PREVENTIVE HEALTHCARE: TOPICAL ISSUES OF HEALTH RISK ANALYSIS

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Research article

MODERN APPROACHES TO THE ASSESSMENT AND CLASSIFICATION OF THE HAZARD POSED BY SUBSTANCES WITH MUTAGENIC EFFECTS

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There are no lists of chemicals with mutagenic effects in the Russian Federation and in the states of the Eurasian Economic Union. Therefore, within the framework of the program 'Development of integrated approaches to testing, assessing hazards and risk of exposure to chemicals for human health and improvement of the evidence base of toxicological research results' (deadlines: 2024–2025), the Russian Register of Potentially Hazardous Chemical and Biological Substances – Branch of F.F. Erisman Federal Scientific Center of Hygiene of the Rospotrebnadzor has completed several work tasks concerning selection of substances with mutagenic effects, assessment and classification of their hazard.

Data available in international legislation, documents issued by the United Nations structures, scientific articles, monographs, and official national and foreign databases were analyzed in order to identify candidate substances with genotoxic/mutagenic effects and to form their toxicological profiles to assess the degree of hazard. Classifications of potential mutagens were based on the principles stated in the Globally Harmonized System of Classification and Labeling of Chemicals and Mixtures.

Selection of substances, assessment and classification of hazards is a complex process that requires in-depth analysis of the entire set of obtained data. An approach based on the principles of a step-by-step comprehensive assessment and classification of hazards posed by chemicals with mutagenic effects made it possible to scientifically substantiate and form a national list of mutagens. This list was employed as the basis for a number of normative and methodological documents, including Methodological Recommendations 'Assessment and Classification of the Hazard of Mutagens', appendices to the Procedure for creating and maintaining a register of chemicals and mixtures of the Eurasian Economic Union Technical Regulations 'On Safety of Chemical Products' (TR EAEU 041/2017), as well as the draft national Technical regulation 'On safety of chemical products'. The official status of the mutagen list will contribute not only to making relevant management decisions but also to resolving disputes arising between the business community and regulatory authorities due to differences in interpretation of research results.

Keywords: *mutagen, mutagenic effect, classification, toxicity, hazard, chemical safety, regulation, exposure risk.*

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Creation of national lists of supertoxicants is an effective tool applied to provide chemical safety. Such lists contain carcinogens, mutagens, reproductive toxicants and endocrine disruptors and are widely used in international legislation to ensure relevant decision-making aimed at minimizing risks of exposure to hazardous chemicals at every stage of their life cycle [1–5].

The Russian Register of Potentially Hazardous Chemical and Biological Agents – the branch of the F.F. Erismann's Federal Scientific Center for Hygiene of Rospotrebnadzor has developed lists of reproductive toxicants and endocrine disruptors. They were used as grounds for methodical guidelines approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing[1] as well as the Technical Regulations of the Eurasian Economic Union 'On Safety of Chemical Products' (TR EAEU 041/2017) and the RF National Technical Regulations 'On Safety of Chemical Products'[2]. As for carcinogens, the list of chemicals that are labeled as carcinogens by the International Agency for Research on Cancer (IARC) is included into SP 2.2.3670-20 'Sanitary-Epidemiological Requirements to Working Conditions'[3]. Meanwhile, current regulations in the Russian Federation and other EAEU states do not contain any lists of chemicals with mutagenic effects.

Therefore, **the aim of this study** was to select chemicals with mutagenic effects and to provide scientific substantiation for approaches to assessing and classifying their hazards in order to create an appropriate national list of mutagens.

Materials and methods. Data available in international legislation[4], documents issued by the United Nations structures, scientific articles, monographs, the Russian Register of Potentially Hazardous Chemical and Biological Agents[5] and other official national and foreign

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[1] MR 1.2.0321-23. Otsenka i klassifikatsiya opasnosti reproduktivnykh toksikantov: metodicheskie rekomendatsii, utv. Rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom Rossiiskoi Federatsii 04.04.2023 [Assessment and classification of hazards posed by reproductive toxicants: Methodical guidelines, approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the Chief Sanitary Inspector of the Russian Federation on April 04, 2023]. *KonsultantPlus*. Available at: https://www.consultant.ru/document/cons_doc_LAW_467057/ (October 16, 2024) (in Russian); MR 1.2.0313-22. Otsenka i klassifikatsiya opasnosti endokrinnykh razrushitelei: metodicheskie rekomendatsii, utv. rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom Rossiiskoi Federatsii 30.12.2022 [Assessment and classification of endocrine disruptors: Methodical guidelines, approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the Chief Sanitary Inspector of the Russian Federation on December 30, 2022]. *GARANT: information and legal support*. Available at: https://base.garant.ru/407868127/ (October 16, 2024) (in Russian).

[2] TR EAES 041/2017. O bezopasnosti khimicheskoi produktsii: Tekhnicheskii reglament Evraziiskogo ekonomicheskogo soyuza, prinyat Resheniem Soveta Evraziiskoi ekonomicheskoi komissii ot 3 marta 2017 g. № 19 (ne vstupil v silu) [TR EAEU 041/2017. On the Safety of Chemical Products: Technical Regulations of the Eurasian Economic Union, approved by the Decision of the Council of the Eurasian Economic Commission on March 3, 2017 No. 19 (has not come into force so far)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/456065181 (October 16, 2024) (in Russian).

[3] SP 2.2.3670-20. Sanitarno-epidemiologicheskie trebovaniya k usloviyam truda: sanitarnye pravila, utv. Postanovleniem Rukovoditelya Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom Rossiiskoi Federatsii A.Yu. Popovoi 2 dekabrya 2020 g. № 40 [Sanitary-Epidemiological Requirements to Working Conditions: sanitary rules, approved by A.Yu. Popova, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the Chief Sanitary Inspector of the Russian Federation on December 2, 2020 No. 40]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/573230583?ysclid=m2bi4g8n3t775683371 (October 16, 2024) (in Russian).

[4] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. *European Union: an official website*. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008R1272 (October 16, 2024); Candidate List of substances of very high concern for Authorisation. *ECHA: European Chemicals Agency*. Available at: https://echa.europa.eu/candidate-list-table (October 16, 2024).

[5] Federal'nyi registr potentsial'no opasnykh khimicheskikh i biologicheskikh veshchestv [The Russian Register of Potentially Hazardous Chemical and Biological Agents]. *The Russian Register of Potentially Hazardous Chemical and Biological Substances – the branch of F.F. Erisman Federal Scientific Center of Hygiene of the Rospotrebnadzor*. Available at: https://www.rpohv.ru/online/ (October 15, 2024) (in Russian).

databases were analyzed in order to identify candidate substances with genotoxic/mutagenic effects and to form their toxicological profiles to assess the degree of hazard. Classifications of potential mutagens were based on the principles stated in the Globally Harmonized System of Classification and Labeling of Chemicals and Mixtures[6] [6–10].

Results and discussion. More than 20 tests have been developed and validated by international expert society to assess genotoxicity. They make it possible to identify whether a chemical factor is able to damage genetic material in cells thereby inducing certain mutations. There is not any universal test that allows assessing a chemical's ability to induce various mutations in germ and somatic cells; therefore, a set of tests is usually employed involving use of different test objects under *in vitro* and *in vivo* conditions [11–13]. We analyzed toxicological profiles of candidate chemicals to be included into a national list. This allowed us to identify priority tests aimed at investigating mutagenicity relying on their informative value, representativeness and reproducibility of test results. Table 1 provides the ultimate list of selected tests.

Practice has shown that selection of research techniques has significant influence on levels of representativeness reached in assessment of potential genotoxicity. Attention should be paid to uncertainties that typically occur when research results obtained in animal experiments are extrapolated to humans. In case analyzed data are controversial, it is necessary to search for confirmation that a chemical can really affect a target organ (actual toxicity manifestations, carcinogenic effects included) [13, 16–17].

The principle of stage-by-stage research is recommended by international organizations for mutagen assessment.

The first stage is accomplished prior to making a decision whether it is advisable to conduct any research. It involves assessing all available data on effects produced by an analyzed chemical on humans and animals. The assessment should rely on using official information sources; the priority ones are provided in Table 2.

The second stage involves assessing data obtained by creating models using Structure – Property qualitative and quantitative ratios. It includes analysis of substances with similar structures and biological effects. The QSAR Toolbox system developed by OECD experts is a promising tool eligible for predicting mutagenic effects [18–20]. To introduce predictive systems into Russian practical prevention toxicology, the Branch has issued two manuals, General Manual on Prediction of Chemical Toxic Properties[7] and Prediction of Mutagenic Effects Produced by Chemicals[8].

At the first and second stages, an expert is able to officially use data on chemical hazards and risk assessment accumulated by the international scientific society. An analog approach, which was successfully used in the Soviet Union to create safety standards, is widely employed nowadays to predict chemical hazards.

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[7] Obshchee posobie po prognozirovaniyu toksicheskikh svoistv khimicheskikh veshchestv [General Manual on Prediction of Chemical Toxic Properties]: manual. Moscow, The Russian Register of Potentially Hazardous Chemical and Biological Substances – the branch of F.F. Erisman Federal Scientific Center of Hygiene of the Rospotrebnadzor, 2023, pp. 1–307. Available at: https://www.rpohv.ru/files/QSAR.pdf (September 29, 2024) (in Russian).

[8] Prognozirovanie mutagennogo deistviya khimicheskikh veshchestv [Prediction of Mutagenic Effects Produced by Chemicals]: manual. Moscow, The Russian Register of Potentially Hazardous Chemical and Biological Substances – the branch of F.F. Erisman Federal Scientific Center of Hygiene of the Rospotrebnadzor, pp. 308–378. Available at: https://www.rpohv.ru/files/QSAR.pdf (September 29, 2024) (in Russian).

Table 1

Priority tests to investigate mutagenicity

OECD test No.[9]	Name	Type	Test organism (species)	Metabolic activation	Research principle
471	The Ames test – assessment of bacterial reverse mutations	*in vitro*	1) *Salmonella typhimurium* 2) *E. coli*	+S9/ –S9	Detects reverse mutations in analyzed strains that allow microorganisms to synthesize a certain amino acid [14]
476	Assessment of gene mutations in mammalian cells *in vitro* using Hprt and xprt genes	*in vitro*	Mammalian and human cell cultures (mouse lymphoma cell line L5178Y, cell lines CHO, AS52, V79 of the Chinese hamster; human lymphoblast cell line TK6 and others	+S9/ –S9	Detects gene mutations induced by chemicals
490	Gene mutations assays using mammalian cells *in vitro* and the thymidine kinase locus	*in vitro*	Mammalian and human cell cultures (mouse lymphoma cell line L5178Y, human lymphoblast cell line TK6)	+S9/ –S9	Detects gene mutations induced by chemicals
473	The chromosomal aberration test in mammals *in vitro*	*in vitro*	Mammalian and human cell lines or primary cell cultures (the Chinese hamster fibroblasts, human and mammalian peripheral lymphocytes and others)	+S9/ –S9	Reveals factors that induce structural chromosomal aberrations (chromatid and chromosomal) in cultivated mammalian cells
474	The mammalian erythrocyte micronucleus test	*in vivo*	Mammalians, predominantly mice and rats /erythrocytes/	no	Identifies chemicals that induce cytogenetic damage which results in the formation of micronuclei containing lagging chromosome fragments or whole chromosomes
478	Genetic toxicology: the dominant lethal test on rodents	*in vivo*	Rodents (mice, rats) /germ cells/	no	Assesses embryotic or fetal death
489	The Comet Assay using mammalian cells *in vivo*	*in vivo*	Mammalians, predominantly mice and rats /somatic cells/	no	Detects and measures DNA strand breaks in eukaryotic cells [15]

Table 2

Recommended official information sources eligible for collecting data on effects of chemicals

No.	Name	Available at
1	Database of the Russian Register of Potentially Hazardous Chemical and Biological Agents	www.rpohv.ru
2	Automated Distributed Information Retrieval System 'Hazardous Chemicals'	www.rpohv.ru
3	European Chemicals Agency's (ECHA) Dissemination portal with information on chemical substances registered under REACH	https://echa.europa.eu

[9] Organisation for Economic Co-operation and Development (hereinafter OECD).

End of the Table 2

No.	Name	Available at
4	The Global Portal to Information on Chemical Substances (eChemportal)	www.echemportal.org
5	Toxicity Forecasting database (ToxCast)	https://www.epa.gov/chemical-research/exploring-toxcast-data
6	Guide R.2.1.10.3968-23 Health Risk Assessment upon Exposure to Chemical Pollutants in the Environment / approved by the Order of the RF Chief Sanitary Inspector on September 06, 2023	
7	QSAR Toolbox OECD Database	https://qsartoolbox.org
8	Integrated Risk Information System (IRIS) (US EPA)	https://www.epa.gov/iris
9	IARC monographs on the identification of carcinogenic hazards to humans	https://monographs.iarc.who.int/
10	GESTIS Substance Database	https://gestis-database.dguv.de/
11	Toxicity Reference Database (ToxRefDB)	https://www.epa.gov/system/files/documents/2022-04/281_toxrefdb-2-0-mini-slides-23aug2021_508-final.pdf
12	Canadian Centre Occupational Health and Safety, Registry of Toxic Effects of Chemical Substances (CCOHS RTECS)	https://www.ccohs.ca/products/rtecs
13	Hazardous Substances Data Bank (HSDB), US National Library of Medicine	https://pubchem.ncbi.nlm.nih.gov

The third stage involves investigations (tests) *in vitro* using variable test objects including bacteria, mammalian germ and / or somatic cells.

If necessary, investigations (tests) *in vivo* are conducted at the fourth stage.

Hazard-based classification of chemicals is performed in conformity with the GHS requirements [4, 8].

Classification of hazards includes three stages:

– Identification of the relevant data concerning the hazards of the chemical;

– Subsequent analysis of these hazards in order to assess them;

– A decision whether it is advisable to classify the chemical as hazardous and to establish the degree of its hazard by comparing the obtained data with the approved criteria of hazard classification [3, 8].

Making a decision on assigning a chemical to a certain hazard category is a complicated procedure that requires comprehensive analysis of all obtained data. It can often involve even greater difficulty due to the inconsistency of research findings reported in different publications. International organizations and expert societies who deal with chemical safety are trying to work out an accurate and transparent mechanism for making a decision on hazard classification relying on relevant research methods.

Mutagens are usually assigned to one of two hazard categories.

Within hazard category 1, mutagens are divided into two subcategories:

– category 1A is established by epidemiological studies (heritable mutations in human germ cells);

– category 1B is established in animal studies *in vivo* (heritable germ cell mutagenicity in mammals); or *in vivo* (somatic cell mutagenicity in mammals with some supporting evidence) or mutagenic effects in human germ cells without demonstrations of transmission to progeny [4, 8].

We analyzed information provided in toxicological profiles of more than 700 candidate chemicals that might be included into the national list of mutagens. The analysis established that none of them could be classified as hazard category 1A mutagen due to absence of any epidemiological / clinical data.

Four hundred and thirty-one chemicals (431) chemicals were classified as hazard category 1B mutagens, as a rule, based on several positive results obtained by *in vivo* tests (using mammalian germ and somatic cells) as well as by *in vitro* studies (using germ cells of a test object). In addition, data on carcinogenic effects of the chemical are taken into account when classifying its hazard. Table 3 provides an example of classifying a hazard category 1B chemical considering its carcinogenic effects. Positive results were obtained for 4,4′-Oxydianiline in *in vitro* studies using germ and somatic cells; however, multidirectional effects were established by *in vivo* studies: a statistically significant increase in frequency of micronucleated polychromatic erythrocytes was established by the OECD test 474 but the OECD test 486 established absence of unplanned DNA synthesis in rat hepatocytes. Simultaneously, IARC ranks this chemical as 2B carcinogen based on detected development of liver cancer in rats and mice upon various administration ways. This allowed classifying the chemical as hazard category 1B mutagen.

Table 3

Classification of hazard posed by 4,4'-Oxydianiline per mutagenic effects

<table>
<tr><td colspan="3">4,4'- Oxydianiline (CAS 101-80-4)</td></tr>
<tr><td>Acute toxicity parameters</td><td>Test type</td><td>Test results</td></tr>
<tr><td rowspan="5">DL_{50} 570 – 725 mg/kg, oral, rats
DL_{50} 685 mg/kg, oral, mice
DL_{50} 700 mg/kg, oral, rabbits
DL_{50} 650 mg/kg, oral, guinea pigs
DL_{50} > 2500 mg/kg, dermal, rabbits
DL_{50} 365 mg/kg, intraperitoneal, rats
DL_{50} 300 mg/kg, intraperitoneal, mice
DL_{50} 650 mg/kg, intraperitoneal, rabbits</td><td rowspan="3">in vitro</td><td>test 1:250, 500, 1000, 2500, 5000 μg/plate and test 2: 10, 25, 50, 100, 250 μg/plate, S. typhimurium TA 1535, TA 1537, TA 98 and TA 100, the metabolic activation system being present, a considerable growth in mutation frequency in strains TA 1535, TA 98 and TA 100 (OECD test 471 result is positive)</td></tr>
<tr><td>50, 100, 160, 500, 1000, 1600, 2000, 3000 μg/ml, the metabolic activation system being absent, and 160, 500, 1000, 1600, 2000, 3000, 4000, 5000 μg/ml, the metabolic activation system being present, Chinese hamster ovary cells (CHO) as a test object; a considerable growth in chromosomal aberration frequency in CHO cells (OECD test 473 result is positive)</td></tr>
<tr><td>5; 16; 50 μg/ml, the metabolic activation system being absent, and 160, 500, 1600, 2000, 3000, 4000, 5000 μg/ml, the metabolic activation system being present, Chinese hamster ovary cells (CHO) as a test object; a considerable growth in frequency of sister chromatid exchange in CHO cells (OECD test 479 result is positive)</td></tr>
<tr><td rowspan="2">in vivo</td><td>37.5; 75; 150 mg/kg, intraperitoneal, 3 days, mice as test objects; a statistically significant growth in frequency of micronucleated polychromatic erythrocytes (test 474 result is positive)</td></tr>
<tr><td>40; 180; 725 mg/kg, oral, single dose, rats as test objects; exposure did not result in unplanned DNA synthesis in rat hepatocytes (test 486 result is negative)</td></tr>
<tr><td>Available data
on carcinogenic effects</td><td colspan="2">IARC materials contain sufficient data on carcinogenic effects to animals; the chemical is labeled as 2B. Upon long-term intragastric exposure, both benign and malignant hepatocellular tumors as well as benign and malignant follicular thyroid tumors are detected in rats and mice; subcutaneous exposure led to multiple malignant liver tumors (hepatocellular tumors and cholangiocarcinomas)</td></tr>
<tr><td colspan="3">Hazard category 1B</td></tr>
<tr><td colspan="3">Substantiation for classifying the chemical as having hazard category 1B: the classification is based on the results obtained by three positive in vitro tests performed on bacteria and somatic cells, the metabolic activation system present and absent, and one positive in vivo test as well as IARC data on confirmed carcinogenicity to animals</td></tr>
</table>

Note: oral means oral route of administration; dermal, dermal route of administration; intraperitoneal, intraperitoneal route of administration.

Two hundred and twenty-six chemicals (226) chemicals were labeled as having the hazard category 2. The hazard category 2 should be given to chemicals with mutagenic effects confirmed by *in vivo* studies on mammalian somatic cells and (or) *in vivo* genotoxicity tests on somatic cells confirmed by positive results of *in vitro* mutagenicity tests. In addition, a chemical or a mixture can be classified as hazard category 2 mutagen in case positive results were obtained by *in vitro* tests on mammalian cells and *in silico* tests using QSAR Structure – Activity models.

Hazard category 2 is also assigned in case multidirectional results were obtained by *in vitro* and *in vivo* tests but there are available IARC data on carcinogenic effects (Table 4). Despite multidirectional results obtained by

Table 4

Classification of hazard posed by hydroquinone per mutagenic effects

Hydroquinone (CAS 123-31-9)		
Acute toxicity parameters	Test type	Test results
DL_{50} 320–1050 mg/kg, oral, rats DL_{50} 350 mg/kg, oral, mice DL_{50} > 2000 mg/kg, dermal, rabbits	*in vitro*	10; 33; 100; 333; 666 μg/plate, *S. typhimurium* TA 1535, TA1537, TA98, TA100, the metabolic activation system present and absent, mutagenic activity is absent (OECD test 471 result is negative)
		from 2 to 100 μg/ml for 3-hour treatment, from 5 to 15 μg/ml for 24-hour treatment and 10 μg/ml for 48-hous treatment, human lymphocytes as test objects, the metabolic activation system present and absent, no biologically or statistically significant increase in the number of cells with structural aberrations was detected in the test (OECD test 473 result is negative)
		Test concentrations associated with moderate or significant cytotoxic effects, chromosomal aberrations, micronuclei and sister chromatic exchange detected in mammalian cell cultures and human lymphocytes (OECD test 473, OECD test 479 results are positive)
		1.56; 3.12; 6.25; 12.5; 25; 50 μg/ml, the metabolic activation system being absent and 0.652; 1.25; 2.5; 5; 10 μg/ml, the metabolic activation system being present, mouse lymphoma cells L5178Y (OECD test 476 result is positive)
	in vivo	25; 50; 75 mg/kg, intraperitoneal, single dose, mice as test objects; an increase in frequency of micronucleated polychromatic erythrocytes (OECD test 474 result is positive)
		80 mg/kg, oral, single dose, mice as test objects; a slight increase in micronuclei quantities (OECD test 474 result is positive)
		30; 100; 300 mg/kg, oral, 10 weeks, rats as test objects; did not produce dominant lethality (OECD test 478 result is negative)
		40; 80; 120 mg/kg, intraperitoneal, single dose, mice as test objects; statistically significantly increased frequencies of aberrant cells (chromatide aberrations exclusive gaps) were observed in the mouse spermatocytes (OECD test 483 result is positive)
		25; 50; 100; 200 mg/kg, oral, 4 weeks, male mice as test objects; did not cause any significant increase in mutation frequency (OECD test 488 result is negative)
Available data on carcinogenic effects	IARC labeled the chemical as Group 3 (Not classifiable as to its carcinogenicity to humans). Data on carcinogenicity to animals are considered limited (oral administration resulted in growing number of esophagus and kidney tumors in rats and mice)	
Hazard category 2		
Substantiation for classifying the chemical as having hazard category: the classification is based on multidirectional results obtained by *in vitro* and *in vivo* tests as well as IARC data on limited confirmed carcinogenicity to animals		

Note: oral means oral route of administration; dermal, dermal route of administration.

in vitro and *in vivo* tests, hydroquinone is classified as hazard category 2 chemical based on positive results of *in vivo* studies performed on germ cells as well as data on carcinogenic effects on mice and rats upon oral administration (esophagus and kidney tumors).

If a chemical is classified as hazard category 1 carcinogen according to the GHS but no experimental data have been obtained for it as regards possible mutagenic effects, in this case it is recommended to classify such chemical as hazard category 2 mutagen [6, 7, 16].

A hazard category identified for a given chemical can be revised in case some new experimental data have been obtained concerning its mutagenic and (or) carcinogenic effects.

Limitations of the study. The classification does not cover medical preparations or active ingredients in pesticides and agricultural chemicals.

Conclusions. Comprehensive approach to selecting, assessing and classifying hazards of chemicals with mutagenic effects made it possible to provide scientific substantiation and create the national list of mutagens, which was included into draft methodical guidelines 'Assessment and Classification of Hazards Posed by Mutagens'. Implementation of the list into the methodical and regulatory base of the Russian Federation and Eurasian Economic Union will minimize risks of chemical exposure for human health and the environment, ensure transparency in decision-making and broad public awareness.

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Competing interests. The authors declare no competing interests.

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