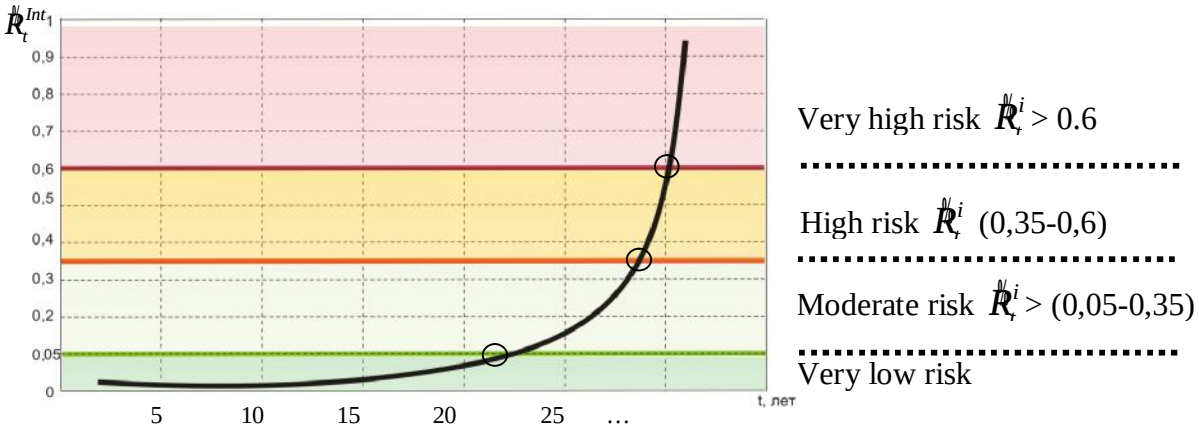

Figure 3. Assessment scale for risk characterization (in terms of reduced health index)

At the level $\tilde{R}$ of 0.05-0.35, the risk is considered moderate (average) risk. The product characterized with such risk level must be accompanied with informational material about possible hazards and health risk. Manufacturers may be recommended to lower the hazard level in the planned products (brands, series).

At the level $\tilde{R}$ of 0.35-0.6, the risk is regarded as high. The product may fall under the category of risk-bearing supply and must provide customers with information about the associated risks. In some cases, it can be decided to limit the production and/or use of the product.

The level $\tilde{R}$ of 0.6 and up is regarded as very high. The product falls under the category of risk-bearing supplies. Consumers and other interested parties must be informed about the product-related risks. The product can be recalled.

The suggested approaches were tested during the validation of food product safety [3,5,24]. Used in the establishing of the safety standards for food products, they helped support the joint position of more than 60 countries, including the EU, China, Russia etc. on the prohibition of meat products that contain ractopamine. It was found that ractopamine consumed with food products, in residual amounts recommended by the Codex Alimentarius Commission, with the account for the volume of real consumption, leads to the impermissible life-long risk of cardiovascular diseases ($\tilde{R}$=0,47) and reduction in life expectancy. Continuous consumption of meat with residual amounts of ractopamine creates a moderate risk of digestive disorders in people aged 28-30, and a high risk in people aged 66-67.

Restrictions on the use of some pre-fabricated buildings structures made of harmful health-risk bearing materials were made - applied for temporary stay of people. It was proven

that the risk groups included pensioners who were under exposure of more than 16 hours a day. Permanent residence in homes with elevated levels of formaldehyde provides them with moderate levels of risk within 3 years, and high levels - in 6-8 years.

As a result, it was decided to re-settle about 180 residents

Among other restrictions related to health risk management, it was decided to limit the period of use of some types of school furniture. The assessment of respiratory risks in children revealed that the maximum of 14 tables of the investigated brand could be put in one room not to exceed the safety level.

This data was taken into account for the product labelling: putting 1 item in a room of less than 16.5 m3 can lead to a moderate risk of respiratory diseases in children.

Overall, the suggested method based on the general principles of risk assessment tested and acknowledged by the international researchers provides additional opportunities for risk analysis method. It is still necessary to further improve the approaches and tools in the sphere of product safety for consumer health, including:

· Converging various scientific and methodological approaches to the assessment and management of consumer health risks;

· Improving the system of registration and accounting for the data on cases of consumer injuries;

· Developing available relevant databases on the mathematical “does-response” models with the account for various ages of consumers, with the integration of information systems and databases of Russia into the information systems of other countries;

· Sharing the experience and having discussions on the practice on consumer health risk assessment and management under exposure to various product-related hazardous factors.

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