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Research Article

Use of Predictive Systems in the Hazards Assessment of New Chemicals Under Notification Procedure

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Abstract

The implementation of the Russian Technical Regulation of the Eurasian Economic Union 041/2017 "On the Safety of Chemical Products" highlights the need to develop and validate alternative methods for assessing the hazard of new chemicals as part of their notification procedure. The objective of this study was to evaluate the possibility of using the QSAR Toolbox software of the Organization for Economic Co-operation and Development to predict toxicity and hazard indicators in accordance with the requirements of the Globally Harmonized System of Classification and Labelling of Chemicals in the framework of the notification procedure. The article analyzes the prognostic ability of the program in relation to assessment of acute toxicity, skin and eyes irritation, mutagenic effects, sensitizing, reproductive toxicity effects and acute toxicity to aquatic biota. Samples of chemicals with known experimental data were used to verify the forecasts. It was found that the accuracy of the forecast varies significantly depending on the estimated effect: the highest rates were achieved for estimation of skin sensitization when using profilers based on the Adverse Outcome Pathway concept (up to 75%), for acute toxicity to aquatic biota with respect to *Daphnia magna* (84%); acceptable accuracy - for acute toxicity with intragastric intake (70%) and for acute toxicity to fish (71 - 75%). It is shown that the Quantitative Structure-Activity Relationship Toolbox can be used as an effective tool at the initial stages of assessment. However, the forecast data obtained require experimental confirmation for hazard classification as part of the notification procedure for new chemicals, especially compounds beyond the scope of the model.

Keywords: *QSAR Toolbox; OECD Methods; Prediction of Toxic Effects; GHS; In Silico Methods; Notification; Technical Regulation*

Abbreviations

GHS: Globally Harmonized System of Classification and Labelling of Chemicals; OECD: Organization for Economic Co-operation and Development; QSAR: Quantitative Structure-Activity Relationship; TG: Test Guideline; AOP: Adverse Outcome Pathway; GLP: Good Laboratory Practice; ADISS: Automated Distributed Information and Search System "Hazardous Substances"; ECHA: European Chemicals Agency; EPA: Environmental Protection Agency; FDA: Food and Drug Administration; IPCS (INCHEM): International Programme on

Chemical Safety; GHS-J: GHS Classification by the Japanese Government; EAEU TR: Technical Regulation of the Eurasian Economic Union; LD_{50}: Median Lethal Dose; LC_{50}: Median Lethal Concentration

Introduction

In 2026, the Technical Regulation of the Russian Federation "On the Safety of Chemical Products" are expected to come into force, with the key regulatory aspects being the assessment of the safety of chemical products on the market and the need to notify new chemicals in accordance with the GHS criteria [1]. Until now, in the practice of domestic preventive toxicology, national criteria and research methods have been used to assess and classify product hazards, which differ significantly from the GHS approaches and OECD test methods [2].

In preparation for the implementation of the requirements of the Technical Regulation, the Scientific Information and Analytical Center "Russian Register of Potentially Hazardous Chemical and Biological Substances" of the F.F. Erisman Federal Scientific Center of Hygiene of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor), taking into account international experience and domestic practice, has developed methodological approaches to the assessment of chemicals with specific and long-term effects (carcinogenicity, mutagenicity, reproductive toxicity, sensitizing effects, effects on the endocrine system), which require priority regulation to minimize the risk of exposure to public health. Methodological approaches made it possible, for the first time in the Russian Federation, to scientifically substantiate national lists of endocrine disruptors, mutagens, reprotoxicants and sensitizers and to update the list of carcinogens, identify substances of priority for hygienic regulation and (or) the introduction of restrictive and prohibitive measures, taking into account these types of exposure [3-6]. The national lists were formed using an integrated approach to hazard assessment and classification, which is a scientifically based combination of *in silico, in chemico, in vitro*, and *in vivo* methods [7].

For many decades, *in vivo* research methods have been a priority in Russian preventive toxicology [2]. Currently, alternative research methods are becoming increasingly used, especially in assessing irritant effects on skin and eyes and mutagenic effects. As for *in silico* methods, they are widely used in the pharmaceutical industry to design active substances with specified pharmacological properties, but are practically absent in domestic preventive toxicology [8].

According to the inventory, there are approximately 80,000 chemicals on the Russian Federation market that must be evaluated and classified according to the Technical Regulation. Given the cost and duration of *in vivo* and *in vitro* studies, in some cases, *in silico* methods can be a useful tool for screening the toxicity and hazard of chemicals [1].

Objective of the Study

The objective of this study is to evaluate the possibility of using *in silico* methods to predict toxicity and hazard indicators in accordance with the requirements of the GHS as part of the notification procedure.

Materials and Methods

The study was performed using the OECD QSAR Toolbox software versions 4.4.1 - 4.8.2, the OECD guidelines for the assessment of acute toxicity, irritation effect, sensitizing effect, reprotoxic, mutagenic effects and acute toxicity for aquatic biota. The Microsoft Excel program was used for statistical processing of the obtained results.

To assess the predictive ability of the program, samples of chemicals were formed with known experimental data for each effect studied. The experimental data sources were databases: ADISS, ECHA, EPA, NITE, FDA, IPCS (INCHEM), GHS-J, OECD. The sample size varied from 30 to 100 substances, depending on the effect being studied, while substances of various GHS hazard classes and various chemical groups were included.

The criteria for the inclusion of substances in the samples were: the availability of experimental data obtained in accordance with the OECD TGs, the GHS classification, the chemical belonging to the group of organic compounds (due to the limitations of the program).

The accuracy of the forecast was assessed by comparing the values of indicators calculated by the program (quantitative or qualitative) with those experimentally established. The prognostic accuracy of the methods was assessed based on the available number of true positive (TP), true negative (TN), false negative (FN) and false positive (FP) results.

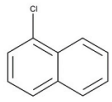
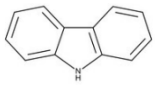
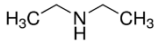
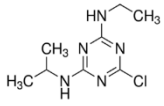
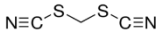
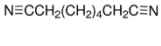
During the analog categorization procedure, after using specific profilers, non-specific ones were used, which were individually selected for each chemical substance, taking into account its belonging to the class of chemical compounds.

Results and Discussion

Acute toxicity

The initial stage of the toxicological assessment as part of the notification of new chemicals is the determination of acute toxicity parameters - LD_{50} for intragastric and cutaneous routes of administration and LC_{50} for inhaled routes of administration. These indicators form the basis for the classification and labelling of chemical products in accordance with the GHS.

The predictive ability of the QSAR Toolbox software in relation to acute toxicity in the intragastric route of admission was evaluated using the "Acute Oral Toxicity" profiler, developed on the basis of experimental *in vivo* LD_{50} data on intragastric admission to rats. The sample included amines, alcohols, heterocyclic compounds, etc. (there are about 50 substances in total). Table 1 presents some examples.

CAS	Name	Structural formula	LD_{50}, intragastric, rats	
			Experiment	Calculation*
90-13-1	1-Chloronaphthalene		1840-2200 (class 4) [25]	2040 (class 5)
109-06-8	2-Methylpyridine		790-1410 (class 4) [25,26]	734 (class 4)
86-74-8	Carbazole		>5000 (not classified) [25,26]	3830 (class 5)
109-89-7	Diethylamine		248-500 (class 3) [25]	203-541** (class 3)
1912-24-9	Atrazine		673-3000 (class 4) [25,26]	1850 (class 4)
88-75-5	2-Nitrophenol		330-4930 (class 4) [25,26]	648 (class 4)
6317-18-6	Methylene bis(thiocyanate)		55 (class 3) [25]	64,9 (class 3)
107-19-7	Propargyl alcohol		20-110 (class 2) [25]	62,8 (class 3)
629-40-3	Octandinitril		150-650 (class 3) [25,26]	360 (class 4)

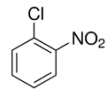
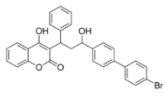
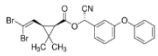
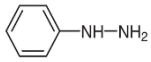
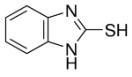
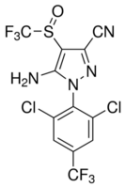
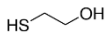
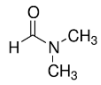
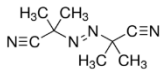
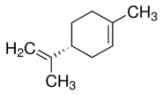
88-73-3	1-Chloro-2-nitrobenzene		144-560 (class 3) [25,26]	528 (class 4)
28772-56-7	Bromadiolone		0,49-1,12 (class 1) [25]	0,581 (class 1)
1453-58-3	3-Methylpyrazole		300-2000 (class 4) [25,26]	1040 (class 4)
52918-63-5	Deltamethrin		31-52 (class 2) [25]	111 (class 3)
100-63-0	Phenylhydrazine		188 (class 3) [25]	343 (class 4)
583-39-1	1,3-Dihydro-2H-benzimidazole-2-thione		208-300 (class 3) [25,26]	421 (class 4)
120068-37-3	Fipronil		92-97 (class 3) [25,26]	249 (class 3)
60-24-2	2-Mercaptoethanol		98-330 (class 3) [25,26]	96,2 (class 3)
68-12-2	N,N-Dimethylformamide		1504-5016 (class 4) [25,26]	1900 (class 4)
78-67-1	2,2′-Azobis(2-methylpropionitrile)		100-1150 (class 3) [25,26]	174 (class 3)
5989-27-5	(+)-Limonene		>2000 (not classified) [25,26]	5050 (not classified)
Note: The hazard class on the parameters of acute toxicity in accordance with the GHS criteria is indicated in parentheses. *Own computations obtained using QSAR Toolbox software versions 4.4.1 - 4.8.2. **Made on different analogues.				

Table 1: *Calculation of indicators of acute toxicity in the intragastric route of admission using the read-across method.*

The obtained LD_{50} value was assigned a hazard class in accordance with the GHS criteria, and the forecast accuracy was about 70%.

This profiler does not work with inorganic substances, organometallic compounds, polymers, and substances with metal ions, which narrows down the number of substances potentially available for analysis by the QSAR Toolbox program.

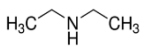
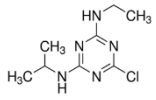
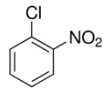
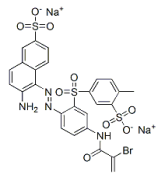
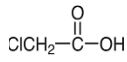
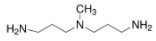
Similarly, the prognostic parameters of LD_{50} were evaluated when applied to rabbit skin irritation. The sample of chemicals was compiled in such a way that the experimental LD_{50} values were mainly in the range up to 2000 mg/kg. Due to the lack of specific profilers

included in the program, a combination of non-specific ones ("Acute Oral Toxicity", "Toxic hazard classification by Cramer", "Protein binding by OASIS") was used.

As a result of the calculations, the accuracy was 62%. The low accuracy of the forecast may be due to several reasons:

- Limited sampling of substances (substances that are known to have a corrosive effect on the skin and eyes and belong to hazard class 1 were not taken into account, since according to the GHS, LD_{50} parameters are not set for them with a cutaneous route of administration, a limited number of substances with pronounced acute toxicity with a cutaneous route of administration, substances with a wide range of applications were mainly considered);
- The difficulty of selecting a sufficient number of analogues with high structural similarity (more than 60%) with established experimental data;
- The absence of a specific profiler (the "Acute Oral Toxicity" profiler was used for calculations, built using LD_{50} data for the intragastric route of administration, the validity of its use in calculating indicators for the cutaneous route of administration is supported by established correlations).

Table 2 presents some examples.

CAS	Name	Structural formula	LD_{50}, cutaneous, rabbits	
			Experiment	Calculation*
109-06-8	2-Methylpyridine		252-410 (class 3) [25,26]	574 (class 3)
109-89-7	Diethylamine		580-628 (class 4) [25,26]	276 (class 3)
1912-24-9	Atrazine		7500 (not classified) [25,26]	2640 (class 5)
88-75-5	2-Nitrophenol		>7940 [25,26]	3220 (class 5)
107-19-7	Propargyl alcohol		16-88 (class 2) [25,26]	486** (class 4)
88-73-3	1-Chloro-2-nitrobenzene		355-450 (class 4) [25,26]	1900** (class4)
85187-33-3	Reactive Red 84		>3000 (not classified) [26]	4860 (class 5)
79-11-8	Chloroacetic acid		175-250 (class 3) [25,26]	141 (class 3)
105-83-9	3,3′-Diamino-N-methyldi-propylamine		126-209 (class 3) [25,26]	329-382*** (class 4)

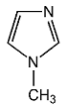
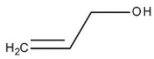
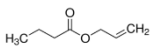
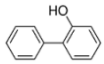
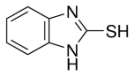
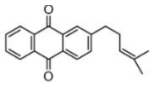
616-47-7	1-Methyl-1H-imidazole		400-640 (class 4) [25,26]	178-191*** (class 3)
107-18-6	Allyl alcohol		89 (class 3) [25,26]	320 (class 4)
2051-78-7	Allyl butyrate		530 (class 4) [25,26]	967 (class 4)
90-43-7	1,1'-Biphenyl-2-ol		>5000 (not classified) [25,26]	5240 (not classified)
4488-57-7	5,6-Dihydrodicyclopenta-diene		>2000 (not classified) [26]	3460 (class 5)
583-39-1	1,3-Dihydro-2H-benzimidazole-2-thione		>2000**** (not classified) [26]	2710-3000 1590**** (class 4)
71308-16-2	2-(4-methyl-3-pentenyl) anthraquinone		>2000 (not classified) [26]	9230 (not classified)
Note: The hazard class on the parameters of acute toxicity in accordance with the GHS criteria is indicated in parentheses. *Own computations obtained using QSAR Toolbox software versions 4.4.1 - 4.8.2; **Low structural similarity of analogues (20 - 30%); ***Depending on the selected analogues; ****Data for rats.				

Table 2: *Calculation of acute toxicity indicators for the cutaneous route of administration using the read-across method.*

The use of the QSAR Toolbox predictive system to calculate LC_{50} for the inhaled route of administration is currently problematic due to the lack of a specific profiler.

Thus, the prediction of acute toxicity by the intragastric and subcutaneous route of administration can be used as an auxiliary tool for the preliminary assessment and categorization of substances for the purpose of notification of new chemicals.

Irritating effect

When notifying chemicals within the framework of the Technical Regulation "On the Safety of Chemical Products" intended for use as raw materials for the production of exported perfumes and cosmetics, it is advisable to use alternative research methods in order to exclude animal testing. Due to the limited use of *in vitro* methods, the possibility of using *in silico* methods is being considered.

The prediction of the irritant effect on the skin was carried out using the profiler "Skin irritation/corrosion Inclusion rules by BfR", based on the experimental results obtained by the method of OECD TG No. 404 "Acute irritation/corrosion of the skin".

To calculate the indicators, a sample of chemicals classified by ECHA as Class 2 was used, as this category of substances presents the greatest challenges in data interpretation. Class 1 substances have a necrosis effect and are generally easy to classify, and the pH value (below 2.0 and above 11.5) can indicate a corrosive effect.

The following indicators were selected as the end points of the calculation: edema score; erythema score; skin irritation\corrosion. The scores obtained as a result of the calculations were compared with the scores of the irritating effect of the experiments (a deviation of +/- 0.5 points from the experimental value was considered acceptable). The forecast accuracy for both erythema score and edema score was 53%. When determining the presence or absence of an irritant effect, taking into account the reversibility of the effect, the accuracy of the forecast increases to 64,3%.

To calculate the indicators of irritation of the mucous membrane of the eyes, by analogy with the skin, a sample of chemicals classified as hazard class 2 in terms of irritant effect in accordance with the GHS was formed. The following parameters are selected as endpoints: conjunctivae score; chemosis score; iris score; cornea opacity score and eye irritation/corrosion.

The prediction of the irritant effect on the eye mucosa was carried out using the profiler "Eye irritation/corrosion Inclusion rules by BfR", based on the results of experiments obtained by the method of OECD TG No. 405 "Acute irritation/corrosion of the eyes".

The calculated scores were compared with the GHS criteria values for the irritant effect on the mucous membrane of the eye of hazard class 2.

The presence or absence of irritation was predicted with an accuracy of 65,4%. When assessing the irritating effect on the mucous membrane of the eyes, comparing calculated scores with experimental ones, the accuracy for conjunctivae score and chemosis score was 48%, for iris score 44%, for cornea opacity score 41%, due to limited laboratory data.

The predictive ability of the QSAR Toolbox to evaluate an irritant for notification purposes is currently limited; the program can only be used at the screening stage (presence/absence of an effect).

Sensitizing effect

Chemicals that cause skin sensitisation pose a risk to human health and are included in the list of indicators evaluated as part of the notification procedure for new chemicals. The OECD QSAR Toolbox software for calculating skin sensitization indicators implements the Adverse Outcome Pathway (AOP) scheme [22,23].

Each key event includes from one to four "key nodes" corresponding to a specific testing method. The interpretation of the results was carried out within the framework of the AOP scheme, where each key node combines a number of methods. The first node covers four *in chemico* methods, the second two *in vitro* methods (KeratinoSens and LuSens), and the third three *in vitro* methods for analyzing dendritic cell activity (h-CLAT, MUSST, and mMUSST).

A comparative analysis of the sensitizing potential of chemicals performed by the calculated method with data from experiments *in chemico* showed that the highest accuracy is observed for the methods:

- *In chemico* glutathione depletion analysis GHS (RC_{50}) - 55%;
- *In chemico* analysis of adduct formation LC-MS - 60%.

The low accuracy rates are explained by the limited experimental data accumulated by *in chemico* methods for assessing the sensitizing potential of chemicals, which makes it difficult to build correct models and select structural analogues for forecasting.

As a result of a comparative analysis of *in vitro* methods, the highest accuracy of the forecast was shown by:

- *In vitro* analysis of dendritic cell activity h-CLAT (CD86 expression) - 48,3%;
- *In vitro* analysis of dendritic cell activity MUSST (CD86 expression) - 57,7%;
- *In vitro* analysis of dendritic cell activity mMUSST (CD86 expression) - 61,1%.

When applying a combined approach to the assessment of the sensitizing effect using the AOR scheme integrated into the QSAR Toolbox software, the forecast accuracy increased to 70 - 75%.

The obtained results correlate with the data of the study, the authors of which analyzed the sensitizing potential of a number of anhydrides, peroxides, acids, phthalates, alcohols using *in vitro* methods (DPRA, KerationSens/LuSens, h-CLAT and U937-CD86/(m) MUSST) using the QSAR Toolbox [12].

Mutagenic effect

Taking into account the medical and social significance of the effects of exposure to chemicals with mutagenic effects, the study of genotoxicity/mutagenicity is extremely relevant.

There is no universal test for unambiguous assessment of the ability of a chemical compound to induce different types of mutations in germ and somatic cells, which makes it necessary to use a set of methods performed on different test objects *in vitro* and *in vivo*. The choice of research methods affects the representativeness of the assessment of potential genotoxicity. In order to reduce the number of experiments performed on animals, computational methods are being actively introduced into toxicological practice, including using the OECD QSAR Toolbox software.

In the course of studying the methodological documents of the OECD regulating the detection of the mutagenic activity of chemical compounds, a list of seven most commonly used methods was determined. These methods allow for the detection of genotoxic effects in various biological models, both in the presence and absence of metabolic activation.

The calculation results are presented in table 3.

OECD test number, name	Type of method	Profiler	Forecast accuracy*
OECD TG № 471 Bacterial Reverse Mutation Test; (Ames test)	*In Vitro*	"DNA alerts for AMES, CA and MNT by OASIS"	+S9 60% –S9 20%
		"*In vitro* mutagenicity (Ames test) alerts by ISS"	+S9 60% –S9 40%
OECD TG № 476 *In Vitro* Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes	*In Vitro*	"DNA binding by OASIS"	62,2%
OECD TG № 490 *In Vitro* Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase	*In Vitro*	"DNA binding by OASIS"	62,2%
OECD TG № 473 *In Vitro* Mammalian Chromosomal Aberration Test	*In Vitro*	"DNA alerts for AMES, CA and MNT by OASIS"	+S9 33,3% –S9 43,75%
		"Protein binding alerts for Chromosomal aberration by OASIS"	+S9 55,6% –S9 75%

OECD TG № 474 Mammalian Erythrocyte Micronucleus Test	*In Vivo*	"DNA alerts for AMES, CA and MNT by OASIS"	36%
		"*In vivo* mutagenicity (Micronucleus) alerts by ISS"	24%
OECD TG № 478 Genetic Toxicology: Rodent Dominant Lethal Test	*In Vivo*	"DNA binding by OASIS"	39,3%
OECD TG № 489 *In vivo* Mammalian Alkaline Comet Assay	*In Vivo*	"DNA binding by OASIS"	66,6%
Note: * Own computations obtained using QSAR Toolbox software versions 4.4.1 - 4.8.2			

Table 3: *Results of calculations of mutagenic effect indicators using the read-across method.*

The conducted research indicates that the prediction of mutagenic effects requires the integration of data from several profilers and consideration of the metabolic profile of substances.

Reprotoxic effect

Assessment of the reprotoxic effect is a mandatory component of the notification procedure for new chemicals [1]. The study of the effect on the reproductive system and developing offspring using the QSAR Toolbox program was carried out using the "DART scheme": chemicals with structural features that potentially have a reprotoxic effect are identified as analogues. The profiler is based on the principle of combining known modes of action and related structural features of chemicals, as well as empirical associations of structural fragments in DART chemical molecules.

To assess the reprotoxic effect, the QSAR Toolbox program analyzed chemicals with approved hazard classes (hazard classes 1 and 2) in accordance with the GHS. As a result of the analysis, the accuracy of the predicted values was 59.4%. The share of uncertain results is 37.5%. The high proportion of uncertain results is explained by the lack of a sufficient number of relevant analogues with the experimental data obtained or by the fact that the structure of the substance exceeds the limits of the applicability of the model.

Prediction of reprotoxic effects in the QSAR Toolbox can only be used as a primary screening tool. The high proportion of uncertain results and insufficient accuracy make it impossible to use this forecast for hazard classification within the framework of notification without experimental confirmation.

Acute toxicity to aquatic biota

Within the framework of the notification, the assessment of acute toxicity for aquatic biota is carried out on different test objects: fish, algae, and daphnia.

The calculation of acute toxicity indicators of chemicals (LC_{50} and EC_{50}) for aquatic biota using the OECD QSAR Toolbox software as part of the notification procedure for new chemicals was carried out using several procedures.

The automatic procedure (based on data on the octanol/water distribution coefficient) makes it possible to calculate the acute toxicity concentration LC_{50}, 96h for *Pimephales promelas*. The following profilers were used automatically for this type of calculation: "US-EPA New Chemical''; ''Acute aquatic toxicity classification by Verhaar''; ''Acute aquatic toxicity MOA by OASIS''; ''Aquatic toxicity classification by ECOSAR''; "Organic Functional Groups"; "Organic Functional Groups US-EPA"; "Organic Functional Groups by Norbert Haider". The calculated LC_{50} values were used to assign a hazard class to the chemical, and the results were compared with experimental data. The predictive accuracy of the LC_{50} calculation using the automatic procedure was 71%.

This procedure has limitations and is not applicable to inorganic substances, organometallic compounds, polymer molecules, chemicals containing metal ions.

When using a standardized procedure for grouping chemicals, specific profilers were used: "Aquatic toxicity classification by ECOSAR" and "Acute aquatic toxicity MOA by OASIS". The approach allows to calculate the predicted values for a larger number of test objects. According to the calculated values of LC_{50}, the hazard class of the chemical was assigned, after which the results were compared with experimental data. The predictive accuracy was:

- LC_{50} (EC_{50}), *Pimephales promelas*, 96h - 62,5%;
- LC_{50} (EC_{50}), *Actinopterygii*, 96h - 75%;
- EC_{50} (LC_{50}), *Branchiopoda*, 48h - 37,5%;
- EC_{50} (IC_{50}, LC_{50}), *Algae Chlorophyceae*, 72 - 96h, by weight - 25%;
- EC_{50} (IC_{50}, LC_{50}), *Algae Chlorophyceae*, 72 - 96h, by the rate of growth - 62,5%.

The low rates of acute toxicity of chemicals for algae and branchiopods are due to the small number of selected analogues with experimental data. The standardized procedure for calculating indicators of acute toxicity of chemicals for representatives of aquatic biota is not applicable for inorganic substances, organometallic compounds, polymer molecules, chemicals containing metal ions.

The prediction of LC_{50}, *Daphnia magna*, 48h, for chemicals was carried out by trend analysis using the profiler "Aquatic toxicity classification by ECOSAR". According to the calculated values of LC_{50}, the hazard class of the chemical was assigned, after which the results were compared with experimental data. The prognostic accuracy was 84%. The high indicator is explained by a large array of accumulated experimental materials, on the basis of which the values of the target chemical are calculated.

The prediction of acute toxicity for aquatic biota in the QSAR Toolbox demonstrates high efficiency for well-studied test objects such as *Daphnia magna* (84%) and some fish species (71 - 75%). However, for less studied taxonomic groups (algae, branchiopods), the accuracy of the forecast remains low, which requires either experimental confirmation or accumulation of additional data to expand the training samples. As with other effects, the program has limitations on the types of chemical compounds.

Conclusion

The conducted research has shown that the OECD QSAR Toolbox software can be considered as a useful tool for preliminary hazard assessment of new chemicals as part of the notification procedure under EAEU TR 041/2017, however, its use has a number of significant limitations and requires careful interpretation of the results. The accuracy of the forecast varies significantly depending on the estimated toxicological parameter. The effectiveness of the forecast directly depends on the availability of relevant structural analogues with high-quality experimental data. It is currently premature to classify and label chemicals according to the GHS hazard criteria.

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