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ON IMPLEMENTATION OF POPULATION LIFE QULITY ASSESSMENT INTO SOCIAL-HYGIENIC MONITORING SYSTEM

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The article dwells on grounds for implementing population life quality assessment into social-hygienic monitoring system; it also outlines some methodical approaches to such assessment. Certain techniques are now applied both in Russia and worldwide but the authors propose to update them by application of approaches oriented at life quality assessment as a combination of life quality potential (in a country, region, or a municipal district) and risks of a decrease in this potential. The suggested approaches allow both to calculate integral indexes and to fragment life quality potential and risks in order to solve managerial tasks. It is shown that social-hygienic monitoring system is able to provide informational, methodical, and analytical base for life quality assessment due to it being a state system that has long been accumulating medical-demographic, social-economic, sanitary-hygienic, and other data on Russian regions functioning.

Implementation of life quality assessment into social-hygienic monitoring system will require to improve and enhance interdepartmental interaction; to make each concerned party have greater interest in obtaining relevant and correct indexes of population life quality and separate components of its potential and risks; to include a substantial sociological component into systems of observations as it will help to assess people's satisfaction with their living standard in general and with its specific components; to develop and implement methodical support, as well as hardware and software for assessment of life quality including its separate components and to enlarge the information fund of social-hygienic monitoring; to develop skills of experts employed at Rospotrabnadzor's bodies and organizations who are responsible for formation of regional and federal information funds and for analytical data processing.

Key words: *social-hygienic monitoring, life quality, living standard, potential, integral index, risk.*

The tasks on improving life quality of Russians are considered as priorities in the Russian Federation strategy for national security [1]. At the same time, “life quality” is considered as an integral index of population satisfaction with the material, social and spiritual aspects of life [1, 2]. The strategy for national security assumes improvement of citizens life quality by ensuring food safety, scaling-up availability of comfortable housing, diversity and safety of goods and services, achieving a high level of education and healthcare, fare

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[1] On the Russian Federation’s National Security Strategy: Presidential Decree No. 683 ddt. 31.12.2015. *ConsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_191669/743474b198a4e9a6e9e181d9451aafc27185f735/ (access date: 22.06.2018) (in Russian).

wages and salaries, creating favorable living conditions, a wide network of accessible social, engineering and transport infrastructures for limited mobility people, etc.

In global practice, "life quality" is being considered in different ways. This term appeared in scientific literature in 1996, with reference of organs transplantation in the perception of patients. Inevitably, measures of "life quality" for a long time have been complied only with the purpose of analyzing medical care effectiveness [3, 4]. This practice still goes on at present, allowing doctors and researchers to evaluate effectiveness and efficiency of therapy according to a system of personal indices [5, 6]. At the same time, many authors recognize the need to take into account a significantly wider range of parameters characterizing population life quality [7–9].

In 2011, experts of Organization for Economic Cooperation and Development (OECD), having summarized multidirectional studies on life quality from economic, sociological, environmental and other points, suggested using the so-called "Better Life Index" [10]. The better life index includes 11 aspects: 1) income and material security; 2) employment and earnings; 3) housing; 4) state of health; 5) work and rest balance; 6) education and skills; 7) socialization; 8) involvement in public life and quality of government control; 9) environmental quality; 10) personal security; 11) perceptions of satisfaction with life. The first three aspects define material well-being, points 4–11: life quality of an individual. All aspects are described by one or two parameters, each, in turn, being represented by one or two indexes. All indexes become normal so that the best score for all countries is “1”, and the worst is “0”. After that, these indexes come to evaluation of the characteristics as the arithmetic average of their normalized values. Similarly, the levels of characteristics are aggregated to obtain a final score in each aspect. Russian Federation is also evaluated in terms of Better life index among other countries [11].

Not all national researchers consider such approach as adequate to the real situation in the Russian society [8]. However, despite the fact that the index chosen by OECD can be discussed, criticized, viewed as insufficiently correct for Russian Federation, it is necessary to take into account the global focus on these indexes, to evaluate parameters that lower Russia's rating, and strive to improve them.

In this regard, it seems relevant to systematically calculate and monitor the life quality index for the country as a whole, its certain regions and municipalities, as well as decomposition of this index into indices actually managed by the state and specifically by certain authorized executive bodies.

In recent years, various approaches to assessing life quality have been proposed, mainly for the rating tasks of Russian regions and cities [7, 12, 13]. The latter is due to the fact that the country as a whole and almost all its territories are interested in the influx of able-bodied population. In a complicated demographic situation in the country, many regions and cities declare an orientation towards the formation of a “health-saving” environment, considering the population high life quality as an important factor of competitiveness and attractiveness of any territory [14]. This trend is global, since population satisfaction with a living standard ensures social stability of a society, and is one of the conditions for the country's sustainable development [15].

In this regard, it appears that any assessments of the population life quality should not only be considered (and not so much) as means of comparing territories, but should be the tools for substantiating control actions, identifying the most acute problems requiring solutions and forming the most efficient and effective measures. Such approach is welcomed by many researchers. At the same time, life quality indexes are considered by some authors as criteria in evaluating government activities [16–18]

The Federal Service for Surveillance over Consumer Rights Protection and Human Well-Being ensures control over compliance with the mandatory requirements for a significant number of indexes that are components of life quality: parameters of habitat, infectious and non-infectious morbidity, working condi-

tions, educational process, etc. The Service monitors these indexes level in all regions of the country and performs an analysis of the effectiveness and efficiency of actions to control these indexes.

Socio-hygienic monitoring (SGM), implemented by Rospotrebnadzor, is a unique interdepartmental state system for collecting and analyzing various medical-demographic, epidemiological, ecological-hygienic and socio-economic data [19]. Currently, SGM Federal Information Fund has accumulated over 65 million units of information on the medical and demographic indexes of the regions over a long-term period, habitat parameters, socio-economic characteristics, etc. Versatility of the collected data, focus on ensuring health and sanitary-epidemiological well-being of the population, the state and interdepartmental nature of the system give SGM an opportunity to act as the basis for an integral assessment of the population life quality. At the same time, this system can be the basis for substantiating decisions on managing certain components of life quality, taking into account the functions and powers of Rospotrebnadzor or other authorities, business and civil society.

In general, the implementation of methods for assessing life quality in SHM will result in a significant expansion of the system analytical capabilities and an increased demand from the Government, civil society, other federal executive bodies, etc. At the same time, it seems reasonable to develop approaches that reflect situation in Russian Federation as closely as possible allowing for the global method of calculating life quality index. The latter will provide an opportunity to obtain the forecast estimates of the Russian Federation rank in global rating, and define measures to improve the country's status at the international level.

In this context, it is important that socio-hygienic monitoring system for many years solves problems of identifying the priority risk factors, including the ones that compromise life quality. Identification, quantification and structuring risk factors allows for better controllability in many social processes, forecasting trends in the indexes and taking preventive measures [20, 21].

In this regard, it seemed relevant to include risk assessment methods in the system of estimated indexes of the population life quality.

The purpose of implementing the population life quality assessment in the system of socio-hygienic monitoring is to provide public authorities, civil society, local governments, other stakeholders with the information and analytical data on the potential of population life quality and risks for deterioration of this quality as a basis for making management decisions at all levels.

The main principles of the system development as related to introducing life quality assessment methods into it are:

1) scientific validity of methodological approaches adapted to the realities in Russian Federation on effective management of the population life quality based on an assessment of the potential and risks for deterioration of life quality;

2) transparency and systematic assessments based on socio-hygienic monitoring data and the associated state and departmental statistics;

3) development of an analytical apparatus that enhances integrated assessment and evaluation of certain components of the potential and risks to life quality at the level of the country and its particular regions (municipalities);

4) transparency of the results for all stakeholders.

Due to the fact that achieving an effective management of environmental quality parameters is eventual provided only a clear targeting to the actions-focus object, the methodological basis for assessing life quality level can be the calculations of life quality potential indexes (in a country, region, city) parallel to the assessment of risks to the citizens life quality.

The general algorithm for assessing life quality level for management tasks and minimizing risks within the framework of social and hygienic monitoring system suggests:

- estimating life quality integral index potential in a territory (allowing for its decomposition to the level required to manage it);

- estimating risks for decline in life quality integral index (allowing for its decomposition to the level required to manage it);

- estimating general life quality level as a value that reflects both the potential and the risks associated with the population life quality;

- trends' analysis and comparative analysis of life quality index at the country, regional, municipal levels.

Monitoring the integral indexes and their certain components, and comparing the indexes periodically will allow for evaluation of the changes dynamics in the potential or risks in a territory, the effectiveness and efficiency of control actions.

The life quality potential reflects a system of indexes, the high level of which (the maximum approximation to the most favorable one, achieved in the country, or a target level, the presence of a pronounced tendency to improvement, etc.) enhances the population life quality. Potential is determined through the integral index, approximated to the "better life index", by the calculation method. For comparison of various characteristics measured in scales of different range and dimension, a relative non-dimensional indicator is determined, reflecting the approximation degree of an absolute index of a characteristic to the best (or target) index (1):

$$f_t^{\text{èíò}} = \frac{1}{N}\sum_{i=1}^{N}\frac{f_{it}}{f_{it}^{\max}}, \quad (1)$$

where $f_t^{\text{èíò}}$ is the integral index of the population life quality at the *t*-th territory; $f_{it}^{\max}$ is the maximum value of the *i*-th index for f_{it} among all the territories; N is the number of factors of a potential being taken into account

The value $f_t^{\text{èíò}}$ is considered as a potential for life quality.

The potential for life quality can be assessed as:

high, at $f_t^{\text{èíò}} \geq 0{,}8$,

average, at $0{,}6 \leq f_t^{\text{èíò}} < 0{,}8$,

low, at $0{,}4 \leq f_t^{\text{èíò}} < 0{,}6$,

extremely low, at $f_t^{\text{èíò}} < 0{,}4$.

Each object under assessment (country as a whole, its separate region, city, any other municipality) is characterized by each individual indicator (*fit*) and the integral index as a whole.

The ratio $f_{it}/f_{it}^{\max}$ characterizes the progress degree of the best (target) index in a territory; the ratio $(f_{it}/f_{it}^{\max})/f_t^{\text{int}}$ is the contribution of a specific group of indexes to the overall life quality index.

The list of indices that truly reflect the population life quality potential should include:

1) material well-being level of a household and/or an individual;

2) population employment and occupational safety;

3) availability of high-quality housing;

4) medical and demographic indices of a society;

5) work and rest balance;

6) level of education and leisure activities;

7) social binds;

8) involvement in public life and quality of government control;

9) environmental quality;

10) personal security;

11) perceptions of satisfaction with life.

If there are data on significance of certain life quality components for the population, the weighting factors can be established for each group of indices.

To obtain correct comparative assessments, all objects (countries, regions, municipalities) should be characterized by a single set of indices.

Calculation of life quality potential should include not only the static indices characterizing the current (or averaged over a given period) state of an object, but also the indices characterizing index dynamics (increase, decrease, rate of change, etc.)

Index decomposition allows you to identify priority problems and determine vectors of actions to improve population life quality. Within the framework of socio-hygienic monitoring, a comparative and (or) dynamic

analysis of life quality components can be performed, which includes interests of certain state (municipal) bodies authorized in a particular field of activity.

Risks that do not allow realize the potential of a territory in terms of population life quality are determined by the parameters characterizing the negative phenomena of social life as regard to violations of individual health, safety, living conditions, quality of environmental objects, etc.

Using the classical definition of risk, as the product of negative events probability and their consequences, the basic formula (2) for assessing risk of decrease in life quality is proposed:

$$R = \frac{1}{N} \sum_{i=1}^{N} p_i g_i , \qquad (2)$$

where p_i is the occurrence probability of a negative event or its frequency over a certain period of time (for example, a year); g_i is the severity of these events consequences in terms of their impact on life quality; N – the number of risk factors being considered.

The task to determine the severity of negative events consequences is exploratory in nature, and is aimed at formalizing causal relationships between the frequency of events and the population life quality of the regions, assessed by a special index or indexes system (3):

$$g_i = f(p_i, \Delta f_t^{\text{èíò}}) , \qquad (3)$$

where $\Delta f_t^{\text{èíò}}$ is the change in life quality index.

The resulting risk index for the rating scale is classified as

high at $R \geq 0{,}6$,
average at $0{,}3 \leq R < 0{,}6$,
low at $0{,}05 \leq R < 0{,}3$,
extremely low at $R < 0{,}05$.

The study of cause-effect relationships involves using systems analysis methods that allow determine main patterns for regional distribution of indexes that reflect life quality.

The source of information to assess probability of negative events that determine life quality is state statistical reporting, compiled by Federal State Statistics Service, the Ministry of Health of Russian Federation, Ministry of Internal Affairs, Ministry of Natural Resources and Ecology, Ministry of Education and other federal executive bodies whose data are accumulated in the hygienic monitoring.

The list of indexes that really reflect the risks to population life quality is formed for the same 11 groups, which determine the life quality potential. An example of the initial data that allows for assessment of the potentials and risks to life quality is given in Table 1.

Since the formula for calculating risk of loss (decrease) in life quality implies a summation of risks formed by different factors, the assessment of individual indexes or indexes groups' shares to the overall risk level characterizes signification of factors and allows for management priorities.

Cross-spectrum analysis of the potential and risk indexes allows us to draw conclusions about the general life quality level of a country's population, focusing on the objects of management (Table 2). Regions (territories) with high potential and low risks, i.e. the leading regions (cities), whose indexes should be looked up to, and whose experience should be adopted.

Regions (territories) with a high potential that can be formed by a high level of employment and wages of the population, growth of the domestic regional product and housing provision at the same time can be featured with high risks of medical and demographic losses due to climatic peculiarities of the subject, population aging, adverse environmental or sanitary epidemiological situation, etc. In these cases, an analysis of life quality assessment results should provide guidance for developing risk management activities.

Table 1

Examples of indexes accumulated in SHM systems for assessing life quality potential and its decrease risks

Life quality potential index	Data source	Risk factor for life quality	Data source
Life expectancy at birth	Federal State Statistics Service (Rosstat). Predictions by calculations method for "Life expectancy at birth (years)" index	Total mortality	Rosstat. Form C51 “Distribution of the deceased by sex, age groups and causes of death in the specified year”.
Share of economically active population of a territory in the total population (country, region, etc.)	Rosstat Tables 1ВСН-П "Population size by sex and age, as of January, 1st of the specified year"; FIF SHM, Section 1. “Medical-demographic indexes	Adult mortality excluding deaths of retirement age people	Rosstat Form 1-У “Information on the deceased”, Rosstat Tables 1ВСН-П "Population size by sex and age, as of January, 1st of the specified year"; FIF SHM, Section 1. “Medical-demographic indexes”
		Share of people working in contact with harmful and adverse factors of occupational environment and labor process	FIF SPM, Table 8.2 "Number of people working in contact with harmful and adverse factors of occupational environment and labor process by type of factors per economic activity"
Share of population provided with drinking water	Federal State Statistics Service. Ф-18 "Information on sanitary condition of the subject of the Russian Federation"	Percentage of drinking water samples studied that do not meet sanitary and epidemiological requirements	Federal State Statistics Service. Ф-18 "Information on sanitary condition of the subject of the Russian Federation"
Number of living space per person (m2/person)	FIF SHM. Section 3 "Information on social and economic status of a territory"	Share of dilapidated and emergency housing	Federal State Statistics Service. Calculations method for "Share of dilapidated and emergency housing in the total amount of housing stock of a constituent entity of the Russian Federation" index

Table 2

Matrix for determining population life quality level as a combination of potential and risks parameters

Potential index	Risk			
	Extremely low	Low	Moderate	High
High	High level	High level	Moderate level	Low level
Moderate	High level	Moderate level	Moderate level	Low level
Low	Moderate level	Moderate level	Low level	Extremely low level
Extremely low	Low level	Low level	Extremely low level	Extremely low level

Regions (territories) with low potential and high life quality risks require principal programs of a complex development, etc.

Decomposition of both the indexes of potential and risk makes it possible to identify vectors of actions that, with the same integral indexes, can be completely different in different regions.

As of today, the data accumulated in the federal information fund system, state and industry statistics allow for an in-depth analysis of risks to life quality within the minimum period of time. The most significant problems for obtaining the objective assessments of life quality are the preparation and processing data from sociological studies on citizens’ perceptions of

life quality in the regions. However, the experience of such studies in the country is available, including the experience gained by scientific organizations of Rospotrebnadzor [22, 23]. Completing the social and hygienic monitoring system with sociological research data will expand the scope of application of the methodology for assessing and managing risks of a different nature, including risks to the population life quality [24].

In general, the implementation of life quality assessment in the system of social and hygienic monitoring will require:

- strengthening and intensifying the interdepartmental interaction, increasing the involvement of each of the parties in obtaining adequate and correct indexes of population life quality and certain components of its potential and risks;

- mainstreaming into the monitoring system of an essential sociological component, which makes it possible to assess the population satisfaction with the living standard in general and with its certain quality components;

- development and implementation of methodologies and hardware-software for assessing life quality and its certain components, and expansion of SHM federal information fund;

- professional development of Rospotrebnadzor bodies and organizations' experts, staffing the regional and federal information funds and performing analytical data processing.

The development of SHM system in terms of launching new functions is supposed to be implemented, having worked out the approaches to assessing the potential and risks to life quality on the example of several pilot regions (municipalities) with identification of effective mechanisms for applying results when making management decisions. The final step should be a systematic assessment of life quality of the country as a whole and of separate regions, informing the government, regional and municipal authorities and civil society on the results obtained.

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References

1. Zalevskiy G.V., Loguntsova O.I., Nepomnyashchaya V.A. Kachestvo zhizni kak kompleksnaya kharakteristika zhiznedeyatel'nosti cheloveka [Quality of life as a complex characteristic of life activity]. *Sibirskii psikhologicheskii zhurnal*, 2002, no. 16–17, pp. 102–103 (in Russian).

2. Malikov N.S. K voprosu o soderzhanii ponyatiya "kachestvo zhizni" i ego izmereniyu [On content of "life quality" concept and its measuring]. *Uroven' zhizni naseleniya regionov Rossii*, 2002, no. 2, pp. 17–23 (in Russian).

3. Libis R.A., Kots Ya.I., Ageev F.T., Mareev V.Yu. Kachestvo zhizni kak kriterii uspeshnoi terapii bol'nykh khronicheskoi serdechnoi nedostatochnost'yu [Life quality as a criterion of successful therapy for patients with chronic cardiac insufficiency]. *Russkii meditsinskii zhurnal*, 1999, vol. 7, no. 2, pp. 55–59 (in Russian).

4. Ware J.E., Snow K.K., Kosinski M., Gandek B. Sf-36 Health Survey: Manual and Interpretation Guide. Boston: The Health Institute, New England Medical Center, 1993, 316 p. Available at: https://www.researchgate.net/profile/John_Ware/publication/247503121_SF36_Health_Survey_Manual_and_Interpretation_Guide/links/56a0e80b08ae21a5642d5ad3/SF36-Health-Survey-Manual-and-Interpretation-Guide.pdf (22.06.2018).

5. Akinyemiju T.F., Zhao X., Sakhuja S., Jolly P. Life-course socio-economic status and adult BMI in Ghana; analysis of the WHO study on global ageing and adult health (SAGE). *International Journal for Equity in Health*, 2018, vol. 15, no. 1, pp. 1–8.

6. Provotorov V.M., Kotochigova T.V. Kachestvo zhizni bol'nykh khronicheskoi obstruktivnoi bolezn'yu legkikh s khronicheskoi serdechnoi nedostatochnost'yu [Quality of life of patients with chronic obstructive pulmonary disease with chronic heart failure]. *Vrach-aspirant*, 2011, vol. 48, no. 5.1, pp. 237–240 (in Russian).

7. Makhmudova M.M., Koroleva A.M. Kachestvo zhizni naseleniya: sushchnost', metodiki otsenki i sovremennoe sostoyanie v Ural'skom federal'nom okruge [The quality of life of the population: essence, assessment methods and state-of-the-art in the Ural Federal District]. *Vestnik Chelyabinskogo gosudarstvennogo universiteta*, 2014, vol. 353, no. 24, pp. 21–26 (in Russian).

8. Golovin A.A., Vlasova T.A., Koroleva N.M. Metodika otsenki kachestva zhizni naseleniya [Методика оценки качества жизни населения]. *Vestnik Belgorodskogo universiteta kooperatsii, ekonomiki i prava*, 2018, vol. 71, no. 4, pp. 115–122 (in Russian).

9. Pineo H., Glonti K., Rutter H., Zimmermann N., Wilkinson P., Davies M. Characteristics and use of urban health indicator tools by municipal built environment policy and decision-makers: a systematic review protocol. *Systematic Reviews*, 2017, vol. 6, pp. 2. DOI: 10.1186/s13643-017-0406-x

10. What's the Better Life Index? *Better Life Index.* Available at: http://www.oecdbetterlifeindex.org/about/better-life-initiative/ (01.08.2018).

11. Russian Federation. *Better Life Index.* Available at: http://www.oecdbetterlifeindex.org/countries/russian-federation/ (01.08.2018).

12. Volkov V.N. Reitingi gorodov Rossii po kachestvu zhizni naseleniya kak otrazhenie effektivnosti obrazovatel'nykh sistem [Life quality ratings of the Russian cities as a reflection of the educational system efficiency]. *Nepreryvnoe obrazovanie: XXI vek*, 2016, vol. 13, no. 1, pp. 50–60 (in Russian).

13. Fomina E.S., Ivanova T.A. Opredelenie reitinga sub"ektov rf po urovnyu kachestva zhizni s pomoshch'yu postroeniya integral'nogo indikatora [The rank determination of the federal subjects of russia based on qol (quality of life) level by building an integral indicator]. *Prilozhenie matematiki v ekonomicheskikh i tekhnicheskikh issledovaniyakh*, 2014, vol. 4, no. 1, pp. 192–197 (in Russian).

14. Kemalov A.M. Metodika otsenki kachestva zhizni naseleniya gorodov-millionnikov [Procedure of population life quality assessment in cities with over a million dwellers]. Alleya nauki, 2017, vol. 2, no. 10, pp. 184–190 (in Russian).

15. Wu S., Li D., Wang X., Li S. Examining component-based city health by implementing a fuzzy evaluation approach. *Ecological Indicators*, 2018, vol. 93, pp. 791–803.

16. Tkachev A.N., Lutsenko E.V. Kachestvo zhizni naseleniya kak integral'nyi kriterii otsenki effektivnosti deyatel'nosti regional'noi administratsii [Population life quality as an integral criterion for assessing efficiency of activities performed by regional administration]. *Nauchnyi zhurnal Kubanskogo gosudarstvennogo agrarnogo universiteta*, 2004, vol. 4, no. 2, pp. 171–185 (in Russian).

17. Tatarkin A.I., Kuklin A.A., Vasil'eva E.V., Nikulina N.L. Kachestvo zhizni kak sistemnaya dominanta povysheniya ekonomicheskoi bezopasnosti regiona [Quality of life as the main factor in increasing the economic security of the region]. *Vestnik Tyumenskogo gosudarstvennogo universiteta*, 2012, no. 11, pp. 38–49 (in Russian).

18. Akhremenko A.S., Evtushenko S.A. Kachestvo zhizni regionov Rossii: politologicheskii aspekt, metodologiya i metodika izmereniya [Quality of life in Russian regions: politological aspect, method and methodology of measurement]. *Vestnik Moskovskogo universiteta. Seriya 12: Politicheskie nauki*, 2010, no. 1, pp. 67–83 (in Russian).

19. Vereshchagin A.I., Fokin M.V., Kalinovskaya M.V. Formirovanie federal'nogo informatsionnogo fonda sotsial'no-gigienicheskogo monitoringa [Forming of federal infor mation fund of social-hygienic monitoring]. *Zdorov'e naseleniya i sreda obitaniya*, 2006, vol. 163, no. 10, pp. 11–15 (in Russian).

20. Onishhenko G.G., Zaitseva N.V., May I.V. [et al.]. Health risk analysis in the strategy of state social and economical development. In: G.G. Onishhenko, N.V. Zaitseva eds. Perm', Publishing house of the Perm National Research Polytechnic University, 2014, 738 p. (in Russian).

21. Korotenko G., Shevchenko K. Perspektivy primeneniya ontologicheskikh modelei dlya otsenki znachimosti pokazatelei i indikatorov, primenyaemykh v sotsial'no-gigienicheskom monitoringe [Prospects of ontological models application in assessing significance of parameters and indicators in social-hygienic monitoring]. *Sovremennyi nauchnyi vestnik*, 2013, vol. 5, no. 2, pp. 84–90 (in Russian).

22. Barg A.O., Nesevrya N.A. Sotsial'nye faktory riska zdorov'yu: teoretiko-metodologicheskie problemy analiza [Social health risk factors: theoretical and methodological issues in analysis]. *Vestnik Permskogo universiteta. Filosofiya. Psikhologiya. Sotsiologiya*, 2010, vol. 1, no. 1, pp. 99–108 (in Russian).

23. Lebedeva-Nesevrya N.A., Barg A.O., Solov'ev S.S. Zdorov'e v sub"ektivnykh otsenkakh rabotayushchego naseleniya Rossii [Self-Rated Health of the Working Population in Russia]. *Izvestiya Ural'skogo federal'nogo universiteta. Seriya 3: Obshchestvennye nauki*, 2017, vol. 12, no. 3 (167), pp. 108–115 (in Russian).

24. Popova A.Yu., Gurvich V.B., Kuz'min S.V., Orlov M.S., Yarushin S.V., Mishina A.L. Nauchnaya kontseptsiya razvitiya normativno-metodicheskoi osnovy obespecheniya sanitarno-epidemiologicheskogo blagopoluchiya naseleniya [The paradigm of the development of the regulatory and methodological framework aimed to maintain sanitary and epidemiological welfare of the population]. *Gigiena i sanitariya*, 2017, vol. 96, no. 12, pp. 1226–1230 (in Russian).

Popova A.Yu., Zaitseva N.V., May I.V. On implementation of population life qulity assessment into social-hygienic monitoring system. Health Risk Analysis, 2018, no. 3, pp. 4–12. DOI: 10.21668/health.risk/2018.3.01.eng

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NOISE AT A WORKPLACE: PERMISSIBLE NOISE LEVELS, RISK ASSESSMENT AND HEARING LOSS PREDICTION

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Introduction. Noise is a major occupational risk factor that causes hearing loss, one of the most widely spread occupational diseases. Recently some new standards that regulate noise at workplace have been fixed and risk assessment in the sphere has become necessary, so now it is vital to get better insights into the matter. The purpose of the work was to analyze peculiarities of occupational risk assessment performed for workplaces where there was a lot of in-plant noise taking into account international documents and national practices. Analysis of legal grounds for occupational risk assessment revealed that the most important issue in it was to determine probability of a damage to a worker's health. Only an employer can manage risks as it is him who has created them; hygienists, as per ILO Convention No. 161, are responsible for informing and giving recommendations to workers and employers on prevention measures. Methodology of occupational risk assessment that is applied in occupational medicine is a scientific foundation in the process. Analysis of risk assessment principles revealed it was necessary to determine tolerable risk, and not an acceptable one. Necessary and sufficient condition of evidential risk assessment is a hazardous factor existing at a workplace that exceeds maximum allowable concentrations or permissible exposure levels and prediction of a disease caused by this factor. According to the Guide P 2.2.1766-03, occupational risk is considered to be proven when there are data on workers' health; but as per data of working conditions assessment and criteria set forth by the Guide P 2.2.2006-5 it is thought to be only suspected. So, data obtained via specific assessment of working conditions are not sufficient to assess actual occupational risks. In 2010 the ILO issued an important document on emerging risks and new prevention forms. EU Strategic Framework on Health and Safety at Work 2014-2020 focuses on new and emerging risks as well as on probable new occupational diseases and work-related diseases. Recently some scientific works have been published that dwell on predicting risks caused by new technologies, physical, biological, psychosocial, and chemical factors. Directive 2003/10/EC issued in the EU differentiates noise standards as per urgency of measures taken, and these standards allow for means of individual protection applied to protect hearing organs; all the standards are also supplemented with practical guides. The Noise Regulations issued in Great Britain in 2005 give the following definition for risk assessment: it is determination of exposure to noise, account of risks borne by exposed groups of workers, assessment of combined effects produced by noise and ototoxic substances, as well as by noise and vibration. The author provides data that validate effects of occupational exposure to noise (the WHO, 2004) and notes that though an increase in permissible noise level from 80 to 85 dB is considered to be acceptable, the idea is rather controversial. The State Standard P ISO 1999–2017 on prediction of hearing loss caused by noise is well in line with the opinion expressed by the WHO experts that exposure to noise can cause disability. Conclusion. There is a logical chain for occupational risk assessment in case of noise: exposure assessment – determination of working conditions category (hazard degree) – calculation of hearing loss probability as per State Standard P ISO 1999–2017 – prevention measures – necessity to work out specific programs aimed at hearing preservation recommended by the ILO. These programs can reduce risk and extra-aural noise effects; they should be drawn up as Sanitary rules or a State Standard and help to preserve health and provide safe and productive work.

Key words: *noise, occupational medicine, working conditions, hearing loss, risk assessment, prediction, prevention.*

Noise is one of the most widely spread adverse factors at a workplace. As per data provided by the Federal State Statistics Service[1], in 2016 38.5% workers were employed at work places with adverse and hazardous working conditions; 18.2% out of them were exposed to noise, ultra- and infrasound; that is, almost each 5th workplace is hazardous as per acoustic factors. Pa-

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[1] Russian Statistics Yearbook. 2017: Statistic data collection / Federal State Statistics Service. Moscow, 2017, 686 p. (in Russian).

thologies caused by physical factors occupy the first place in occupational morbidity structure; their share increased in 2017 and reached 47.82%. Hearing loss caused by noise and diagnosed as sensorineural deafness prevails among such pathologies as its share amounts to 58.84 %[2].

The analysis performed for five basic economic branches (mining; processing industries; production and supply of electricity, water, and gas; transportation and communication; construction) has shown that hygienic standards are not met at workplaces; each 10th noncompliance was related to noise, and each 5th occupational disease was caused by it [1].

As per data provided by the WHO, 360 million people worldwide (5% of the world population) live with disabling hearing loss. There are a lot of unemployed among such people or they frequently have very low-paid occupations. Hearing loss among elderly people leads to social isolation, anxiety, depression, a decrease in cognitive abilities, and dementia[3].

As per data of the US National questioning on healthcare, 23% out of workers exposed to noise had hearing troubles, 5% suffered from tinnitus, and 9% had both conditions; the same parameters among those who had never been exposed to noise amounted to 7%, 5%, and 2% correspondingly (P<0.0001) [2].

Issues related to etiology, pathogenesis, diagnostics, and prevention of noise-induced hearing loss have been studied [3, 4]. Validity of extra-aural noise effects is becoming higher. Earlier non-specific noise effects weren't always considered to be proven [5]; but recent research has revealed that exposure to noise significantly correlates with cardiovascular diseases, notably, arterial hypertension, although a correlation between noise and mortality caused by cardiovascular diseases turned out to be weak [6].A greater attention is paid to traumatism as an occupational risk factor [7], especially for noisy occupations [8], as well as to fitness for work responsibilities fulfillment as per hearing or so called "hearing fitness" [9]. Hearing loss criterion in its essence is not primarily oriented at health preservation, but at providing safe and efficient work, especially in case of occupations that involve great neuro-emotional tension (public transport drivers, civil aviation pilots etc.) [10, 11].

The question of risk assessment associated with noise exposure at a workplace becomes truly vital in relation to approval on Sanitary-Epidemiologic Rules and Norms SanPiN 2.2.4.3359-16[4], that set maximum permissible noise levels at 80 and 85 *dB(A)* and require obligatory risk assessment in the last case, as well as introduction of the State Standard GOST R ISO 1999-2017[5]

The research goal was to analyze peculiarities of occupational risks assessment for workers exposed to noise at their workplaces taking into account international documents and national practices.

Legal grounds for occupational risk assessment. A concept of "risk" first appeared in occupational health 50 years ago in a document issued by the International Organization for Standardization (ISO), namely ISO/R 1999:1971 recommendation[6] on how to assess occupational exposure to noise in order to preserve a person's hearing. There was a table in the document with "Risk, %" column as hearing loss probability in per cent that depended on a noise level in dB(A) and duration of service in noisy conditions. The International Labor Organization (ILO) fixed in its Convention No. 148[7] ((ratified by the Russian Federation), Clause 3, that "the term noise covers all sound which can result in hearing impairment or be harmful to health or otherwise

[2] On sanitary-epidemiologic welfare of the population in the Russian Federation in 2017: State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being Publ., 2018, 268 p. (in Russian).

[3] Prevention of deafness and hearing loss: The Secretariat Report (A70/34 On May 04, 2017). *World Health Organization*. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_34-ru.pdf (access date: 14.07.2018) (in Russian).

[4] SanPiN 2.2.4.3359-16. Sanitary-Epidemiologic Rules and Norms for physical factors at workplaces. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/420362948 (access date: 14.07.2018).

[5] State Standard R ISO 1999-2017. Acoustics. Assessment of hearing loss caused by exposure to noise at workplaces. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200157242 (access date: 14.07.2018).

dangerous". The Convention introduced a concept of occupational risk. Clause 4 states that "measures be taken for the prevention and control of, and protection against, occupational hazards in the working environment due to ... noise and vibration".

As per Clause 8 of the Convention, "The competent authority shall establish criteria for determining the hazards of exposure to air pollution, noise and vibration in the working environment and ... shall specify exposure limits on the basis of these criteria. The criteria and exposure limits shall be established, supplemented and revised regularly in the light of current national and international knowledge and data, taking into account as far as possible any increase in occupational hazards resulting from simultaneous exposure to several harmful factors at the workplace."

The RF Labor Code[8] contains Clause 209 that defines an occupational risk as "a probability of damage to health caused by exposure to adverse and (or) hazardous occupational factors when a worker fulfils his or her duties according to a labor contract or in any other cases identified by the present Code or other federal laws. A procedure for occupational risk assessment is to be fixed by a federal executive body that is responsible for state policy development and legal regulation in the sphere of labor taking into account opinions expressed by the Russian tripartite commission for regulation of social and labor relations".

Occupational risks management is a set of activities that are components in the system of labor protection management; they include measures aimed at detecting, assessing, and reducing occupational risks.

Therefore, the primary task in occupational risk assessment is to determine probability of damage to health. A procedure for occupational risk assessment is fixed by the RF Labor Ministry taking into account opinions expressed by The Tripartite Commission. Occupational risks management as a set of organizational and technical activities is a part of the labor protection system and it goes beyond responsibilities of hygienists. Therefore, a risk is managed by those who create it, in this case, by employers. Hygienists act within their competence determined in the ILO Convention No. 161 or "Occupational Health Services Convention" (not ratified by the Russian Federation); they give advice to workers on risks at their workplaces, protection and prevention measures; and they give advice to employers on prevention measures required to manage risks.

Methodology of occupational risks assessment in occupational health is scientific grounds for hygienic assessment and prevention. Its foundations were set 25 years ago in research supervised by Academician N.F. Izmerov [12]; they were then generalized in a reference guide [13]; and its principles, methods and criteria were systematized in further research[9] [14]. These domestic works (co-written with other scientists) were given the Russian Federation Government Award in science and technology (2002) and F.F. Erisman's Award in Hygiene granted by the Presidium of the Russian Academy of Medical Sciences (2004).

The methodology spots out ***a priori*** hygienic and ***a posteriori*** medical and biological occupational risks assessment [13]. Its advantages are the scales with quantitative assessment criteria: a) a risk doubles per each harm category of working conditions in the Guide R 2.2.2006-05[10] and b) an occupational disease index also doubles per each harm category of working conditions [11].

In particular, the Guide R 2.2.2006-05 implies scales for vibration and acoustic factors

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[6] ISO/R 1999:1971. Acoustics – Assessment of occupational noise exposure for hearing conservation purposes. *International Organization for Standardization*. Available at: https://www.iso.org/ru/standard/56849.html (access date: 14.07.2018) (in Russian).

[7] Working Environment (Air Pollution, Noise, and Vibration) Convention: Convention No. 148. KODEKS: an electronic fund of legal and reference documentation. Available at: http://docs.cntd.ru/document/1900829 (access date: 14.07.2018) (in Russian).

[8] Labor Code of the Russian Federation. KODEKS: an electronic fund of legal and reference documentation. Available at: http://docs.cntd.ru/document/901807664 (access date: 14.07.2018) (in Russian).

[9] Occupational risk: Electronic interactive reference catalogue. Edited and compiled by a member of Russian Academy of Science, Academician N.F. Izmerov, Professor E.I. Denisov, Doctor of Biological Sciences I.V. Stepanyan. Available at: http://medtrud.com/ (access date: 14.07.2018) (in Russian).

that have steps for noise, whole-body and hand-arm vibration equal to 10, 6 and 3 dB respectively and it reflects their different biologic efficiency (doubling of loudness, kinematic parameter, and a dose accordingly).

A significant task in the methodology is to determine a probability of occupational and work-related diseases as well as to account their categories of risk, severity of illness, and degree of work-relatedness (causality) as it allows to obtain single-number indexes that *are very convenient for managing risks*[12].

Risk assessment principles: risk tolerability or acceptability. There is a principle in the world practice stating that a polluter has to pay or "polluter pays principle" (PPP); it was introduced by a recommendation of the Organization for Economic Cooperation and Development in 1972; it was accepted by the European Union in 1987 and included as Principle No. 16 in Rio-de-Janeiro Declaration of 1992. There is another principle, a precautionary principle, approved by the European Union[13] in 2000 and UNESCO [14] in 2005. The principles allow to manage probable risks in a case when there aren't enough scientific data, for example, risks related to nanotechnologies, genetically modified organisms, etc.

There are three possible attitudes towards risks, namely avoidance, acceptance, and regulation; world practice mostly inclines towards regulation, or risk management [as per 13], that was earlier called prevention.

First works on risks were published in the UK and the USA [15–17]. Foreign researchers in their works on risk assessment procedures examined a number of criteria for risks acceptance/tolerance such as ALARA, ALARP, FAPRA and others, that differed only in their legal subtleties. ALARA principle (the abbreviation for As Low As Reasonably Achievable) was formulated in 1954 by the International Commission on Radiological Protection. It was further developed in ALARP principle, or "As Low As Reasonably Practicable".

In 1974 the "Health and Safety etc. at Work Act" was issued in the UK [15] according to it, people who control production premises or activities are to reduce risks as per SFARP criterion (the abbreviation for So Far As is Reasonably Practicable). The UK Health and Safety Executive issued a controversial document "Reducing risks, protecting people" [17] where it fixed criteria for risks tolerance as per the following gradations: unacceptable, tolerable, quite acceptable, negligible, and we can see that the terms are rather inconsistent. Since there is a principle in occupational health and industrial ecology stating that "Acceptance of a priori hazard and harm for health is incompatible with zero risk principle and implies there is a residual risk determined by deontology and prevention capabilities" [as per 13], it is necessary to speak about social tolerance of occupational risks [13, p. 100].

The Guide R 2.2.1766-0311 sets an association between working conditions categories and occupational risks categories: optimal 1 catego-

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[10] R 2.2.2006-05. The Guide on hygienic assessment of factors related to working environment and labor process. *KODEKS: an electronic fund of legal and reference documentation.* Available at: http://docs.cntd.ru/document/1200040973 (access date: 10.07.2018) (in Russian).

[11] R 2.2.1766-03. The Guide on assessment of occupational risks for workers' health. Organizational and methodical grounds, principles, and assessment criteria. Guide. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/9019020533 (access date: 10.07.2018) (in Russian).

[12] Risk management methodology in occupational medicine: hygienic assessment of working conditions, prediction and causation of occupational diseases related to work (harmonized collection of methodological materials) / approved by the Scientific Council No. 45 "Medical and ecological issues related to workers' health" of the Russian Academy of Medical Sciences. Moscow, NII MT RAMS Publ., 2012, 23 p. (in Russian).

[13] Communication from the Commission on the precautionary principle. Brussels, 2.2.2000, COM (2000) 1 final. Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2000:0001:FIN:EN:PDF (access date: 10.07.2018)

[14] UNESCO. The Precautionary Principle. World Commission on the Ethics of Scientific Knowledge and Technology (COMES). Available at: http://unesdoc.unesco.org/images/0013/001395/139578e.pdf (access date: 10.07.2018) (in Russian).

[15] Health and Safety at Work etc. Act 1974. Available at: http://www.legislation.gov.uk /ukpga/1974/37/contents (access date: 10.07.2018).

ry– no risk; acceptable 2– negligible (tolerable) risk; hazardous 3.1– small (moderate) risk; hazardous 3.2– average (considerable) risk; hazardous 3.3– high (intolerable) risk; dangerous (extreme) 4– ultra high risk and risk for life that is characteristic for this particular occupation. And we can see that here a term "tolerance", and not "acceptance" is applied. Therefore, according to risk management principle (Clause 209 of the RF Labor Code) we should rely on a concept of risk tolerance, and not risk acceptance.

OEL or risk assessment? For many years, a paradigm based on OEL (MPC and MPL) was a central one in occupational hygiene, its main assumption being that conformity to them was obligatory and possible at any workplace and it could guarantee health preservation. Indeed, MPC and MPL are true bases of safety but they are far from being always adhered to. Therefore, it became necessary to assess consequences of their violation, to determine prevention tactics and measures of social protection for those who have to work under adverse conditions. Finding solutions to these tasks required new theories that include risk assessment and management and that have been developing rapidly over recent years. As social and economic changes occurred in the country, and it made a scientific paradigm in occupational health shift from MPC/MPL to a methodology of occupational risk assessment [13].

As opposed to traditional hygienic assessment of working conditions when all values higher than hygienic standards were fixed without taking into account an extent to which they were higher or what possible consequences for health it would mean, risk assessment pays greater attention to quantitative estimation of probable damage to health in order to choose efficient risk management activities, i.e. prevention [13].

MPC and MPL as bases of hygiene don't give any information on probability or severity of consequences, i.e. risk assessment. There is a true paradox here: risk assessment is based on MPC and MPL, however, MPC and MPL are obligatory but not sufficient for risk assessment. A "dose – effect" relationship is sufficient here as it gives grounds for predicting probable health disorders.

The ILO in its "Technical and ethical guidelines for workers' health surveillance" [18]. item 2.7, states that "surveillance programs should be used for prevention purposes and in particular to predict the occurrences of occupational injuries and diseases". And here (item 3.19) "priority should be given to environmental (exposure) limits over biological (biological exposure limits) criteria". That is, medical examinations with an occupational disease prediction (given in italics by us – E.D.) are a basis of prevention activities with priority given to criteria of working environment assessment, i.e. MPC/MPL.

Consequently, evidence-based risk assessment in full conformity with the letter and the spirit of the requirements fixed by the RF Labor Code (Clause 209 and others) and the ILO documents should include obligatory and sufficient such components as assessment of a degree of excess the MPC/MPL by harmful factor at a workplace and prediction of probability of an occupational disease caused by this factor.

Special assessment of working conditions (SAWC) according to the Federal Law NO. 426[16]. Clause 13 of the Law contains the following definition: Special assessment of working conditions is a unified set of activities aimed at identifying adverse and (or) hazardous factors related to working environment and working process and assessing their effects on a worker taking into account deviations in their actual values from fixed standards (hygienic standards) existing for these working conditions and application of individual and collective protection means".

SAWC replaces a certification of workplaces and state examination of working conditions and takes into account actual impacts on a worker's body exerted by adverse and (or) hazardous factors related to working environment and working process. Categories (sub-categories) of working conditions at specific workplaces are fixed as per SAWC results; these categories are taken into account when insurance fees are paid to pension funds, compensations are given to workers, individual protection means provided, medical examinations organized, occupational risks assessed, accidents and occupational diseases investigated, etc.

SAWC is performed according to an established procedure[17], that includes: 1) identifi-

cation of potentially adverse and (or) hazardous occupational factors; 2) examinations (tests) and measurements of such factors; 3) assignment of working conditions into a specific category (subcategory) according to a degree of their adverse and (or) hazard health effects; 4) presentation of results. In spite of several drawbacks [19], SAWC is an acting system for occupational risk assessment.

It should be noted that, according to the Guide ₽ R 2.2.1766-03[11], an occupational risk is considered to be proven (category 1A) on the basis of data on workers' health obtained via periodical medical examinations; while results of working conditions hygienic assessment performed as per criteria given in the Guide R 2.2.2006-05[10] are to be considered only as a suspected risk (category 2). So, if one wants to assess an actual occupational risk, SAWC results are not sufficient and they should be supplemented with data obtained via periodical medical examinations.

The European Union strategy on health and safety at work (2014–2020) and new emerging risks. A framework strategy adopted in the EU[18] highlighted problems small and middle-sized businesses had to face, new emerging risks, and ageing of workforce. There are 7 strategic goals outlined in the document, and No. 5 goal directly focuses on ageing of workforce, new and emerging risks (and new occupational diseases) as well as prevention measures. The purpose of the strategy is to promote better working conditions and processes, higher labor satisfaction, higher competitiveness of European companies and lower expenses borne by social insurance systems. A most significant part in the EU strategy is recognition of new and emerging risks and new occupational and work-related diseases. There isn't any similar document issued in our country.

We should mention a most significant document issued by the ILO that dwells on emerging risks and new prevention techniques in a rapidly changing labor world [20]. It was followed by works on prediction of new risks caused by new technologies [21] as well as by physical [22], biological [23], psychosocial [24], and chemical [25] factors.

New and emerging physical risk factors are linked with a role that physical loads play in development of disorders in the musculoskeletal system; such risks also include those caused by noise, vibration, thermal factors, ionizing radiation, machinery and equipment etc. Such risks can also emerge from absence of physical activity, or combined effects produced by physical loads and psychosocial risks; they can be related to multiple factors or caused by a complex interaction within "a man – a machine" system etc. [22]. New biological risks are linked with the global epidemiologic situation, impacts exerted by antimicrobic-resistant pathogens in public healthcare and food industry, as well as with endotoxins, mold fungi at workplaces, solid wastes etc. [23]. Works are being published on risk analysis and prediction in relation to advanced processing technologies [26].

It is obvious that all the above-mentioned issues ought to be examined in depth bearing in mind future prospects for research; there is a wide range of them, starting from disorders in the musculoskeletal system and to combined effects by physical and psychosocial loads, issues related to "a man – a machine" interactions etc.

The EU Guide on occupational risks assessment [27] consists of 4 parts: 1) introduction, definitions, and procedures, 2) basics (data collection, detection of hazards, risk assessment, prevention measures, documenting), 3) checklists (safety rules, chemicals, noise, vibration, illumination, stress at work), 4) detection of hazards and prevention measures for specific activities (work in an office, construction, food industry, wood pro-

[16] On special assessment of working conditions: The RF Federal Law issued on December 28, 2013, No. 426. *Konsultant Plus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_156555/ (access date: 09.07.2018) (in Russian).

[17] On Approval of Procedure for conducting a special assessment of working conditions, Classifier of adverse and (or) hazardous production factors, reporting form on a specific assessment of working conditions and instructions how to fill it in: The Order issued by the RF Ministry for labor and Social Protection on January 24, 2014 No. 33n. *Garant.* Available at: http://base.garant.ru/70583958/ (access date: 09.07.2018).

[18] Communication from the Commission to the European Parliament, the Council, the European economic and social committee and the Committee of the regions on an EU strategic framework on health and safety at work 2014–2020 Available at: http://ec.europa.eu/social/BlobServlet?docId=11828&langId=en (access date: 09.07.2018).

cessing, car repairing, agriculture, open-cut mines). This Guide can be useful for both employers and their employees as it explains basic issues related to labor protection and occupational medicine in such a way that they can be understood easily. However, it doesn't contain any quantitative criteria of occupational risks assessment or any literature reference and it makes its scientific value rather limited.

The EU Directive 2003/10/EC on noise[19]**.** Item 7 in the preamble contains the following: "to introduce measures protecting workers from the risks arising from noise owing to its effects on the health and safety of workers, in particular damage to hearing".. Clause 4 "Determination and assessment of risks" states in item 6e that "…any indirect effects on workers' health and safety resulting from interactions between noise and warning signals or other sounds ... need to be observed in order to reduce the risk of accidents". Thus the Directive regulates limitation of noise required for both hearing preservation and labor safety.

The document also fixes exposure limit values and exposure action values in respect of the daily noise exposure levels and peak sound pressure. The lower and upper exposure action values require some measures to be taken, and the exposure limit values suppose that personal protection of hearing organs ought to be applied (Table).

Permissible noise levels as per the Directive 2003/10/EC

№	Parameter	$L_{EX,\ 8h}$	P_{peak}	dB(C) re. 20 μPa
1	Exposure limit values	87 dB (A)	200 Pa	140 dB
2	Upper exposure action values	85 dB (A)	140 Pa	137 dB
3	Lower exposure action values	80 dB (A)	112 Pa	135 dB

As one can see from the Table (the difference between lines 1 and 2-3), when hearing protectors (earmuffs, earplugs, helmets etc.) are applied, their expected efficiency is within 2-7 dB. It corresponds to a 1.15-1.6 times decrease in noise loudness and this decrease can be subjectively noticeable [13].

One should also mention "Non-binding guide to good practice for the application of Directive 2003/10/EC"[20]; this guide dwells on issues related to measuring and assessing exposure to noise as well as prevention measures. Therefore, there are noise standards in the EU that are differentiated as per urgency of measures to be taken and that account for PPE for hearing organs; these are supplemented with a guide to good practice.

An experience of Great Britain on risk assessment of noise at work. "Control of Noise at Work Regulations"[21] fix a procedure for risk assessment in case of noise exposure at a workplace. An employer is to assess a health risk for workers caused by noise in order to determine what measures should be taken to meet the requirements set forth by the Regulations. And here noise is to be estimated via observations over working practices and taking into account data on possible noise levels generated by used equipment; when necessary, an employer should measure noise levels and compare them with the existing standards.

Risk assessment includes considering the following: a) level, type, and duration of exposure to noise, including exposure to a peak sound pressure: b) impacts exerted by noise on workers whose health is at specific risk of such exposure; c) any consequences for workers' health and safety that result from interactions between noise and ototoxic substances or between noise and vibration; d) any indirect consequences for workers' health and safety that result from interactions between noise and acoustic alarms or any other sounds that are to be heard to reduce risks at a workplace.

So, risk assessment here involves determina-

[19] On the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (noise) (The 17th separate Directive in Clause 16(1) of Directive 89/391/EEU): Directive by the European Parliament and the European Union Council 2003/10/EU issues on February 6, 2003. Available at: http://docs.pravo.ru/document/view/44436558/50529867/ (access date: 09.07.2018) (in Rissian).

[20] Non-binding guide to good practice for the application of Directive 2003/10/EC. Luxembourg: Office for Official Publications of the European Communities, 2008, 169 p. DOI: 10.2767/61482

[21] Control of Noise at Work Regulations 2005. Available at: http://www.legislation.gov.uk/uksi/2005/1643/contents/made (access date: 09.07.2018)

tion of noise exposure, account of risks for vulnerable groups of workers, assessment of combined effects produced by noise and ototoxic substances, as well as by noise and vibration.

New noise standards. New Sanitary-Epidemiologic Rules and Norms SanPiN 2.2.4.3359-16[4] fix maximum permissible noise levels for certain industries at 80 and 85 dBA provided that acceptability of risk for workers' health is confirmed by occupational risks assessment and results obtained during periodical medical examinations of people who are exposed to noise higher than 80 dBA. The document also requires prohibition of any works under noise levels higher than 80 dBA. These statements raise a number of issues.

Validity of OEL (MPL) for noise. The WHO document that focuses on assessing burden of diseases caused by work-related hearing loss [28] contains Table 1 "Assessment of reported responses to occupational noise exposure" where evidence is considered to be limited for performance, biochemical and immune effects, and birth weight, and where it is considered to be sufficient for the following:

- annoyance at noise being <55 *dB(A)* in offices and <85 *dB(A)* in industry,
- hypertension at 55-116 *dB(A)*,
- hearing loss (adults) at 75 *dB(A)* and (unborn children) at < 85 *dB(A)*.

In relation to that we can't agree with some authors who state that it is quite acceptable to increase MPL for noise from 80 to 85 *dB(A):* "In-plant noise equal to 80 *dB(A)* is theoretical minimum exposure that doesn't cause higher risks of hearing loss. Compliance with the noise standard equal to 85 *dB(A)* fully allows to reduce prevalence of noise-induced hearing loss" [29]. This tirade contradicts arguments given by the WHO.

After the State Standard GOST R ISO 1999-2017[5] has been introduced, it is advisable to make some corrections into item 3.2.6 of the SanPiN 2.2.4.3359-16[4] and fix that occupational risk assessment is to be performed via calculation of hearing loss probability for workers and audiometric testing during periodical medical examinations when noise level is higher than 80 *dB(A)*. These measures will reduce both risks of hearing loss and extra-aural effects of noise.

A new standard for hearing loss prediction, GOST R ISO 1999-2017[5]. There is a specific risk assessment system that has developed in relation to the issue of noise in world literature and practices; this system differs from that applied when chemical factors are assessed [30] and is based on predicting probability of hearing loss as an officially recognized occupational disease caused by noise. It started as far back as in 1971 when the Recommendation ISO/R 1999:1971 was first published; it then became the Standard ISO 1999:1975, which was then revised as ISO 1999:1990 and finally as ISO 1999:2013, and then introduced in Russia as the State Standard GOST R ISO 1999-2017. As opposed to the first edition, the Standard doesn't contain any definite formula for risk assessment, but it determines techniques that can be applied within national systems to predict hearing loss.

The Standard introduces a number of notions that are very important for occupational health [22]:

- hearing loss – deviation or a change for the worse of the threshold of hearing from normal;
- hearing disability – effect of hearing loss on activities in daily living (Note 1 to entry: This is sometimes called “activity limitation” (WHO);
- risk of hearing disability – percentage of a population sustaining hearing disability;
- risk of hearing disability due to noise – risk of hearing disability in a noise-exposed population minus the risk of hearing disability in a population not exposed to noise but otherwise equivalent to the noise-exposed population.

These terms enrich the methodology of occupational risks assessment. It is also important that the Standard adheres to the WHO position on disability that can be a consequence of expo-

[22] Original text to be found in ISO 1999:2013 Acoustics – Estimation of noise-induced hearing loss. *Online Browsing Platform*. Available at: https://www.iso.org/obp/ui/#iso:std:iso:1999:ed-3:v1:en (access date: 09.07.2018).

[23] State Standard R ISO /IEC 31010-2011. Risk management. Risk assessment techniques. Moscow, Standartinform Publ., 2012, 74 p. (in Russian).

sure to noise [28].

Conclusion. Fundamentals of risk management have been developed in great detail and documented in standards[23] and guides, starting from pragmatic [31, 32] to academic ones with economic and psychosocial estimates [33] and taking into account occupational and non-occupational exposures [34].

There is Guidance on risk assessment at work [35] and a standard on risk assessment techniques [36] adopted in the EU; Health and Safety Executive (HSE) in the UK has developed "Risk Assessment Tool and Guidance (including Application Guidance)" [37].

But the issue of noise at a workplace has its peculiarities because it is related not only to health but also safety [10, 11], and involves not only risk assessment but also prediction of possible effects. Starting from early works with predictions as per Monte Carlo method [38], the methodology of occupational risks assessment is so well grounded by scientific works, developments, and state standards, that it makes the noise issue truly international. We can compare it to a project by the US National Institute for Occupational Safety and Health (NIOSH) dedicated to assessment of new risk factors (including nano-materials) suggested for general discussions [39].

A logic chain for noise is as follows: exposure assessment – determination of working conditions category (degree of harm) – calculation of hearing loss probability as per GOST R ISO – a set of prevention measures (PPE, rest rooms, vitamin prophylaxis etc.); all these require development of Hearing Conservation Programs recommended by the ILO and documented as sanitary rules or a state standard.

Thus, in relation to State Standard GOST R ISO 1999-20175 introduction it is advisable to make changes into item 3.2.6 of the Sanitary-Epidemiologic Rules and Norms4 and state that occupational risk assessment is to be performed via calculation of hearing loss probability for workers and their audiometric testing during periodical medical examinations when noise level is higher than 80 dB(A). These measures will reduce both risks of hearing loss and extra-aural noise effects. In a very distant future, “deserted work” in the noisy conditions will be performed by the so-called cyber-physical systems (robots and autonomous devices based on artificial intelligence), which is envisaged by the course of digitalization of the Russian economy.

Conclusions:

1. From the standpoint of evidence-based medicine, an adequate assessment of occupational risk under exposure to noise should include both an assessment of the excess of the maximum permissible level and a prediction of the probability of hearing loss with audiometric control during a periodic medical examinations.
2. Occupational risk assessment under exposure to noise in world practice includes detection of hazard sources, exposure assessment, determination of vulnerable workers' groups (teenagers, pregnant and recently delivered women, breast-feeding mothers, workers with chronic diseases, migrants, and others) and selection of prevention measures.
3. Noise exposure monitoring, a prediction of hearing loss probability, audiometric control during periodical medical examinations, and prevention activities are to be fixed as a set of measures in programs for hearing preservation documented as a state standard, a system of labor safety standards, or sanitary-epidemiologic requirements.

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References

1. Kostenko N.A. Usloviya truda i professional'naya zabolevaemosti v nekotorykh vidakh ekonomicheskoi deyatel'nosti Rossiiskoi Federatsii v 2004–2013 gg. [Working conditions and occupational morbidity in

some branches of economic activity of Russian Federation in 2004–2013]. *Meditsina truda i promyshlennaya ekologiya*, 2015, no. 4, pp. 43–45 (in Russian).

2. Masterson E.A., Themann C.L., Luckhaupt S.E., Calvert G.M. Hearing difficulty and tinnitus among U.S. workers and non-workers in 2007. *Am. J. Ind. Med*., 2016, vol. 59, pp. 290–300. DOI: 10.1002/ajim.22565

3. Zinkin V.N., Sheshegov P.M., Chistov S.D. Klinicheskie aspekty professional'noi sensonevral'noi tugoukhosti akusticheskogo geneza [The clinical aspects of occupational sensorineural impairment of hearing of the acoustic origin]. *Vestnik otorinolaringologii*, 2015, vol. 80, no. 6, pp. 65–70. DOI: 10.17116/otorino201580665-70

4. Le T.N., Straatman L.V., Lea J., Westerberg B. Current insights in noise-induced hearing loss: a literature review of the underlying mechanism, pathophysiology, asymmetry, and management options. *J. Otolaryngol. – Head and Neck Surg.*, 2017, vol. 46, pp. 41. DOI: 10.1186/s40463-017-0219-x

5. Occupational exposure to noise: evaluation, prevention and control. In: B. Goeltzer, C.H. Hansen, G.A. Sehrndt eds. Dortmund, Germany: WHO, 2001, 336 p.

6. Skogstad M., Johannessen H.A., Tynes T., Mehlum I.S., Nordby K.-C., Lie A. Systematic review of the cardiovascular effects of occupational noise. *Occupational Medicine*, 2016, vol. 66, no. 6, pp. 1–16. DOI: 10.1093/occmed/kqw113

7. Bukhtiyarov I.V., Izmerov N.F., Tikhonova G.I., Churanova A.N. Proizvodstvennyi travmatizm kak kriterii professional'nogo riska [Occupational injuries as a criterion of professional risk]. *Problemy prognozirovaniya*, 2017, no. 5, pp. 140–149 (in Russian).

8. Toppila E., Pyykkö I., Pääkkönen R. Evaluation of the increased accident risk from workplace noise. *Int. J. Occup. Saf. Ergon. (JOSE)*, 2009, vol. 15, no. 2, pp.155–162.

9. Tufts J.B., Vasil K.A., Briggs S. Auditory fitness for duty: A review. J. *Am. Acad. Audiol.*, 2009, vol. 20, pp. 539–557. DOI: 10.3766/jaaa.20.9.3

10. Denisov E.I., Adeninskaya E.E., Eremin A.L., Kur'erov N.N. Professional'naya poterya slukha – problema zdorov'ya i bezopasnosti [Occupational deafness – problem of health and safety]. *Meditsina truda i promyshlennaya ekologiya*, 2014, no. 7, pp. 45–47 (in Russian).

11. Sovershenstvovanie kriteriev poteri slukha ot shuma i otsenka professional'nogo riska / I.V. Bukhtiyarov, E.I. Denisov, N.N. Kur'erov, L.V. Prokopenko, M.V. Bulgakova, O.O. Khakhileva [Improvement of noise-induced hearing loss criteria and occupational risk assessment]. *Meditsina truda i promyshlennaya ekologiya*, 2018, no. 4, pp. 1–9 (in Russian).

12. Izmerov N.F., Kaptsov V.A., Denisov E.I., Ovakimov V.G. Problema otsenki professional'nogo riska v meditsine truda [Evaluation of occupational diseases according to risk and severity categories]. *Meditsina truda i promyshlennaya ekologiya*, 1993, no. 3–4, pp. 1–4 (in Russian).

13. Professional'nyi risk dlya zdorov'ya rabotnikov [Occupational health risk]. In: N.F. Izmerov, E.I. Denisov, eds. Moscow, Trovant Publ., 2003, 448 p. (in Russian).

14. Izmerov N.F., Denisov E.I. Otsenka professional'nogo riska v meditsine truda: printsipy, metody i kriterii [An assessment of the occupational risk in the medical sphere: principles, methods and criteria]. *Vestnik Rossiiskoi akademii meditsinskikh nauk*, 2004, no. 2, pp.17–21 (in Russian).

15. Risk: Analysis, Perception and Management. Report of the Royal Society Study Group. London, 1992. Available at: https://royalsociety.org/topics-policy/publications/1992/risk/ (18.07.2018).

16. Vincent T.C., Milley W.M. Risk assessment methods: approaches for assessing health and environmental risks. New York: Plenum Press, 1993, 267 p.

17. Reducing risks, protecting people. HSE's decision-making process (HSE.r2p2). Crown, 2001, 88 p.

18. Technical and ethical guidelines for workers' health surveillance (OSH No 72). Geneva, International Labour Office, 1998, 41 p.

19. Prokopenko L., Lagutina A., Kur'erov N. Metodika trebuet peresmotra [The procedure needs to be revised]. *Okhrana truda i sotsial'noe strakhovanie*, 2014, no. 9, pp. 72–77 (in Russian).

20. Emerging risks and new patterns of prevention in a changing world of work. Geneva, International Labour Organization, 2010, 19 p.

21. Ellwood P., Reynolds J., Duckworth M. Green jobs and occupational safety and health: Foresight on new and emerging risks associated with new technologies by 2020. Luxembourg, European Agency for Safety and Health at Work, 2014, 40 p. DOI: 10.2802/92105

22. Flaspöler E., Reinert D., Brun E. Expert forecast on emerging physical risks related to occupational safety and health. Luxembourg, European Agency for safety and health at work, 2005, 76 p.

23. Expert forecast on emerging biological risks related to occupational safety and health. Luxembourg, European Agency for Safety and Health at Work, 2007, 145 p.

24. Expert forecast on emerging psychosocial risks related to occupational safety and health. Luxembourg, Office for Official Publications of the European Communities, 2007, 126 p.

25. Expert forecast on emerging chemical risks related to occupational safety and health. Luxembourg, European Agency for Safety and Health at Work, 2009, 197 p.

26. Fernándeza F.B., Péreza M.Á.S. Analysis and modeling of new and emerging occupational risks in the context of advanced manufacturing processes. *Procedia Engineering*. 2015, vol. 100, pp. 1150–1159. DOI: 10.1016/j.proeng.2015.01.478

27. Osnovy otsenki riskov. Okhrana truda – delo kazhdogo. – Evropeiskoe agentstvo po okhrane truda (per. po zakazu Minzdravsotsrazvitiya Rossii) [Basics of risk assessment. Labor protection concerns everybody. European Agency for Health and safety at Work (translation ordered by the RF Ministry for Public Healthcare and Social Development)]. 2008, 56 p.

28. Concha-Barrientos M., Campbell-Lendrum D., Steenland K. Occupational noise: assessing the burden of disease from work-related hearing impairment at national and local levels. WHO Environmental Burden of Disease Series, no. 9. Geneva, World Health Organization, 2004, 41 p.

29. Mazitova N.N., Adeninskaya E.E., Pankova V.B., Simonova N.I., Fedina I.N., Preobrazhenskaya E.A., Bomshtein N.G., Severova M.M., Volokhov L.L. Vliyanie proizvodstvennogo shuma na slukh: sistematicheskii obzor zarubezhnoi literatury [Influence of occupational noise on hearing: systematic review of foreign literature]. *Meditsina truda i promyshlennaya ekologiya*, 2017, no. 2, pp. 48–53.

30. Principles for modelling dose-response for the risk assessment of chemicals. Environmental Health Criteria 239. Geneva, WHO, 2009, 137 p.

31. Risk assessment and workers' participation. Workshop on making modern OSH legislation. Tirana, Albania, 2012, 34 p. Available at: https://www.ilo.org/wcmsp5/groups/public/---ed_dialogue/---lab_admin/documents/presentation/wcms_184162.pdf (18.07.2018).

32. Risk-Controlling the risks in the workplace. *Health and Safety Executive*, 2014. Available at: http://www.hse.gov.uk/Risk/controlling-risks.htm (18.07.2018).

33. Galizzi M., Tempesti T. Workers' perceptions of risk and occupational injuries. University of Massachusetts Lowell. *Risk, Perception, and Response: Conference*. Harvard University, 2014, 58 p.

34. Lentz T.J., Dotson G.S., Williams P.R.D., Maier A., Gadagbui B., Pandalai S.P. [et al]. Aggregate exposure and cumulative risk assessment – Integrating occupational and non-occupational risk factors. *J. Occup. Environm. Hyg.*, 2015, vol. 12, pp.112–126.

35. Guidance on risk assessment at work. Luxembourg: Office for Official Publications of the European Communities, 1996, 64 p.

36. Risk management – Risk assessment techniques (IEC/ISO 31010:2009 (EQV). Brussels, CENELEC, 2010, 15 p.

37. Risk Assessment Tool and Guidance (Including guidance on application). No. OQR012. UK: Health and Safety Executive, 2008, 13 p.

38. Kravets V.A., Denisov E.I., Zyabkina T.I. Ispol'zovanie matematicheskogo modelirovaniya dlya prognoza vliyaniya proizvodstvennogo shuma. Okhrana truda na stroitel'stve ob"ektov neftyanoi i gazovoi promyshlennosti. Moscow, Informneftegazstroi, 1980, vol. 1, pp. 18–23.

39. Current Intelligence Bulletin: NIOSH Practices in Occupational Risk Assessment. External review Draft. *Regulations.Gov.*, 2018. Available at: https://www.regulations.gov/document?D=CDC-2018-0060-0002 (18.07.2018).

Denisov E.I. Noise at a workplace: permissible noise levels, risk assessment and hearing loss prediction. Health Risk Analysis, 2018, no. 3, pp. 13–23. DOI: 10.21668/health.risk/2018.3.02.eng

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VULNERABILITY AS A SPECIFIC CATEGORY OF CONSUMER RISK

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Regulation of legal relationships involving consumers which is adopted in the Eurasian Economic Union countries doesn't highlight peculiarities related to providing consumer rights of specific population groups; people who belong to such groups can't evaluate a situation correctly when they act as consumers due to various reasons, such as their age, physical peculiarities, or some other circumstances.

The author performed this research on the following object: legal relationships which exist between subjects acting on a consumer market, one party here being a consumer who is more vulnerable than others around due to his or her age or disability.

The research goal was to give a definition for "vulnerability" as a specific category of consumer risk which determines basic mechanisms of consumer rights protection.

To achieve this, the author analyzed and assessed consumer risks which occur in such situations when consumers are under a certain age, elderly people, or disabled people. The paper also dwells on some peculiarities of deals which are made by people from the above-mentioned population groups.

The performed research allowed to characterize a consumer "vulnerability" as an increased risk that a deal made by a consumer can have negative consequences due to his or her social or behavioral peculiarities. These peculiarities are shown to influence a person's ability to obtain or understand information; to make a free choice on a product or service; to perceive certain marketing practices adequately (perception of aggressive advertising); being financially capable to make deals. It was proved that specific population groups (young or elderly people, disabled people) are especially prone to consumer risks due to their age or physiologic peculiarities. People from such groups are too gullible and usually unable to adequately estimate all the consequences of a deal they have just made; they can also have limited physical abilities to fulfill their right to cancel a deal they made in due time.

Having performed this research, the author came to a conclusion that it is advisory to spot out specific groups of "vulnerable" consumers in order to protect their rights in a more proper way; it is necessary to supplement legislation on consumer rights protection with specific norms which can help to protect their rights and legitimate interests. As all the EEU countries are now trying to integrate their development processes, common grounds and approaches to national legislation development should be found in international legal acts adopted by the Eurasian Economic Union (EEU).

Key words: *consumer, consumer behavioral risks, consumer protection, disabled people, elderly people, underage people, consumer risks, risk assessment, vulnerability, the Eurasian Economic Union legislation.*

Consumer risk is given little attention as an issue to be examined; but simultaneously it is a rather complicated category that includes physical, economic, social, legal, and behavioral aspects. There are several types of consumer risks described in scientific works; they are physical (physiological), property, and economic ones [1–3]. If we consider a consumer risk to be a specific barrier that prevents a consumer from complete fulfillment of his or her rights, it is advisable to start examining the issue from a physical (physiological) aspect of consumer vulnerability.

Such definitions as "vulnerability" and "vulnerable groups" are used in many spheres associated with social relations and their essence tends to vary depending on a particular sphere. As regards consumer rights protection, experts on consumer risks are of the opinion that a level of risk directly depends on factors that influence consumer behavior: conditions of a deal not being well-defined; amount of knowledge and information a consumer has on the matter; occurrence of hazards, and adequate estimation of a situation and possible damage by consumers themselves [4].

Given all the above said, consumer vul-

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nerability can be defined as an increased risk that a deal made by a consumer can have negative consequences due to his or her social or behavioral peculiarities. These peculiarities influence a possibility to get free access to information, to make a free choice on a product or a service, to adequately perceive specific marketing information (susceptibility to aggressive advertising), a financial capability to make a deal (susceptibility to unfair practices when loan commitments are imposed on a consumer who is not able to pay for a product or a service with available financial resources).

This characteristics allows to examine a situational essence of risks and consumer vulnerability, and it means that 1) consumer "vulnerability" directly depends on a specific situation which a consumer is in; 2) certain consumer groups can be exposed to greater risks in comparison with others.

This research considers the following consumer groups to be "vulnerable": elderly people, disabled people, and young people. This differentiation is determined by objective factors that make these consumer groups "vulnerable". Among such factors there are specific needs that are to be satisfied for complete fulfillment of consumer rights (a consumer is not always able to adequately estimate conditions of a deal or quality of a product he or she buys due to his or her physical and mental abilities, or age) and peculiarities related to protecting rights of such consumer groups (they are not able to defend their rights themselves, and they don't understand basic principles of protection applied in situations when their rights are violated). The above-mentioned circumstances predetermine higher risks for such consumers concerning violations of their consumer rights and legal interests.

As a rule, consumers who belong to the above mentioned groups don't focus their attention on safety as a primary factor influencing their choice of a product or a service. Unfortunately, safety becomes the most significant in such situations when a consumer has to face consequences of a deal when he or she bought a hazardous product or a service. Thus, specific risks are caused for children, elderly people, and disabled people because they, due to their physiological peculiarities, most strongly react to negative impacts caused by nutrition-related factors. Nutrition-related diseases lead to such serious outcomes as renal and hepatic failure, disorders in the brain and nervous system functioning, reactive arthritis, cancer, and death. As per the WHO estimation, diseases caused by low quality food and water annually result in 2.2 million deaths, most of the deceased being children [5].

Electronic commerce (or e-commerce for short) is another sphere where specific consumer risks can occur. Each 7th online purchase involving cross-border transaction entails impossibility to detect a person responsible for consumer rights observance. As services are rendered by a number of providers working together, it is sometimes hard to determine who is responsible – a seller, an Internet provider, a device itself, or a channel. As for electronic sales, there are also several participants in the process, starting from payment services providers to a national mail service, and it is too difficult to determine who is responsible for a quality of a product or a service.

And finally, direct deals between consumers are becoming more and more popular, and it makes the issue even more complicated as here we actually can't find a particular company that renders a service. This international labyrinth of transactions and purchases makes a determination of people responsible for sales of low quality products next to impossible. Thus, the repost issued by the Organization for Economic Cooperation and Development (OECD) stated that 68 % goods sold via the Internet and detected by inspections were forbidden for sales in offline retail outlets [6].

All the above mentioned means it is hard for consumers to protect their rights, and it is practically next to impossible for people with age or physical peculiarities.

As practice shows, legislation adopted in the Eurasian Economic Union countries (EAEU) that regulates relations in the sphere of consumer rights protection is quite generalized and covers all the consumers without any vulnerable consumer categories being singled out. But at the same time contemporary development of social relations implies that certain differentiation in the sphere of consumer right protection is necessary.

According to a definition adopted by the WHO, disabled people are people with limited capabilities who face functional difficulties due to

a disease, deviations, or development malformations, health state, or appearance; their capabilities can also be limited because the environment is not adapted to their specific needs or due to prejudices that a society has in relation to disabled people [7]. As per statistic data collected by the WHO, more than 1 billion people all over the world have this or that disability. It is rather frightening that disability figures are growing rapidly due to population aging and global increase in chronic diseases. It accounts for approximately 15% of the world population (from 110 to 190 million adult people) [8].

In order to reduce impacts exerted by these limitations, the EAEU member-states develop systems of state guarantees on social protection of disabled people that include a) creation of equal possibilities for such people to fulfill their economic, social, cultural, personal, and political rights; b) elimination of limitations on their life activity in order to recover their social status and to help them achieve material independence.

But still, consumer risks for disabled people are often related to limited physical possibility to buy a product due to absence of available infrastructure in retail outlets or due to absence of information about a product which is provided in a way convenient for understanding by people with sensory functions disorders.

We should also mention absence of information about peculiarities related to use of a product by disabled people among consumer risks for them.

Besides, as practice shows, people with limited capabilities often become victims of discrimination, especially by transport companies (it is especially widely spread in case of airlines), when they are refused transportation.

In many EAEU countries it is impossible to acknowledge a disabled person to be a consumer in situations when deals in favor of disabled people are made at the expense of insurance companies or social protection authorities. The issues requires consideration and solving at the legislative level.

Earlier, issues related to protection of elderly consumers rights were not given any special attention. Meanwhile, as per data provided by the WHO, a number of people aged 60 and older will grow from 900 million in 2015 to 2 billion in 2050 (from 12% to 22% of the overall world population).

Population aging is becoming faster and faster. Thus, for example, it took France more than 150 years to adapt to a growth in a share belonging to elderly people in the overall population from 10% to 20%; it will take such countries as Brazil, India, or China just a bit longer than 20 years to adapt to the same changes [9].

A drastic increase in a share of elderly people in the overall world population calls for reconsideration of attitudes towards protection of their rights to consume products or services that are suitable for use taking into account individual peculiarities of such people.

Elderly people, due to their physical and mental age-related peculiarities, can often become victims of circumstances. While still being legally capable at the moment a deal is made, they often don't fully understand the meaning of their actions or they are unable to manage them properly. In this case a deal can be acknowledged as being invalid by court in accordance with the civil legislation.

Mental disorders are widely spread among people older than 60. As per the WHO data, more than 20% people aged 60 and older suffer from mental or neurologic disorders (excluding disorders related to headache), and 6.6% disabilities among people older than 60 are caused by neurologic and mental disorders. Dementia and depression are the most widely spread neuropsychiatric disorders among people belonging to this age group [10].

According to experts research performed in the Russian Federation [1], disputed deals made by elderly people most frequently included the following: sales contracts (22.12%) and deeds of gift (22.12%), last wills (38.46%), renunciation of inheritance (2.88%), giving a power of attorney to dispose of property (3.85%), order to withdraw a last will (0.96%), a contract on a rent with life-long residence (7.69%), a contract on non-repayable transfer of a share in a LLC authorized capital (0.96%), and a contract on handing over a living space into ownership (0.96%) [1].

Besides, people belonging to this group of vulnerable consumers face another serious problem, or so called "discrimination" when elderly people are not treated by financial organizations as a priority target group and consequently they

become the most financially excluded population group.

Thus, as per data of research performed in Russia in 2016, payments for communal services were the most popular financial service among elderly citizens. It was detected that 40% elderly people didn't use plastic cards, 70% didn't have a bank account except one for pension payments, 91% didn't bought insurance services, and 93% never bought products or services in the Internet [11].

Apart from some objective barriers (low incomes, limited access to digital products, low consumer and digital literacy, physical inaccessibility for people with limited abilities) there are also subjective ones (psychological barriers as understanding of one's' incompetence, a fear to make a mistake or to become a victim of a fraud, unwillingness to master new technologies etc.).

Children with their specific habits and preferences are another specific consumer group. And it is important to note that their habits and preferences are often formed not by their parents but by commercials, TV, or the Internet. More and more children aged 3-12 have their own TV set and their own gadget and are active users of social Internet networks. Children buy products themselves and can act both as direct consumers (even at such an early age as 3-5) and as major and active mediators in the process of buying. Children's habits and preferences influence consumer behavior of their parents thus creating a consumer basket of a family. Adult people often choose an internet-content depending on their children's preferences.

Basic consumer risk here is that children most frequently become victims of unfair marketing in online games, mobile applications, and social media-sites. As practice shows, most online games downloaded via popular applications contain built-in or context advertising (regardless of whether a game is free or it was paid for). Consumers of such game content frequently have to pay additional fees to get rid of advertising. Most games also include offers a consumer has to pay for (to buy a game continuation, or bonuses necessary to continue a game). Therefore, a child (being partially capable) is involved into making a deal which is not always approved by his parents.

These are only several aspects that call for necessity to develop specific regulation related to protection of specific "vulnerable" consumers.

Another risk existing for children-consumers in the Internet is related to so called "free" content that is often given in exchange for personal data; parents' control over purchase of such content is practically impossible in spite of the fact that they are actual buyers here. That is, a child can download "free" content (which can be hazardous for a child's psyche) without any preliminary check by parents who would like to make sure that this content is appropriate in terms of a child's age, development, culture, etc.

Lack of attention paid to vulnerable customer groups has become obvious recently, especially under globalization and constantly increasing necessity to develop comparable international legal regulation and specific mechanisms for consumer rights protection concerning various groups of population.

Despite a lot of works on examining risks related to consumption and behavioral peculiarities of consumers [2, 3, 12], an issue of protecting consumer rights of disabled people and socially vulnerable population groups was first raised on the international level only in the revised "UN Guidelines for Consumer Protection" approved by the UN General Assembly in 2015 [13].

National strategies developed in the EAEU countries also include the issue into priority lists; in particular, "The strategy for the state policy in the sphere of consumer rights protection in the Russian Federation for the period up to 2030"[2].

In 2018, when the Russian Federation has taken presidency over the EAEU, issues related to development of human potential, cooperation in social and humanitarian sphere and protection of public interests have been declared as the most significant trends in the further development of the Eurasian integration[3].

Development of harmonized EAEU policy in the sphere of consumer rights protection is based on national legislation harmonization taking into account legal acts adopted by the Eura-

[1] Tyul'kina O.Yu. Forensic-psychiatric expertise of organic mental disorders in elderly people who made property deals: abstract of a thesis for ... Candidate of Medical Sciences. Moscow, 2013, pp. 6.(in Russian).

sian Economic Commission. Recommendations given by the Commission to the EAEU member states are a "soft" administrative mechanism that will allow to implement unified regulation of the consumer rights protection on the whole EAEU territory.

Development of common approaches to protecting rights of vulnerable consumer groups is a new line in the EAEU countries cooperation; it is of great interest both for population (people are sure they purchase a qualitative product or service) and for business (companies can attract more consumers, products manufactures in the EAEU are popularized, imports are replaced).

Finding solutions to problems of disabled people and other socially vulnerable consumers are an unconditional priority and uniqueness of a document that determines unified approaches to protecting rights of specific consumer groups adopted in the EAEU countries.

There are not many examples of specific protection given to such people in world practice; development of a system approach to improvement of their situation can be considered advanced and unique experience.

Nowadays there are no unified (standard) solutions to problems in the sphere of protecting rights of vulnerable consumers in the EAEU countries. Therefore, development of common measures aimed at greater consumer safety in the EAEU countries should take into account aspects of protecting rights of vulnerable consumers in specific spheres of legal relations associated with considerable consumer risks. Such aspects include:

– issues related to provision of information about application and storage of a product (if it is unsafe for a consumer) when a product (service) is sold;

– advertising; notably, elimination of unfair communicative influences (aggressive advertising or advertising that influences specific consumer groups such as children or people who can't adequately estimate and understand their actions and their outcomes) that can cause a damage to consumers; ban on advertising of specific products (tobacco and alcohol in sensitive spheres or in contents oriented at children, teenagers, elderly or disabled people); creations of standards for advertising in the financial sphere;

– the financial sphere concerning availability of bank operations (comprehension of financial risks, restructuring of accounts payable for specific population groups);

– issues related to protection of young consumers when they use communicative technologies (smartphones, pads, or computers);

– updating of electronic commerce and greater digital literacy;

– a prohibition to discriminate vulnerable consumers (no one can be refused to make a deal with on the basis of his or her "vulnerability");

– development of transportation and tourism.

Besides, specific requirements to protection of vulnerable consumers should be introduced at all the stages in a product (service) life cycle:

– manufacturing: specific marking should be made on a product that helps people with limited abilities perceive information about it or that contains additional information if it is required by legislation of those countries where this product will be sold;

– pre-sale stage: a consumer should be given information about peculiarities related to safe use of a consumer product, about a product being appropriate for consumers of a certain age (age limitation), about possible suffocation, about noise levels, a product composition or any other possible hazards; a consumer should be given clear instructions on how to operate a product so that he or she can determine obvious possible hazards before he or she starts using it;

– operation: a consumer should be given a clear and easily comprehended instruction (taking into account requirements existing for specif-

[2] On Approval of the strategy for the RF state policy in the sphere of consumer rights protection for the period up to 2030: The RF Governmental Order issued on August 28, 2017 No. 1837-r. *Official internet-portal of legal information*. Available at: http://www.pravo.gov.ru (access date: 08.06. 2018) (in Russian).

[3] The Message by the RF President to the heads of the Eurasian Economic Union member states. *The RF President: official internet-portal*. Available at: http://kremlin.ru/events/president/news/56663 (access date: 08.06. 2018) (in Russian).

ic consumer groups, for example, Braille, a voice message, etc.) on how to assemble a product and use it safely, information on safe maintenance, storage, lifetime, and utilization of a consumer product, and any other necessary service information.

Development of public interests protection at the overall EAEU level should be based on stronger legal grounds that include transparent requirements for doing business and greater market integration. And a priority task here is to involve businesses into development of specific regulation that takes into account needs of certain consumer groups; efficiency of specific mechanisms for protection of "vulnerable" customers depends on whether a solution to this task is found.

A consumer exposed to increased risks can never actively participate in economic relations associated with production development. As N.I. Golub notes in his research, "the greater consumption is, the more demanding people are to conditions of labor, life, and work" [1]. For example, when assessing people's life and health (on the basis of expenses spent on providing proper life conditions and health), American experts estimated "a price of life" as being equal to 1.5 – 3.0 million US dollars; German experts, 0.5 – 1.0 million US dollars; experts from the Moscow Institution for Issues of Nuclear Energy Development of the Russian Academy of Science, 0.09-0.19 million US dollars [14].

Marketing research on consumer behavior tends to focus on an individual consumer. Peculiarities and needs of an individual consumer are examined in order to get commercial benefits. Such examinations should be aimed at providing "vulnerable" consumers with a possibility to make safe deals without any high consumer risks; deals that can bring additional revenues to businesses.

For example, as D.G. Alekseeva rightly points out, there are spheres where a risk to lose business reputation is especially high. Nowadays there are risks caused by new hazards for lending organizations credibility in relation to changes in the essence and conditions of bank operations; these risks can lead to a loss of business reputation. It makes financial organizations take additional measures aimed at providing safety of such consumer deals[4] [15]. Expenses on providing safety are incomparable with profits brought by concluding safe deals.

Variability of consumer risks determines multiple approaches to managing such risks that should include social, legal, and economic aspects. On the unified EAEU market, management of such risks can be optimized only provided that all the countries, businesses, and communities take active part in the process. Efficiency of a risk-based approach to providing consumer rights is recognized and validated on the international level [16]. The common goal of protecting vulnerable consumer groups should be a possibility for each representative of such groups to completely fulfill his or her consumer rights. This goal can be achieved in the EAEU only if encouragement and protection of vulnerable consumers' rights becomes subject to specific legal regulation on the interstate level.

This approach will make for implementation of protection for socially vulnerable consumer groups and will become one of the most significant components in common work done by the EAEU member states on creation of as comfortable and safe consumer environment for socially vulnerable population groups as only possible.

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References

1. Golub N.I. Klassifikatsiya riskov v lichnom potreblenii [Classification of risks related to private consumption]. *Sotsiologicheskie issledovaniya*, 1999, no. 8, pp. 139–141 (in Russian).

[4] The strategy for increasing financial availability in the Russian Federation in 2018 - 2020 (approved by the Board of Directors of the Central Bank of Russia on March 26, 2018). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_295167/ (access date: 08.06. 2018) (in Russian).

2. Heuze V. Une reconsideration du principe de reparation integrale. *Cycle Risques, assurances, responsabilite – Groupe de travail sur «Incertitude et reparation», Cour de Cassation*. Paris, 2005. Available at: https://www.courdecassation.fr/venements_23/colloques_activites_formation_4/2005_2033_publique_incertitude_8058.himl (16.11.2014).

3. Robentson Thomas S. Consumer behavior. Cambridge, Harvard University, 1999, 800 p.

4. Vasilenko I.V., Tkachenko O.V. Sotsial'nyi risk: k opredeleniyu ponyatii [Social risk: to the definition of the concept]. *Vestnik Volgogradskogo gosudarstvennogo universiteta*, 2014, no. 3, pp. 32–45 (in Russian).

5. Zabolevaniya pishchevogo proiskhozhdeniya [Food-related diseases]. *Vsemirnaya organizatsiya zdravookhraneniya: ofitsial'nyi sait*. Available at: http://www.who.int/foodsafety/areas_work/foodborne-diseases/ru/ (08.06.2018) (in Russian).

6. Protecting consumers in a globalised world: time for a global approach to product safety? *Consumers International: ofitsial'nyi sait*. Available at: https://www.consumersinternational.org/news-resources/blog/posts/a-global-approach-to-product-safety/ (08.06.2018).

7. World report on disability. *World Health Organization*. Available at: http://www.who.int/disabilities/world_report/2011/report/en/ (08.06.2018).

8. 10 faktov ob invalidnosti [10 facts about disability]. *Vsemirnaya organizatsiya zdravookhraneniya: ofitsial'nyi sait*. Available at: http://www.who.int/features/factfiles/disability/ru/ (08.06.2018) (in Russian).

9. 10 faktov o starenii i zdorov'e [10 facts about growing old and health]. *Vsemirnaya organizatsiya zdravookhraneniya: ofitsial'nyi sait*. Available at: http://www.who.int/features/factfiles/ageing/ageing_facts/ru/ (08.06.2018) (in Russian).

10. Psikhicheskoe zdorov'e i pozhilye lyudi [Mental health and elderly people]. *Vsemirnaya organizatsiya zdravookhraneniya: ofitsial'nyi sait*. Available at: http://www.who.int/mediacentre/factsheets/fs381/ru/ (08.06.2018) (in Russian).

11. Antonyan S.S., Imaeva G.R., Aimaletdinov T.A., Korkonosova E.I., Buimuratova L.R., Sharova O.A., Tomilova O.V. Finansovoe povedenie pozhilykh lyudei v Rossii v kontekste digitalizatsii: Issledovanie CGAP/NAFI [Financial behavior of elderly people in Russia in the context of digitalization: research performed by CGAP/NAFR (National Agency for Financial Research)]. Available at: https://wciom.ru/fileadmin/file/nauka/grusha2017/prez/24_antonyan.pdf (08.06.2018) (in Russian).

12. Slater D. Consumer Culture & Modernity. Cambridge, Polity Press, 1998, 139 p.

13. Resolution adopted by the General Assembly on 22 December 2015: 70/186 Consumer protection. Available at: http://unctad.org/en/PublicationsLibrary/ditccplpmisc2016d1_ru.pdf (08.06.2018).

14. Korchagin V.P., Narozhnaya V.L. Ekonomicheskaya otsenka ushcherba ot lyudskikh poter' [Economic assessment of damages caused by population losses]. *Problemy prognozirovaniya*, 1998, no. 5, pp. 112 (in Russian).

15. Alekseeva D.G. Bezopasnoe osushchestvlenie bankovskoi deyatel'nosti: pravovye problemy [Safe banking activities: legal issues]. *Bankovskoe pravo*, 2011, no. 1, pp. 35–40 (in Russian).

16. Better regulation in Europe: Executive summaries. *OECD*, 2010, 157 p. Available at: www.oecd.org/gov/regulatory-policy/45079126.pdf (08.06.2018).

Osaulenko L.N. Vulnerability as a specific category of consumer risk. Health Risk Analysis, 2018, no. 3, pp. 24–30. DOI: 10.21668/health.risk/2018.3.03.eng

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THE RF FEDERAL LAW “ON CHEMICAL SAFETY” AS A TOOL FOR MINIMIZING POPULATION HEALTH RISKS CAUSED BY DEALING WITH HAZARDOUS CHEMICAL WASTES

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The article contains information on hazardous chemical wastes, reasons that cause their occurrence and accumulation in the environment as well as issues related to accumulation of persistent organic pollutants (POPs) in the environmental objects. The authors outline specific features of POPs and their possible influence on the environment and a human body; they also dwell on priority activities accomplished in the RF in relation to POPs after Stockholm Convention on Persistent Organic Pollution was ratified. Provisions of international law in the sphere of providing chemical safety are being consolidated now and operating bodies of Basel, Rotterdam, and Stockholm Conventions interact with each other in order to fix concentrations for chemicals which are persistent organic pollutants and to determine their low contents in wastes. The European Union countries and Canada have submitted their proposals on concentrations of 21 various chemicals in wastes for consideration by all the concerned parties. Scientific validity of the proposed concentrations has been analyzed; the analysis results are given in the article. Given the hazards caused by chemicals wastes that contain POPs for people and the environment, the authors suppose that additional research should be performed on substantiation of POPs safe concentrations in wastes. Taking into account national security and common provisions of international laws related to solving global, national, and regional tasks, the authors note that it is necessary to update legislation on state regulation in the sphere of providing chemical safety; they also give grounds and outline conceptual approaches to creation of the Federal Law "On chemical safety". The article gives a basic idea of this law; its purpose; an object of its regulation; people or economic entities whose activities are subject to its force; a place this law, when passed, is going to have in the RF federal legislation and a system of international agreements that are ratified by the RF. It should be noted that when the Federal Law "On chemical safety" is adopted, it will allow to reduce negative effects produced by hazardous chemical wastes on population and the environment and will have both medical and social-economic outcomes.

Key words: *chemical wastes, persistent organic pollutants, stability, bioaccumulation, cross-border transfer, toxicity, chemical safety, international conventions, federal laws.*

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Occurrence and long-term storage of hazardous chemical wastes, both industrial and consumer ones, is a burning issue all over the world and in the Russian Federation as well; chemicals from such wastes can penetrate the environment and harm human health and environmental objects. The overall volume of industrial and consumer wastes accumulated and accounted in the country amounted to approximately 40.7 billion tons by the end of 2016[1] . But the actual amount can be even greater due to wastes accounting being a rather complicated procedure as some wastes were generated many years ago and they have been stored ever since on non-organized ("spontaneous") dumps that are detected annually. Besides, previously accumulated wastes decay, become diluted, they are exposed to weathering and wash-out, they become covered with dust or hidden by plants that grow on dumps, and experts face serious problems when they try to objectively describe consequences of these processes. Approximately 2% out of the overall wastes mass (about 800 million tons) are hazardous wastes. Over 2006-2016 approximately 140-98 million tons of wastes belonging to the I-IV danger categories were annually generated in Russia.

Dumps where solid household and communal wastes are stored pollute the atmospheric air, soils, underground and surface waters with heavy metals [1–4], polycyclic aromatic hydrocarbons and other persistent organic pollutants [5–8]. Hazardous pollutants penetrate natural water objects including those which drinking water is taken from to be supplied to population [9, 10]. Some authors note that impacts exerted by such dumps cause unacceptable population health risks [11–13]. Experts detect hazardous chemical admixtures in plants tissues [14] and in biological media of animals [15, 16] in zones influenced by dumps where wastes are stored. Experimental and epidemiologic research confirms that hazardous chemicals typical for household and industrial wastes dumps exert negative impacts on population health, including cellular level [16–18]. Medical and demographic losses, in their turn, cause substantial economic losses, both at a regional and a country level [19, 20].

There are the following basic reasons that cause generation and accumulation of hazardous chemical wastes:

– wide application of chemicals with high toxic, mutagenic, and carcinogenic properties in industry, agriculture, and households;

– synthesis and implementation of principally new industrial chemicals that later occur in wastes but their impacts on human health and the environment are not studied sufficiently yet;

– accumulation of persistent organic pollutants (POPs) in the environment due to past-time activities;

– absence of efficient technical solutions concerning processing and recycling of hazardous chemical industrial and communal wastes, as well as absence of efficient techniques for polluted soils recultivation;

– insufficient legislative and regulatory grounds for a system of hazardous wastes treatment in the Russian Federation [21, 22].

World practice shows that legal regulations are widely used to minimize chemical risks caused by industrial and communal wastes. Thus, the Stockholm Convention[2] ratified by 152 countries was adopted in order to limit or even terminate manufacturing and application of all intentionally produced persistent organic compounds (POPs); and gradually reduce and, if possible, completely terminate introduction of unintentionally produced POPs, such as dioxins and furans, into the environment. Implementation of the best available technologies is a basic way that should be applied when treating hazardous wastes.

Activities aimed at identification of dioxins and furans sources and development of emis-

[1] On the situation and protection of the environment in the Russian Federation in 2016: State Report. Moscow, the RF Ministry of Natural Resources and The Environment; NIA-Priroda Publ., 2017, 760 p. (in Russian).

[2] Stockholm Convention on Persistent Organic Pollutants. Available at: http://chm.pops.int/Portals/0/sc10/files/a/stockholm_convention_text_r.pdf (access date: 15.08.2018) (in Russian).

[3] Basel Convention on the control of transboundary movements of hazardous wastes and their disposal. – URL: http://www.basel.int/Portals/4/Basel%20Convention/docs/text/BaselConventionText-r.pdf (access date: 15.08.2018) (in Russian).

sion surveys were accomplished within the frameworks of cooperation with the Basel Convention[3] secretariat. Besides, within the Basel convention framework, experts control transboundary movement of hazardous wastes and try to prevent transportation of hazardous wastes for their consequent disposal in countries where there are no relevant enterprises dealing with safe processing of wastes. Annually as many as 8.5 million tons of hazardous wastes are moved across state borders. The convention covers a wide range of wastes that are considered "hazardous" depending on their origin and composition.

There are more than 20 legislative acts adopted in the European Union (EU) that regulate wastes treatment. We can mention the EU Council Directive 96/61/ec dated September 24, 1996 on integrated pollution prevention and control; the EU Council Directive 2000/76/eu on incineration of wastes dated December 4, 2000; the EU Council Directive 99/31/eu on landfill of wastes dated July 16, 1999, and others. These documents envisage there should be a decrease in wastes volumes aimed for elimination, and a step-by-step transfer to their application as recycled resources. There were certain instruments applied to achieve it, in particular, new taxation on wastes sources, development of processing strategies, updating of existing schemes for quantitative and qualitative wastes parameters.

The Russian Federation is actively developing legal grounds for regulation of wastes treatment. The country ratified the Stockholm Convention in the Federal Law issued on June 27, 2011 No. 164-FL[4] with an initial list containing 12 POPs. Each new chemical included into lists fixed by the Convention is to be ratified separately as per obligations accepted by the Russian Federation. When ratifying the Stockholm Convention, The Russian Federation determined the following priority activities: a ban on manufacturing and application of certain pesticides; a ban on manufacturing and application of polychlorinated biphenyls (PCBs) by 2025 and complete elimination of PCB-containing equipment by 2028; minimization and, if possible, elimination of unintentionally occurring POPs; control over recycling of POP-containing wastes. Polychlorinated biphenyls are industrial products that are being applied at the moment and that are to be eliminated. It is forbidden to produce them in Russia, however at present there are at least 30 thousand tons of them kept in warehouses or in technical appliances (transformers, condensers, etc.) But at the same time, the second hazardous industrial product, hexachlorobenzene, is used in pyrotechnic compounds and is still produced in the country.

The Federal Law "On industrial and consumer wastes"[5]. issued on June 24, 1998 No. 89-FL is constantly updated. More than 80 technical, essential, and organizational corrections have been made into it since it was issued [23].

But at the same time, some issues remain vital; it is especially true for the sphere of providing chemical safety for the population [11, 24, 25]. Several authors note that legal regulation of public relations existing in the sphere can be described as disjoint; it doesn't have a unified legal ground; it can solve only some specific tasks related to providing chemical safety in different legislation spheres [26, 27].

Given all the above mentioned, lawmakers and experts **have developed a draft of a basic federal law that will be entitled "On chemical safety".**

A basic idea of this law, "On chemical safety", is to systematize separate legal standards concerning chemical safety issues and contained in legal acts issued in different legislative spheres; to exclude duplications and existing contradictions between such acts as regards requirements to and necessary activities aimed at providing chemical safety; to fix a set of activities necessary to ensure implementation of state policy for providing chemical safety.

The goal of the law is to create a legal

[4] On ratification of the Stockholm Convention on persistent organic pollutants: Federal law issued on June 27, 2011 No. 164-FL. *President of Russia: the official web-site.* Available at: http://kremlin.ru/acts/bank/ (access date: 17.08.2018) (in Russian).

[5] On industrial and consumer wastes: The Federal Law issued on June 24, 1998 No. 89-FL (last edited on December 31, 2017). *KonsultantPlus* Available at: http://www.consultant.ru/document/cons_doc_LAW_19109/ (access date: 17.08.2018) (in Russian).

framework for implementing activities aimed at gradual reduction of risks caused by negative impacts exerted by hazardous chemical factors on population and the environment until such risks become acceptable.

The law will cover activities performed by state authorities, local authorities, juridical persons, private entrepreneurs, and citizens who participate in chemical safety provision. It is necessary to separate spheres of responsibility between state and local authorities, and it is also quite important to clarify and to enhance rules and responsibilities of citizens, private entrepreneurs, and juridical persons in the sphere of chemical safety.

This law is primarily aimed at implementation of Clauses 41 and 42 of the RF Constitution; these Clauses state that any citizen has the right for protection of his or her health and for the favorable environment; they also state that the Russian Federation is to fulfill its international legal obligations in the sphere of chemical safety.

The draft law contains a set of activities that are necessary to implement the state policy for providing chemical safety; it includes basic measures and activities performed within the frameworks of the existing Federal Laws, such as "On the basics of citizens' health protection in the Russian Federation, " On sanitary-epidemiologic welfare of the population" , "On environmental protection" , "On industrial and consumer wastes" , "On safe handling of pesticides and agrochemicals" , "On industrial safety of hazardous industrial objects" , "On technical regulation"[6], as well as more than 30 other federal laws dealing with some specific matters in the chemical safety sphere.

A true innovation of the law is a definition given in it to chemical safety; it is defined as *"...a situation in which population and the environment are protected from hazardous chemical factors; in which acceptable levels of chemical risks are secured"* (Clause 1). And here chemical risk is determined as per its classical definition, and it is *"...a probability of damage done (taking its severity into account) to human health and (or) damage done (taking its severity into account) to the environment by hazardous chemical factors"*.

The law contains a definition of chemical carcinogens; they are substances that *"cause oncologic diseases or greater risks of their occurrence"*.

It is extremely important that there is an attempt to determine acceptable risk in the law (Clause 1, Item 27): *"an acceptable chemical risk is a level of chemical risk detected via comparison with a risk that exists in everyday life, and probable negative outcomes of which are so negligible that this risk can be considered acceptable by the society and by the state as benefits gained from a chemical factor related to the risk are worth it"*. At present it is the only legislative document in the RF that gives at least some criteria for assessing human health risks.

The law also envisages additional activities aimed at reducing threats, hazards, and risks for the environment and human health; they in-

[6] On the basics of citizens' health protection in the Russian Federation: the Federal Law issued on November 21, 2011 No. 323-FL (last edited on December 29, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_121895/ (access date: 29.07.2018) (in Russian); On sanitary-epidemiologic welfare of the population: the Federal Law issued on March 30, 1999 No. 52-FL (edited on July 29, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_22481/ (access date: 05.02.2018) (in Russian); On environmental protection: the Federal Law issued on January 10, 2002 No.7-FL (edited on December 31, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_34823/ (access date: 05.02.2018) (in Russian); On industrial and consumer wastes: the Federal Law issued on June 24, 1998 No.89-FL (edited on December 31, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_19109/ (access date: 05.02.2018) (in Russian); On safe handling of pesticides and agrochemicals: the Federal Law issued on July 19, 1997 No. 109-FL (edited on April 17, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_15221/ (access date: 05.02.2018) (in Russian); On industrial safety of hazardous industrial objects: the Federal Law issued on July 21, 1997 No. 116-FL (edited on March 07, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_15234/ (access date: 05.02.2018) (in Russian); On technical regulation: the Federal Law issued on December 27, 2002 No.184-FL (edited on July 29, 2017). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_40241/ (access date: 05.02.2018) (in Russian).

clude development of efficient technical solutions as regards processing and recycling of chemically hazardous industrial and consumer wastes, recultivation of polluted soils; implementation of best available environmentally friendly technologies for treatment of chemically hazardous wastes; elimination of stocks containing plant protectors and agrochemicals that are no longer fit for use and persistent organic pollutants in conformity with international agreements which the Russian Federation joined.

Clause 6 enlists powers that belong to the RF federal public authorities in the economic safety sphere; among them it fixes monitoring of chemical risks with assessing efficiency of performed activities that are aimed at step-by-step risks reduction until they become acceptable.

The legal act highlights the significance of prophylaxis measures that are aimed at neutralizing chemical threats, preventing and reducing chemical risks. Basic measures here are provision of safe operations at chemically hazardous industrial objects; greater chemical safety of products; handling of pesticides strictly according to the standards, including their active substances and agrochemicals.

The law also fixes the significance of activities aimed at prevention and reduction of chemical risks occurring in situations when highly toxic chemicals and hazardous persistent chemical compounds are applied.

The law also envisages some measures for preventing and reducing chemical risks caused by sources of chemical hazards. Such measures include:

– preventing emergencies and (or) sabotage at potentially hazardous chemical objects;

– eliminating idle sources of chemical hazards or their processing; development and implementation of up-to-date technologies for chemical safety provision;

– working out efficient technical solutions for processing (recycling) of chemically hazardous industrial and consumer wastes as well as recultivation of polluted territories including:

– ranking and classifying potentially hazardous chemical objects and polluted territories taking into account chemicals properties, and population mortality and morbidity that depend on the environment;

– conducting inspections at potentially hazardous chemical objects and polluted territories, including inventories of enterprises that used to produce hazardous chemicals but don't function any more as well as inventories of territories polluted due to economic activities previously performed on them;

– preparing medical and sanitary profiles for territories where potentially hazardous chemical objects are located and working out measures for their elimination (processing) and (or) chemical risks reduction;

– creating regional databases on how properly and reliably potentially hazardous chemical objects are operated and regional maps showing where chemically hazardous wastes are stored in the RF regions etc.

Another substantial component of the law that helps to protect population from chemical hazards is related to measures fixed in it (Clause 15) and aimed at preventing occurrence and prevalence of health disorders caused by hazardous chemical factors; such measures include technologies applied for diagnostics, correction and prevention of health disorders associated with chemicals factors, control over threats and hazards, and a system for wider spread of information on health risks among population.

Chemical risks are gradually reduced to acceptable levels due to enhancement and development of the national system for chemical safety in the Russian Federation. This national system for chemical safety includes the following basic elements: state authorities, local authorities, juridical persons, private entrepreneurs, and citizens taking part in providing chemical safety in accordance with the RF legislation.

The national system for chemical safety has the following functions:

- monitoring of chemical risks;
- updating of legal regulation and public administration taking into account newly detected chemical risks;
- providing resources for functional elements of the national system for chemical safety;
- developing and implementing activities aimed at neutralization of chemical hazards, chemical risks prevention and reduction, providing greater security of population and territories from hazardous chemical factors as well as assessing how

efficient all the implemented measures are.

When the Federal Law "On chemical safety" is issued, it will allow to reduce negative impacts exerted by hazardous chemical factors on population and the environment and will have both medical and socioeconomic outcomes. In particular, the law will provide additional conditions for health preservation, reduction in population mortality and morbidity, preservation of the country gene fund and keeping it at a level necessary for proper development of the society; it will help to ease social tension caused by occurrence or probability of damaging chemical factors that exert negative impacts on the country population; it will allow to decrease losses due to breaks in economic activities performed by workable population in the RF, burdens on the public healthcare system in the country, and economic damage caused by emergencies and disasters at hazardous chemical objects.

The law will become even more significant for the legal system in the RF after some provisions for implementation of international legal obligations accepted by the Russian Federation in the chemical safety sphere are included into it. It will determine political outcomes that will become obvious through greater international prestige enjoyed by the Russian Federation as well as through greater development of regional and international relations in the chemical safety sphere.

But at the same time, when the law is issued, it will require development of domestic sub-legislative scientific and methodical base as regards:

- working out up-to-date techniques for indication of the most significant hazardous chemicals in environmental objects and human biological media;
- working out up-to-date selective and sensitive identification techniques for new chemicals and mixtures for their consequent classification and marking;
- hygienic regulation for new chemicals and mixtures;
- substantiation of limitation imposed on distribution of chemicals causing the highest risks for population health and environmental objects;
- creation of state standard samples and a databank of hazardous persistent chemicals including persistent organic pollutants;
- development and implementation of up-to-date techniques, means and technologies for protection of population and the environment from hazardous chemical factors;
- development and application of means and technologies for diagnostics, treatment and prevention of health disorders caused by hazardous chemical factors;
- substantiation and implementation of medical and prevention activities for people exposed to chemical risks at potentially hazardous chemical objects as well as in zones influenced by such objects;
- creation of an efficient system for risk communications in order to improve overall culture of the RF population in the sphere related to providing chemical safety.

It will also be necessary to train and develop staff required for providing chemical safety and to improve a system of training for experts in the field including creating better conditions for:

- eliminating shortage of experts in the sphere of toxicology and occupational medicine via optimization of their training as well as making these occupations more attractive and prestigious;
- improving skills of staff, including servicing personnel, necessary for providing chemical safety when potentially hazardous chemicals objects are being operated, as well as for solving issues related to anti-terrorist and anti-sabotage protection of such objects;
- development of educational centers created in federal state scientific and educational establishments in the RF regions;
- development and implementation of educational programs and programs for subject updating on issues related to chemical risks analysis and application of chemical risks management technologies;
- performing drills on organization of interdepartmental interaction including elimination of emergency situations consequences at potentially hazardous chemical objects.

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References

1. Popova E.I. Soderzhanie tyazhelykh metallov v pochve i rastitel'nosti na territorii khraneniya tverdykh bytovykh otkhodov [Heavy metals in soil and vegetation storage area solid waste]. *Sovremennye problemy nauki i obrazovaniya*, 2015, no. 5, pp. 652 (in Russian).

2. Yanturin S.I., Khisametdinova A.Yu., Khisametdinov F.Z. Soderzhanie rtuti v gruntovykh vodakh v okrestnostyakh sela Semenovskoe Baimakskogo raiona respubliki Bashkortostan [The content of mercury in groundwater in the vicinity of the village of Semenovskoye in the Baimaksky district of the Republic of Bashkortostan]. *Ilishevskie chteniya: Sbornik materialov I Vserossiiskoi nauchno-prakticheskoi konferentsii*. In: R.R. Baizigitova, ed. Sibai, 2017, pp. 161 (in Russian).

3. Shilova Yu.O., Vitkovskaya S.E. Otsenka vozdeistviya poligona tverdykh bytovykh otkhodov na soderzhanie tyazhelykh metallov v pochve i rasteniyakh [Assessment of the impact of the solid domestic waste landfill on the content of heavy metals in soil and plants]. *Tendentsii razvitiya agrofiziki: ot aktual'nykh problem zemledeliya i rastenievodstva k tekhnologiyam budushchego: materialy mezhdunarodnoi nauchnoi konferentsii, posvyashchennoi 85-letiyu Agrofizicheskogo NII*. St. Petersburg, 2017, pp. 536–539 (in Russian).

4. Hussain R., Lu K., Chao Z., Xiaofeng Z. Trace elements concentration and distributions in coal and coal mining wastes and their environmental and health impacts in Shaanxi. *Environmental Science and Pollution Research China*, 2018, vol. 25, no. 20, pp. 19566–19584.

5. Rocco C., Seshadri B., Adamo P., Bolan N.S., Mbene K., Naidu R. Impact of waste-derived organic and inorganic amendments on the mobility and bioavailability of arsenic and cadmium in alkaline and acid soils. *Environmental Science and Pollution Research*, 2018, vol. 25, no. 26, pp. 25896–25905.

6. Dagvadorzh M., Chonokhuu S., Davaasuren D., Dorzhsuren B., Borkhuu S. Soderzhanie tyazhelykh metallov v pochvakh poligona po zakhoroneniyu otkhodov v Ulan-Batore [The content of heavy metals in the soil of the landfill for waste disposal in Ulan-Bator]. *Molodoi uchenyi*, 2016, no. 4, pp. 169–181 (in Russian).

7. Grebeneva O.V., Sakiev K.Z., Otarbaeva M.B., Zhanbasinova N.M. Problemy zagryazneniya pochvy tverdymi otkhodami promyshlennykh predpriyatii v Kazakhstane [Problems of soils pollution with solid industrial waste in Kazakhstan]. *Meditsina truda i promyshlennaya ekologiya*, 2014, no. 8, pp. 9–13 (in Russian).

8. Nie E., Zheng G., Shao Z., Yang J., Chen T. Emission characteristics and health risk assessment of volatile organic compounds produced during municipal solid waste composting. *Waste Management*, 2018, no. 79, pp. 188–195.

9. Petrovic M., Sremacki M., Radonic J., Obrovski B., Miloradov M. Health risk assessment of PAHs, PCBs and OCPs in atmospheric air of municipal solid waste landfill in Novi Sad. Serbia. *Science of The Total Environment*, 2018, vol. 644, pp. 1201–1206. DOI: 10.1016/j.scitotenv.2018.07.008

10. Turetskaya I.V., Potaturkina-Nesterova N.I., Shrol'O.Yu., Panteleev S.V., Nemova I.S. Otsenka zagryazneniya tyazhelymi metallami poverkhnostnykh vod ozera v raione poligona [The estimation of open lake water pollution with heavy metals in the area of industrial waste burial]. *Fundamental'nye issledovaniya*, 2012, no. 3–3, pp. 539–541 (in Russian).

11. Kleyn S.V., Vekovshinina S.A., Balashov S.Yu., Khoroshavin V.A., Ukhabov V.M. Gigienicheskaya otsenka kantserogennogo riska zdorov'yu naseleniya, prozhivayushchego v zone vliyaniya mest skladirovaniya otkhodov gorno-obogatitel'nogo kombinata [Hygienic evaluation of the carcinogenic risk to health of the population living in the zone of the exposure to places of the burial storage of waste of mining and processing enterprises]. *Gigiena i sanitariya*, 2018, vol. 97, no. 1, pp. 10–15 (in Russian).

12. Hsieh Y.-K., Chen W.-S., Zhu J., Wu Y.-J., Huang Q. Health risk assessment and correlation analysis on PCDD/FS in the fly ash from a municipal solid waste incineration plant. *Aerosol and Air Quality Research*, 2018, vol. 18, no. 3, pp. 734–748.

13. Yushin V.V. faktory riska zdorov'yu naseleniya ot vozdeistviya vybrosov poligona TKO g. Kurska [Risk factors to the health of the population from the impact of the emissions from the Kursk landfill site]. *Pokolenie budushchego: vzglyad molodykh uchenykh: sbornik nauchnykh statei 4-i mezhdunarodnoi molodezhnoi nauchnoi konferentsii: v 3 tomakh*, Moscow, 2016, pp. 154–157 (in Russian).

14. Barquero J.I., Rojas S., Esbrí J.M., García-Noguero E.M., Higueras P. Factors influencing mercury uptake by leaves of stone pine (Pinus pinea L.) in Almadén (Central Spain). *Environmental Science and Pollution Research*, 2017, pp. 1–9. DOI: 10.1007/s11356-017-0446-8

15. Rumak V.S., Umnova N.V., Levenkova E.S., Turbabina K.A., Pivovarov E.A., Shelepchikov A.A., Pavlov S.D. Dioksiny v srede i organizme zhivotnykh vblizi poligona otkhodov proizvodstva i potrebleniya: k metodologii otsenki riska dlya zdorov'ya naseleniya [Dioxins in the environment and the body of animals near landfill: to the methodology of public health risk evaluation]. *Ekologiya cheloveka*, 2017, no. 10, pp. 9–15 (in Russian).

16. Luzhetsky K.P., Kleyn S.V., Vekovshinina S.A., Tsinker M.Yu. Faktory riska narushenii lipidnogo obmena u naseleniya, prozhivayushchego v usloviyakh mnogosredovoi ekspozitsii kadmiem i mysh'yakom [Risk factors of lipid metabolism disorders in residents of multi-environmental exposure to cadmium and arsenic]. *Meditsina truda i promyshlennaya ekologiya*, 2016, no. 12, pp. 25–29 (in Russian).

17. Zemlyanova M.A., Tarantin A.V. Narusheniya belkovogo profilya cheloveka v usloviyakh vozdeistviya tyazhelykh metallov [Violations of human protein profile in heavy metals exposure]. *Ekologiya cheloveka*, 2012, no. 7, pp. 7–14 (in Russian).

18. Amirova Z.K., Speranskaya O.A. Novye stoikie organicheskie supertoksikanty i ikh vliyanie na zdorov'e cheloveka [New persistent organic supertoxicants and their effect on human health]. Moscow, 2016, 169 p. (in Russian).

19. Popova A.Yu., Zaitseva N.V., May I.V., Kir'yanov D.A. Metodicheskie podkhody k raschetu fakticheskikh i predotvrashchennykh mediko-demograficheskikh i ekonomicheskikh poter', assotsiirovannykh s negativnym vozdeistviem faktorov sredy obitaniya [Methodological approaches to the calculation of actual and prevented as a result of the control and supervisory activities, medical-demographic and economic 95 losses, associated with the negative impact of environmental factors]. *Gigiena i sanitariya*, 2015, vol. 94, no. 7, pp. 95–99 (in Russian).

20. Ryzhakov S.A., Zaitseva N.V., May I.V., Alekseev V.B., Podluzhnaya M.Ya., Kir'yanov D.A. Makroekonomicheskii analiz poter' zdorov'ya, veroyatnostno obuslovlennykh emissiyami zagryaznyayushchikh veshchestv v atmosfernyi vozdukh [Macroeconomic analysis of health losses probabilistically caused by emissions of pollutants into the atmosphere]. *Permskii meditsinskii zhurnal*, 2009, vol. 26, no. 3, pp. 139–143 (in Russian).

21. Yastrebov A.E. Pravovye aspekty ekonomicheskogo regulirovaniya v oblasti obrashcheniya s otkhodami proizvodstva i potrebleniya [Legal aspects of economic regulations of production and consumption waste management]. *Severo-Kavkazskii yuridicheskii vestnik*, 2016, no. 2, pp. 85–91 (in Russian).

22. Kozhevnikov O.A. Sovershenstvovanie sudebnoi praktiki po voprosam obrashcheniya s otkhodami proizvodstva i potrebleniya kak odna iz zadach "obnovlennogo" Verkhovnogo Suda RF [Improvement of judicial practice on the management of production and consumption wastes as one of the tasks of the "renewed" Supreme Court of the Russian Federation]. *Administrativnoe i munitsipal'noe pravo*, 2014, vol. 81, no. 9, pp. 975–980 (in Russian).

23. Ostrovskii N.V. Evolyutsiya federal'nogo zakona "Ob otkhodakh proizvodstva i potrebleniya" [Evolution of the federal law "on production and consumption waste"]. *Voprosy upravleniya*, 2015, vol. 32, no. 1, pp. 170–176 (in Russian).

24. Stepanova I.P., Krasil'nikova S.D. Otsenka kantserogennogo riska dlya zdorov'ya naseleniya v rezul'tate vozdeistviya khimicheskikh veshchestv pri khranenii tverdykh gal'vanicheskikh otkhodov [Assessment of the carcinogenic risk for public health as a result of exposure to chemicals in the storage of solid galvanic waste]. *Uchenye zapiski Komsomol'skogo-na-Amure gosudarstvennogo tekhnicheskogo universiteta*, 2013, vol. 1, no. 2 (14), pp. 111–116 (in Russian).

25. Rastanina N.K., Krupskaya L.T., Golubev D.A., Cherentsova A.A. Otsenka riska dlya zdorov'ya naseleniya, svyazannogo s tekhnogennym zagryazneniem ot otkhodov byvshego gornogo predpriyatiya "Khrustal'nenskii GOK" [Evaluation of health risk due to pollution with waste of the abandoned khrustalnensky mining and processing plant]. *Gornyi informatsionno-analiticheskii byulleten' (nauchno-tekhnicheskii zhurnal)*, 2017, no. 12, pp. 88–95 (in Russian).

26. Vekovshinina S.A., Kleyn S.V., Khankhareev S.S., Makarova L.V., Madeeva E.V., Boloshinova A.A. Otsenka kachestva sredy obitaniya i riskov dlya zdorov'ya naseleniya g. Zakamenska – territorii dlitel'nogo khraneniya otkhodov dzhidinskogo vol'framo-molibdenovogo kombinata [The assessment of

environmental quality and risks for thepopulation of the city of Zakamensk – territory of long-term storage of waste of dzhidinsky tungsten-molybdenum combine]. *Gigiena i sanitariya*, 2017, vol. 96, no. 1, pp. 15–20 (in Russian).

27. Rakhmanin Yu.A., Sinitsina O.O. Sostoyanie i aktualizatsiya zadach po sovershenstvovaniyu nauchno-metodologicheskikh i normativno-pravovykh osnov v oblasti ekologii cheloveka i gigieny okruzhayushchei sredy [Status and actualization of tasks to improve the scientific-methodological and regulatory frameworks in the field of human ecology and environmental hygiene]. *Gigiena i sanitariya*, 2013, no. 5, pp. 4–10 (in Russian).

Pushkareva M.V., Shevyreva M.P., Goncharuk N.N., May I.V., Andrishunas A.M. The RF Federal law “On chemical safety” as a tool for minimizing population health risks caused by dealing with hazardous chemical wastes. Health Risk Analysis, 2018, no. 3, pp. 31–39. DOI: 10.21668/health.risk/2018.3.04.eng

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ON ASSESSING POTENTIAL RISK OF DAMAGE TO HEALTH WHEN DEALING WITH WATER COLLECTION AND PURIFICATION AND PROBABILITY OF ITS OCCURRENCE

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The paper dwells on the assessment of potential health risk (R^1) that can occur in the sphere of water collection and purification. It was shown that activities related to water collection and purification held the leading place ($6.10 \cdot 10^{-3}$) as per $R^1_{average}$ in the priority group "Activities in the sphere of public healthcare, provision of communal, social, and private services" (30.9 %). A share of juridical persons and private entrepreneurs whose activities were ranked as having the 1st and 2nd hazard degree as per health risks amounted to 36 % of all the economic entities who provide water collection and purification for drinking water supply system in the RF regions. Our research object was a typical juridical person that provided a large settlement (more than 19 000 thousand people living there) with drinking water taken from a surface source. Water chlorination is a necessary stage in the technological process of water treatment. Chlorinated organic admixtures are detected in drinking water in concentrations which reach up to 1.3 MPC. The object is ranked as having the 1st hazard degree as per health risk ($R^1 = 2.98 \cdot 10^{-3}$). We quantitatively assessed damage to children's health caused by activities performed by the examined economic entity. We found out that oral introduction of chlorinated organic compounds and their additive effects caused increased non-carcinogenic risk that had the following hazard indexes: functional disorders in the liver HI = 1.74: in the kidneys, HI = 1.72; in the neuroendocrine system (HI = 1.56); in the central nervous system, HI = 1.55; the circulatory system, HI = 1.48. Chloroform makes the greatest contribution into the hazard index value (up to 99.75 %). In-depth research proved there was damage to health of 33 % of the examined children. Damage was estimated as mild in 84 % cases, and as moderate, in 16% cases. Given the gravity of negative outcomes for health, risk realization amounted to approximately 6.5 % of the calculated value of potential risk R^1 for children. It means more than 5,400 additional morbidity cases occur annually at the population level; they are digestive organs diseases, nervous, endocrine, and urinary system diseases. Economic losses amounted to more than 100 million rubles. The authors applied a system of parameterized models that describe cause-and-effect relationships for children population to determine reference chloroform concentrations; they amounted to 0.0031 mg/dm^3 in blood; 0.07 mg/dm^3, in drinking water; reference dose load amounted to 0.0095 mg/(kg · day).

Key words: *sanitary-epidemiologic well-being, economic entity, control and surveillance activity, drinking water, exposure, chlorinated organic compounds, population health, potential health risk, evidences, actual damage to health.*

Basic regulatory public documents issued in the Russian Federation[1] define population health as a primary factor that determines social and economic development of the country and as a most signifi-

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cant individual and public resource. These documents fix the necessity to preserve and to improve health of the country population; it is stressed in them that to achieve this goal it is necessary to provide high standards of sanitary and epidemiologic welfare. And quality of the environment is a significant determinant of health [1–4].

As per data obtained during domestic epidemiologic research, over the last five years on average approximately 5.5 – 10 million additional morbidity cases and 26 – 28 thousand additional deaths in the RF were related to adverse impacts exerted by environmental factors; such factors arose from environmental quality that didn't conform to hygienic standards[2].

Nowadays more than 60% of the RF population live in such conditions where environmental quality is unsatisfactory as it has been revealed by Rospotrebnadzor bodies. In 2015–2017 approximately 9–12% of the RF population weren't provided with good quality water and conditionally good quality water. In 2017 the greatest number of drinking water samples that deviated from the standards as per sanitary and chemical parameters were detected for water taken from centralized water supply systems (13.5%); a number of water samples deviating from the standards as per microbiological and parasitological parameters amounted to 2.9 % and 0.07 % correspondingly [5].

Given all that, it is still vital to get better insight into issues related to possible negative effects that are produced by economic entities and their activities on population health in cases when sanitary legislation is violated [5–7].

A special attention is paid not only to control and surveillance over compliance with the obligatory requirements fixed in the RF legislation on providing sanitary-epidemiologic welfare of the population but also to detection of correlations between population health and impacts exerted on it by environmental factors the quality of which was determined mostly by specific economic entities and their activities [5–9]. Examination of impacts exerted by environmental factors on population health is a complicated process as responses from a body can have multiple causation, they can be reversible and distributed over time, bodies of exposed people can have their peculiarities, sometimes there are no direct cause-and-effect relations etc. [10–21].

A necessity to enrich and deepen knowledge in the sphere is confirmed by issues that arise during practical activities performed by Rospotrebnadzor experts, in the course of control and surveillance activities, sanitary-epidemiologic examinations, assessments, and inspections [5, 7].

Our research goal was to assess structural and spatial distribution of potential health risks caused by economic activities in the "Water collection and purification" sphere and actual damage done by them to exposed population's health (the value of risk realization).

Data and methods. We analyzed quantitative characteristics of the results obtained by Rospotrebnadzor during surveillance and control activities over 2017; we took all the necessary data from "Information on state control (surveillance) and municipal control" 1-control form for federal statistic observation. The structure of the Register that comprised economic entities (juridical persons and private entrepreneurs) whose activities were subject to state sanitary-epidemiologic control (surveillance) was analyzed as per its state on the May 15, 2017.

Potential population health risk (R^l) caused by

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[1] The Constitution of the Russian Federation. Available at: http://constitution.kremlin.ru/ (access date: 04.06.2018) (in Russian). On fundamentals of citizens' health protection in the RF: The Federal law passed on November 21, 2011 No. 323-FL. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_121895/ (access date: 04.06.2018) (in Russian). On sanitary and epidemiologic welfare of the population: The Federal Law passed on March 30, 1999 No. 52-FL. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_22481/ (access date: 04.06.2018) (in Russian).The Message by the RF President to the Federal Assembly on March 01, 2018. *The Official Web-site of the RF President*. Available at: http://kremlin.ru/events/president/news/56957 (access date: 04.06.2018) (in Russian).

[2] On sanitary-epidemiologic welfare of the in the Russian Federation in 2013: The State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2014, 191 p. On sanitary-epidemiologic welfare of the in the Russian Federation in 2014: The State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2015, 206 p. On sanitary-epidemiologic welfare of the in the Russian Federation in 2015: The State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2016, 200 p. On sanitary-epidemiologic welfare of the in the Russian Federation in 2016: The State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2017, 220 p. On sanitary-epidemiologic welfare of the in the Russian Federation in 2017: The State Report. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2018, 268 p.

an economic entity of *l*-th type was determined as a product of how probable a violation of legislation was, gravity of consequences for health (relative damage to health) when legislation was violated, and a scale of impacts exerted on population by an economic entity in accordance with MG 5.1.0116-17[3].

To assess actual realization of a potential health risk, we performed selective profound medical-biological examinations; as a result, we managed to detect morbidity cases that were proven to be associated with impacts exerted by examined risk factors. Any fact of damage to health related to negative impacts exerted by an economic entity's activity was detected in conformity with the MG 2.1.10.3165-14[4]. Our evidence was based on the following chain of cause-and-effect relations: "An activity performed by an economic entity in the sphere of water collection and purification – Environmental factors – Markers of exposure – Indicators of a response – Health disorders"; the chain was epidemiologically and biologically substantiated.

A value of proven damage done to each individual (realized individual risk) was determined as per the following formula: $Rv = 1 - \prod_j (1 - g_j d_j)$, where d_j was a binary parameter characterizing that a damage as a *j*-th disease was proven ($d_j = 0$, if damage wasn't proven, and $d_j = 1$, if damage was proven); g_j was gravity of a disease. Realized individual risk Rv was classified as per the following criteria: $Rv \le 0.05$ meant a damage was low (mild as per risk realization); $0.05 \le Rv \le 0.35$ meant average damage (moderate, average as per its realization); $0.35 \le Rv \le 0.6$ meant high damage (grave, high as per its realization); $Rv > 0.06$ meant damage was extremely high (extremely grave, extremely high as per its realization).

Aggregate realized risk as per a sampling was determined as per the following formula: $Rv^{выб} = \sum_i Rv^i$, and was recalculated into population one as per the following formula: $Rv^{поп} = Rv^{выб} \frac{N}{n} 10^{-6}$, where N was a number of people in an examined population; n was a sampling volume. We calculated an arithmetic fraction $Rv^{поп}$ from R_j^l to assess realization of a potential health risk R_j^l for a *j* contingent caused by an *i* type activity performed by an economic entity.

Hygienic assessments of conditions under which damage to health occurred was done by the example of a zone influenced by a representative economic entity; it was located in Perm region, belonged to the1st risk category, dealt with water collection and purification, and applied chlorination as a basic water disinfection technology. Drinking water quality was hygienically assessed as per five chlorinated organic compounds (chloroform, carbon tetrachloride, 1,2-dichloroethane, dichlorobrommethane, and dibromchloromethane); the assessment was performed as per data collected over 2013-2016 and provided by the Perm Region Center for Hygiene and Epidemiology and Federal Management Center for Medical and Preventive Health Risk Management Technologies, the primary target was to check compliance with the SER 2.1.4.1074-01 and HS 2.1.5.1315-03[5]. To determine any other sources of chlorinated organic compounds, we analyzed emissions with contaminants from stationary sources on the examined territory and revealed there weren't any chlorinated organic compounds in the structure of such emissions. Therefore, the subsequent risk analysis was focused on drinking water only. Health risk was assessed in conformity with the Guide P 2.1.10.1920-04[6].

Epidemiologic assessment and statistical analysis of population health were performed as per data provided by the Territorial Fund for Ob-

[3] MR 5.1.0116-17. Risk-oriented model for control and surveillance activities in the sphere of providing sanitary-epidemiologic welfare. Classification of economic entities, types of activities, and objects under surveillance as per potential health risk applied for organization of scheduled control and surveillance activities: Methodical recommendations. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, 2017, 31 p. (in Russian).

[4] MG 2.1.10.3165-14. A procedure for application of results obtained via medical and biological examinations aimed at proving damage done to population health by negative impacts exerted by chemical environmental factors: Methodical guidelines. Moscow, Federal Center for Hygiene and Epidemiology of Rospotrebnadzor, 2014, 66 p. (in Russian).

[5] SER 2.1.4.1074-01. Drinking water. Hygienic requirements to quality of water from centralized water supply systems. Quality control. Hygienic requirements to provision of hot water supply systems safety. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/901798042 (access date 04.06.2018) (in Russian).
HS2.1.5.1315-03. Maximum permissible concentrations (MPC) of chemicals in water taken from water objects used for communal and drinking water supply. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/901862249 (access date: 04.06. 2018) (in Russian).

ligatory Medical Insurance and official statistic data collected in 2011–2016; to perform them we applied spatial-dynamic analysis and calculated odds ratio and risk difference.

Our profound medical and biological examinations comprised 93 children aged 4-7 who lived on the examined territory and 46 children of the same age who lived on a reference territory where quality of the environmental objects conformed to all the hygienic standards. An accomplished questioning and examinations revealed that the reference group was similar to the examined one in terms of age and sex structure, and social and economic living conditions, but children from the reference group weren't exposed to adverse impacts exerted by factors related to drinking water. An individual environmental exposure, body burden, and health risk parameters were calculated for each examined child. Medical and biological examinations were relevant to an environmental risk profile. Overall, we performed more than 3,600 detection of analyzed chemical elements in blood, examined more than 120 clinical and laboratory parameters with unified clinical, biochemical, immune-enzyme, and immunologic research techniques.

To reveal any clinical peculiarities of children, we accomplished a medical and social questioning, had all the children examined by a pediatrician, gastroenterologist, and neurologist, assessed their somatic state and physical development, determined their health groups, analyzed their development history cards (112/u form), assessed their psychoemotional strain; all the children had electrocardiography, heart rate measuring, and electroencephalography; each child had the thyroid gland, gall bladder, pancreas, liver, spleen, adrenals, and kidneys examined with ultra-sound. We performed a sociological questioning with our own toolset in order to reveal any other initiating factors that could cause health disorders similar to an examined factor.

We detected cause-and-effect relations within "Concentration (dose) of a factor in (from) an environmental object – concentration in blood – response" system with linear and non-linear regression analysis. Our calculation of reference (threshold) level of exposure markers and markers of adverse effects was based on creation of regression models that reflected an influence exerted by exposure on odds ratio (OR) as a parameter characterizing how strong a correlation existed between exposure and a response to it. OR ≥ 1 was considered a criterion showing that a correlation existed. We applied Fischer's test (F) to check statistical hypotheses. Discrepancies were assumed to be statistically significant at $p \leq 0.5$.

Economic component of losses was calculated in accordance with MG 5.1.0095-14 and MG "A procedure for calculating economic losses caused by mortality, morbidity, and disability among employed population of the country"[7].

Results and discussion. As per data taken from departmental statistical reports [8] the overall number of economic entities in the RF with their activities being subject to state sanitary and epidemiologic control (surveillance) amounts to more than 1,005 thousand. We analyzed the structure of the Register that enlisted economic entities taking into account their activities and revealed that such activities as "Healthcare, communal, social and personal services" (30.93%) and "Food stuffs production, catering and food stuffs trade" (35.28%) prevailed in the RF. "Healthcare, communal, social and personal services" activity was also among the top three priority activity types as per an average potential health risk per one economic entity (Rlcp= 7.92*10-4).

A more detailed analysis of "Healthcare, communal, social and personal services" activity

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[6] P 2.1.10.1920-04. Guidelines on assessment of population health risk under exposure to chemicals which pollute environment. Moscow, The Federal Center for State Sanitary and Epidemiologic Surveillance, Public Health Ministry of the Russian Federation, 2004, 143 p. (in Russian).

[7] MG 5.1.0095-14. Calculation of economic losses caused by population mortality, morbidity, and disability associated with negative impacts exerted by environmental factors, actual ones and prevented by control and surveillance. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200129398 (acces date 04.06.2018) (in Russian). A procedure for calculating economic losses caused by mortality, morbidity, and disability among employed population of the country / Approved by the Order of the RF Ministry for Economic Development, the RF Ministry for Public Health Care and Social Development, The Ministry for Finance, The Federal Statistics Service on April 10, 2012 г. No. 192/323n/45n/113 Available at: http://docplayer.ru/30329370-Metodologiya-rascheta-ekonomicheskih-poter-ot-smertnosti-zabolevaemosti-i-invalidizacii-naseleniya.html (acces date 04.06.2018) (in Russian).

[8] "Information on state control (surveillance) and municipal control" 1-control form for federal statistic observation with data collected in 2017.

structure revealed that R^l_{cp} reached its maximum values in such spheres as "Water collection and purification" (R^l_{cp} = 6.10*10^{-3}), "Water distribution" (R^l_{cp} = 5.08*10^{-3}), "Sewage disposal" (R^l_{cp} = 1.73*10^{-3}) (Figure 1).

As per data taken from the Federal Register of economic entities that are subject to sanitary and epidemiologic surveillance (hereinafter the Register), 36.0% of economic entities that deal with water collection and purification belong to the extremely high (1st) risk category and high (the 2nd) risk category as per possible health damage; 27.1%, to the 3rd category (considerable risk); 15.5%, to the 4th category (average risk); 7.79%, to the 5th category (moderate risk); and 21.5%, to the 6th category (low risk).

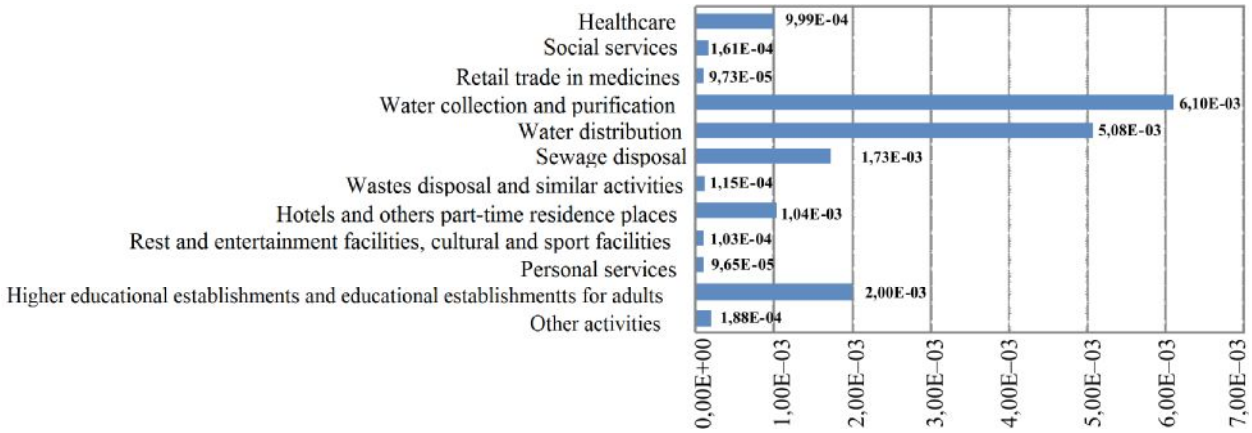

Figure 1. Average potential health risk per one economic entity as per activities performed in the sphere of "Healthcare, communal, social, and personal services"

There are also parameters that characterize average weighted frequency of violations per one inspections (we here speak about probable violations of obligatory requirements, *p(l)*) and parameters that show potential health risks caused by possible non-compliance with obligatory requirements (*u(l)*); they were measured for activities performed in the sphere of water collection and purification for all the economic entities that operated in it, and the obtained values were 4.14 and 0.0367 correspondingly (MG 5.1.0116-17[3]). Discrepancies determining the final value of a potential health risk (R^1) related to "Water collection and purification" activity for each separate economic entity arose from differences in a parameter that characterized a number of population influenced by a *i*-th economic entity (*Mi*, population under exposure, million people). And here the calculated parameter value *u(l)=0,0367* for this activity has potential health risk in its structure that can be caused by possible non-compliance with the obligatory requirements fixed in Clause 19 of the Federal Law passed on the March 30, 1999 No. 52-FL[1]; these potential risks can occur in relation to such health disorders as "Genitourinary system diseases" (u^i*=0.02614)*, "Endocrine, nutritional, and metabolic diseases" (u^i*=0.00668)*, "Diseases of the nervous system" (u^i*=0.00457)*, "Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism" (u^i*=0.00418)*, "Diseases of the digestive system" (u^i*=0.00195)*, "Neoplasms" (u^i*=0.00818)*.

Consumers of services are a basic population contingent that is influenced by activities performed in the sphere of water collection and purification. And as per the data taken from the Register, population under exposure (Mi) to activities performed by economic entities that deal with water collection and purification and belong to the extremely high and high risk categories as per potential health risk is within the following ranges: 0.0066 – 0.84 and 0.00066 – 0.0064 million people correspondingly, and potential health risk (R1) for economic entities form these categories amounts to 1.00*10-3–1.28*10-1 and 1.04*10-4–9.78*10-4 correspondingly.

We analyzed a distribution of economic entities that dealt with this activity as per potential health risk categories in the context of the RF regions (Figure 2); the analysis revealed that economic entities with the 1st and the 2nd categories (extremely high and high health risk) were water supplying organizations located in all the RF regions in large and middle-sized settlements where

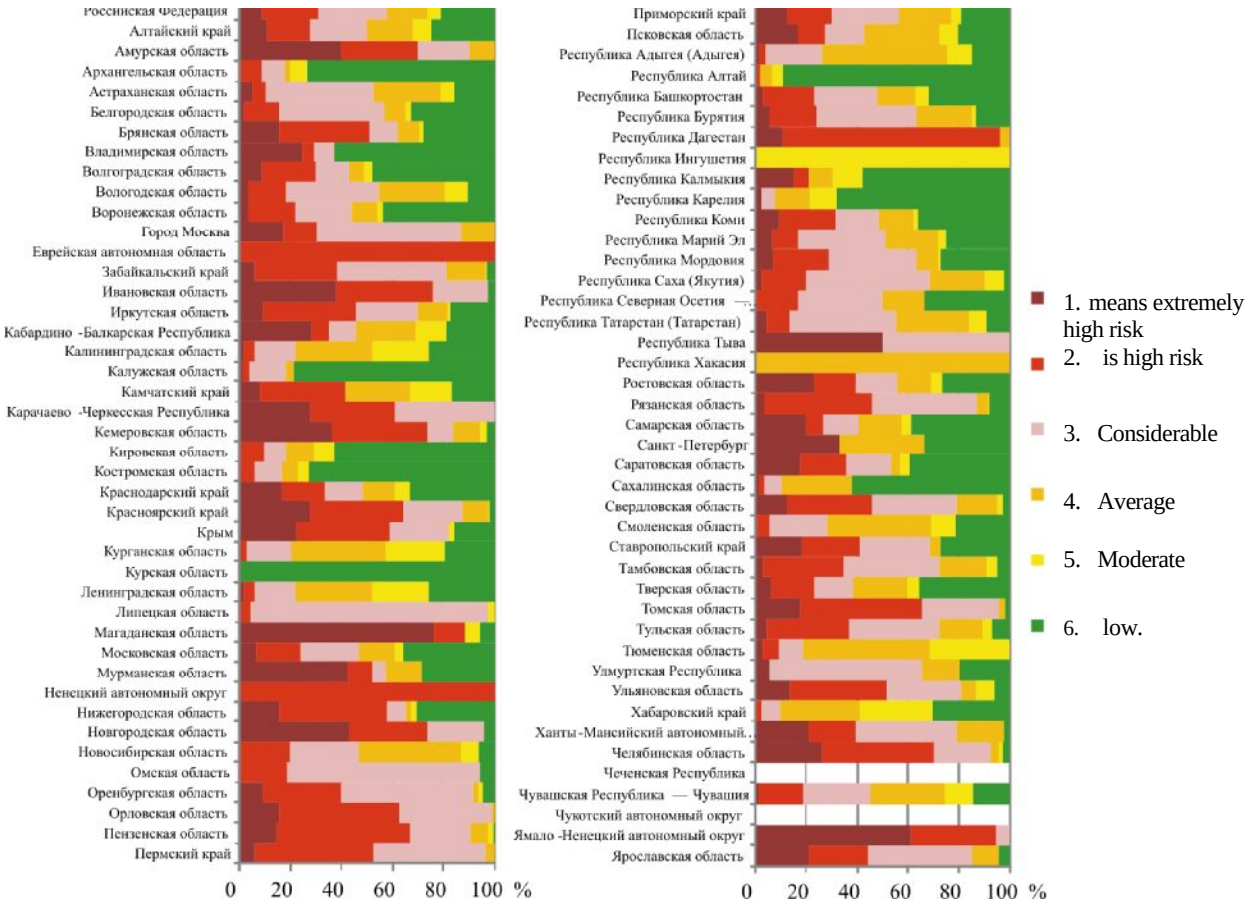

Figure 2. Distribution of economic entities (juridical persons and private entrepreneurs), who deal with water collection and purification (41.00.1), as per health risk categories in all the RF regions (The RF regions are enlisted in the alphabetical order)

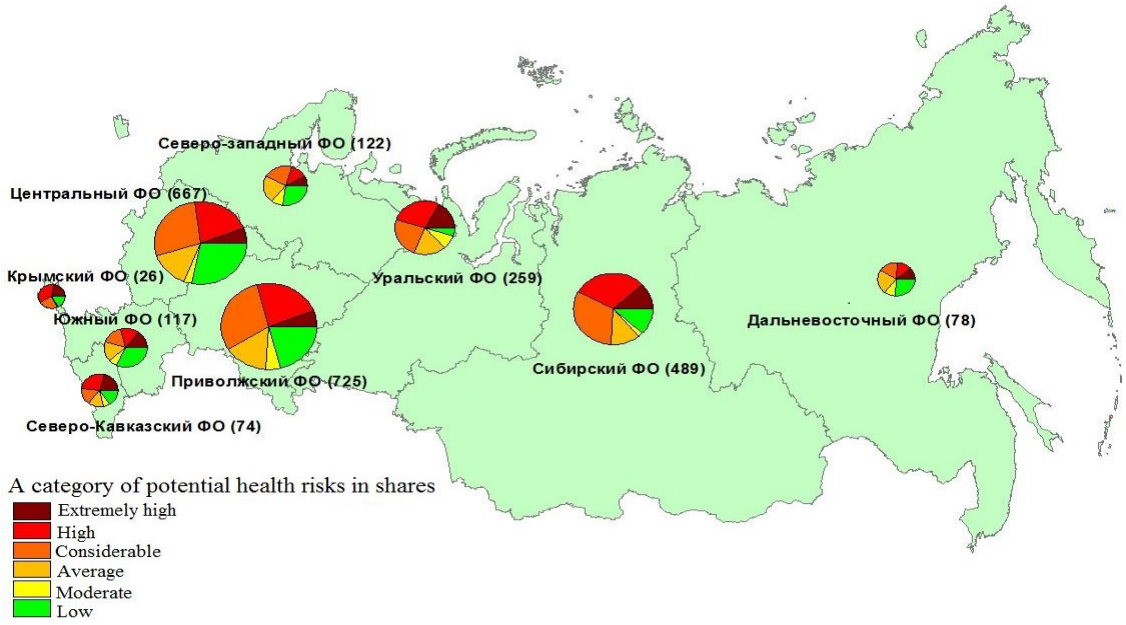

Figure 3. Distribution of economic entities (number and shares) that deal with water collection and purification as per health risks in the RF Federal Districts (the size of a diagram and figures in brackets correspond to the number of economic entities that belong to the 1st and 2nd categories as per potential health risk)

Economic activities performed by economic entities in the sphere of water collection and purification determine quality of water that is taken from centralized water supply systems and used for drinking and domestic consumption. According to data taken from the State Reports "On sanitary and epidemiologic welfare of the population in the RF in 2015 (2016-2017)"[1] approximately 16-19 thousand additional death cases and 1.5 – 2.0 million additional morbidity cases annually are related to drinking water quality. Poor sanitary situation with water sources and secondary water contamination that occurs when water is treated and disinfected are basic reasons for unsatisfactory quality of drinking water. Chlorination as a water disinfection technique is widely spread in the RF; it is one of the cheapest ways to do it and one of the most efficient at the same time. Chlorine disinfection results in formation of toxic compounds, such as chloroform, carbon tetrachloride, dibromchloromethane, dichlorobrommethane, 1,2-dichloroethane and others; these compounds can cause damage to health of population that consume drinking water containing them.

We accomplished a sanitary-epidemiologic examination in order to study influence exerted by economic activities performed by an economic entity that dealt with water collection and purification and violated sanitary legislation in the process; our primary purpose here was to assess impacts on health of exposed children who consumed drinking water with substances formed as a result of hyperchlorination. Our examination revealed that the economic entity took water from a surface water object to supply it to a city population; this surface water object was a pond and it belonged to the 1st risk category. Activities performed by this economic entity belonged to the 1st risk category (extremely high risk), or $R^{1}=2.98*10^{-3}$ (more than 19,000 people under exposure to adverse drinking water contamination).

In 2013 water taken from a surface source for centralized drinking and domestic water supply didn't conform to requirements fixed in sanitary rules and regulations as per sanitary and chemical parameters (iron contents), and microbiological parameters (common and thermal-tolerant coliform bacteria, and coliphages). A share of samples that deviated from standards tended to grow in dynamics and in 2013 amounted to 50% as per sanitary0chemical parameters and to 9% as per microbiological ones.

The stage of hazard identification involves detection of priority chemical compounds that cause the highest population health risks under combined exposure to chemical factors related to drinking water supplied by the examined economic entity dealing with water collection and purification. At this stage we detected the following chemicals that were priority ones in assessing population health risks: chloroform, carbon tetrachloride, 1,2-dichloroethane, dichlorobrommethane, dibromchloromethane, cadmium, manganese, and arsenic. Combined oral introduction of the said chemicals with drinking water (under chronic exposure) can cause health disorders in the kidneys (chloroform, carbon tetrachloride, dichlorobrommethane, and cadmium); liver (chloroform, carbon tetrachloride, dichlorobrommethane, and dibromchloromethane), CNS (chloroform, manganese, and arsenic), neuroendocrine system (chloroform, cadmium, and arsenic), circulatory system (chloroform and manganese), pancreas (carbon tetrachloride). Besides, chloroform, carbon tetrachloride, dichlorobrommethane, dibromchloromethane, cadmium, and arsenic are potential chemical carcinogens as per IARC and(or) U.S.EPA classification.

At the exposure assessment stage, the next one in our examination, we revealed that in 2013-2014 drinking water quality didn't conform to the requirements fixed in SER 2.1.4.1074-01 and HS 2.1.5.1315-03[5] as per chloroform (up to 12.3 MPC), and dichlorobrommethane (up to 4.3 MPC), a share of drinking water samples that deviated from the standards as per contents of these chemicals amounted to 78.6–100.0 %.

At the risk characteristics stage we detected that when chemicals were introduced orally with drinking water, the total individual carcinogenic risk (TCR) for children amounted to 3.89×10^{-5} on the examined territory and it corresponded to the maximum permissible risk. Main contribution into the TCR value was made by dichlorobrommethane (58.1%), chloroform (19.8%), and dibromchloromethane (10.4%).

We assessed non-carcinogenic health risks for children on the examined territory and expressed it in relevant coefficients and hazard indexes; the assessment revealed that hazard index for chloroform was higher than a permissible level and amounted to 1.47. Additive impacts by analyzed chemicals caused increased hazard indexes (HI) for health disorders in the liver, HI 1.74; kidneys, 1.72, neuroendocrine system, 1.56; CNS, 1.55; circulatory system, 1.48. Main contribution into HI value was made by chloroform, including 94.6% in HI for disorders in the neuroendocrine

system; 94.7%, in the CNS; 99.7%, in the circulatory system; 84.6%, in the liver; 85.7%, in the kidneys.

Drinking water quality on the reference territory corresponded to hygienic standards, and carcinogenic and non-carcinogenic health risk parameters related to oral introduction of chemicals in detected concentrations didn't exceed permissible levels.

Therefore, results of environmental risks assessment go in line with the results which were obtained in the course of assessing potential health risks caused by activities performed by an economic entity in the sphere of water collection and purification.

We performed hygienic assessment of conditions that caused damage to health as a result of economic activities performed by an economic entity in the sphere of water collection and purification as these activities led to occurrence of hyperchlorination products in drinking water taken from centralized water supply systems. We also formed an evidence base applying a step-by-step algorithm and accomplishing medical and biological examinations of population health on the examined and reference territories. The assessment and examinations results revealed that morbidity among children (as per data provided by the Territorial Fund for Obligatory Medical Insurance) taken in dynamics over the analyzed period was authentically (pγ0.05) 1.4-5.4 times higher on the examined territory than on the reference one as per classes and nosologies detected at the stages when potential health risks and environmental risks were assessed; these nosologies included diseases of the nervous system (G00-G99 as per ICD-10, including CNS diseases, G10-G47, G90-G99), genitourinary system (N00-N99, including diseases of the urinary excretion system, N00-N39), endocrine system (E00-E99), diseases of blood and blood forming organs (D50-D89), diseases of the digestive system (K71-K77, K20-K31, K55-K63, K80-K83), and congenital malformations (Q00-Q99).

Results of epidemiologic research that was based on the data provided by the Territorial Fund for Obligatory Medical Insurance showed there was an authentic cause-and-effect relationship between the detected risk factors and occurrence of diseases in the nervous system (OR=5.22; DI=4.3-6.4), genitourinary system (OR=2.03; DI=1.6-2.6), endocrine system (OR=1.47; DI=1.1-2.0), blood and blood forming organs (OR=4.08; DI=2.4-7.0), congenital malformations (OR=1.51; DI=1.2-1.9) and others. As per risk ratio, risk of nervous system diseases was 3.0 times higher for children who lived on the examined territory than for those who lived on the reference one; risk of genitourinary system diseases, 1.83 times higher; risk of endocrine system diseases, 1.41 times higher; risk of blood diseases, 3.8 times higher; risk of congenital malformations, 1.39 times higher, etc.

Results of chemical and analytical research showed that dibromchloromethane, chloroform, and carbon tetrachloride were detected in all the examined blood samples taken from children from the examined group; their concentration was authentically up to 5 times higher than in children from the reference group (p γ 0.05). A share of biological blood samples with concentrations of chlorinated organic compounds being higher than in the reference group varied from 5.1% to 90.9%, including those with increased dibromchloromethane (15,9 % samples), chloroform (47.7 % samples), and carbon tetrachloride concentrations (90.9 % samples).

We detected a linear relationship "chloroform concentration in water – chloroform concentration in blood" which was expressed with the following equation: $y=0.00188+0.01782x$ $(F=5.356, p=0.035, R^2=0.26)$, which proves there was a direct correlation between changes in concentration in this substance in blood and changes in its concentration in drinking water; it also explains how chlorinated organic compounds occur in exposed population's blood and a source of this occurrence.

We performed a profound examination of children who lived on the examined territory and detected a set of laboratory parameters deviations in which proved that adverse effects occurred under exposure to drinking water containing products of hyper-chlorination.

Thus, results of biochemical, hematologic, and immune-enzyme research revealed that children from the examined group had the following deviations in their body parameters: imbalance between oxidation and anti-oxidant reactions in a body (an increase in lipid hydroperoxides contents in blood serum, increased 8-hydroxi-2-deoxiguanosine concentration in urine, increased glutathione peroxidase (GlPO), decreased glutathione-S-transferase (GlST) and superoxide dismutase (SOD) in blood serum); imbalance of neuromediators that regulate excitation and inhibition processes in the CNS (increased glutamate concentration and deceased gamma-aminobutyric acid (γ-ABA) in blood serum); filtration functions of kidneys tended to fail (there was an increase in glomerular filtration rate); cytolysis processes was

activated and it was combined with an inflammatory reaction (increased aspartate aminotransferase (ASAT) in blood serum); cytogenetic disorders with increased frequency of cytogenetic abnormalities together with greater destructive changes in cells population on the DNA level. The discrepancies in the said parameters between the examined and the reference groups amounted to 1.2–5 times (p=0.000-0.039).

We detected an authentic cause-and-effect relationship between the following parameters: increased 8-hydroxi-2-deoxiguanosine concentration in urine, increased lipid hydroperoxides in blood serum and increased chloroform and carbon tetrachloride concentrations in blood (R^2=0.51-0.89, 72.1≤F≤520.8, p=0.000); increased chloroform and carbon tetrachloride concentrations in blood and probable increase in GlPO, decrease in GlST and SOD (R^2=0.16-0.88, 11.45≤F≤438.9, p=0.000-0.003); increased chloroform concentration in blood and decreased γ-ABA in blood serum (R^2=0.91, F=725.5, p=0.000); increased chloroform concentration in blood and increased ASAT in blood serum (R^2=0.38, F=48.4, p=0.000); increased chloroform concentration in blood and an increase in glomerular filtration rate in the kidneys (R^2=0.62-0.76 121.85≤F≤241.72, p=0.000); increased carbon tetrachloride concentration in blood and cytogenetic and destructive disorders in buccal epithelium cells (R^2=0.38-0.52, 153.4≤F≤364.9, p=0.000).

Immunologic research performed on children from the examined group allowed to detect disorders in the cellular section of the immunity (inhibited phagocytic activity and T-cells receptors CD4+, CD25+, CD95+), in the humoral section of the immunity (mostly inhibited IgG contends), specific sensitivity to components of factor burden (increased contents of antibodies to chloroform as per IgG criterion), hormonal and mediator regulation (increased free T4 and serotonin contents); all these parameters authentically deviated from the reference level and the same parameters detected in the reference group (p<0.05, the difference was 1.2-2.8 times). Chloroform and carbon tetrachloride were components of factor burden that authentically changed immunity parameters.

We detected an authentic cause-and-effect relationship between the following parameters: an increase in relative and absolute phagocytosis and increased carbon tetrachloride concentration (R^2=0.31-0.70, p<0.05), and increased chloroform concentration (R^2=0.67, p<0.05) in blood; a decrease in IgM concentration under increased chloroform concentration in blood (R^2=0.27, p<0.05), a decrease in IgG concentration under increased carbon tetrachloride concentration in blood (R^2=0.71, p<0.05); a decrease in CD4+, CD25+, CD95+ under increased chloroform concentration (R^2=0.68–0.87, p<0.05); increased serotonin concentration in blood under increased chloroform concentration (R^2=0.43, p<0.05); increased concentration of IgG to chloroform under increased carbon tetrachloride concentration in blood (R^2=0.50, p<0.05).

The results of electrocardiography, heart rate assessment, and clinorthostatic test revealed there was a strain in regulatory-compensatory mechanisms of vegetative regulation as vagotony was the prevailing initial vegetative tone among children from the examined group; it was maintained due to activation of the parasympathetic vegetative nervous system and stronger humoral influences; hypersympathicotonic vegetative reactivity prevailed.

Data obtained via electroencephalography allowed to detect that 2/3 of children from the examined group had functional changes in the brain biorhythms; 90% had signs of dysfunctions in subcortical vegetative brain structures; paroxysmal activity signs (of functional nature) were registered in 20% (discrepancies from the reference group amounted to 3.7-5 times, p<0.05).

Ultrasound research results revealed there was an increase in linear dimensions of the liver and the spleen, reactive changes in the liver and the pancreas parenchyma, disorders in the gall-bladder motility as per hyperkinetic and hypokinetic types; a decrease in the thyroid gland volume, changes in its echostructure (cystic-dilated follicles and diffuse changes), a decrease in peripheral resistance of the vessels; changes in the kidneys structure (hydrocalycosis, cyst, and abnormal development of a kidney), lower renal blood flow rates, increased artery resistance index (frequency of occurrence was up to 3 times higher than in the reference group, p<0.05).

We performed a complex assessment of the somatic state and its results revealed that 36% children from the examined group had drastically disharmonic physical development (boys were excessively high (32.1%), had excessive body weight (18.8%), girls had macrosomia (41.0%), excessive body weight (20.5%), and increased chest circumference (25.7%)), that occurred 1.4 times more frequently than in the reference group (p=0.03-0.046). Only 11.8% children from the examined group had the 1st health group (were practically healthy) that was 2.6 times lower than in the reference group, 30.4% (p=0.00). More than 70% children who lived on the territory where drinking water quality deviat-

ed from standards as per hyper-chlorination products content suffered from functional disorders in their organs and systems (and it was 1.2 time more frequently than on the reference territory); more than 17% children suffered from chronic pathologies with various degree of manifestation (a number of children with the same problems in the reference group was 1.6 times lower).

We analyzed the structure of detected pathology and revealed that the examined children from the both groups most frequently suffered from the digestive organs diseases (38.7% in the examined group, 38.8% in the reference group), nervous system diseases (23.9% and 9.2%, p=0.00), endocrine system diseases (13.2% and 3.1%, p=0.00), and genitourinary system diseases (4.5% and 3,1%, p=0.00). Functional dyspepsia prevailed among the children from the examined group in the digestive organs diseases category (45.4%, that was 3.0 times more frequently than in the reference group, p=0.00); other widely spread disorders were damage to the hepatic-biliary sphere (42.1%, that was 2.2 more frequently than in the reference group, p=0.00). Pathology of hard dental tissues (caries) prevailed in children from the reference group as it was detected in 41.2% cases (28.1% in the examined group, p=0.12).

Pathologies of the nervous system diseases in children from the examined group were represented by astheno-neurotic syndrome (35.6%), vegetative dystonia (17.3%), and neurosis-like syndrome (8.64%), that was 4.0 – 16.4 times more frequently than in the reference group (p=0.00-0.04).

Pathologies in the endocrine system were detected 4.3 times more frequently in the examined group than in the reference one (p=0,00); they were mostly changes in height (being abnormally tall) and nutritional disorders; there were no such pathologies diagnosed on the reference territory (p=0.03-0.04).

Pathologies in the genitourinary systems were mostly represented by neurogenic urinary bladder dysfunction (N31.2, 85.5% of the overall number of diseases in this nosologic category) and it was detected in 13.0% children from the examined group that was 6 times more frequently than in the reference group (p=0.04). Besides, such pathologies as chronic pyelonephritis and congenital pathology in kidneys were detected only in children from the examined group (2.16%, p=0.48); we didn't detect these pathologies in children from the reference group. Diseases in other organs and systems were detected in the examined children from both groups less frequently, and the frequency of their detection didn't have any authentic discrepancies between the two groups.

We detected authentic cause-and-effects relationships between the following: probable occurrence of gastrointestinal tract diseases (functional dyspepsia) under increased chloroform and carbon tetrachloride contents in blood (R^2=0.403-0.61; 51.27≤F≥115.45; p=0.00), and biliary dysfunction under increased carbon tetrachloride concentration in blood (R^2=0.92; F=720.83; p=0.00); probable diseases of the nervous system (neurosis-like and astheno-neurotic syndromes) under increased chloroform and carbon tetrachloride concentration in blood (R^2=0.19-0.73; 17.70≤F≥136.25; p=0.00); probable endocrine system diseases (excessive nutrition) under increased chloroform concentration in blood (R^2=0.59; F=48.98; p=0.00) etc.

Analysis of morbidity among children who lived on the territory where drinking water quality was unsatisfactory as per sanitary-chemical parameters revealed a wide range of combined pathologies, and on average each child suffered from 3.3 various nosologies that was 1.6 times higher than in the reference group.

Our hygienic assessment of conditions that caused damage to health of children who consumed drinking water with hyper-chlorination products was based on the correct choice and analysis of exposure markers and markers of an effect. These markers linked potential damage factors related to activities performed by an economic entity in the sphere of water collection and purification to health disorders. This assessment allowed us to create evidence base and to prove there was damage to children health (for 33% of the examined children) on individual and population levels:

– we showed that activities performed by the analyzed economic entity belonged to the extremely high risk category (R^I=2.98*10^{-3}) and caused potential health risks as per the following nosologies: "Genitourinary system diseases", "Endocrine, nutritional, and metabolic diseases", "Diseases of the nervous system", "Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism", "Diseases of the digestive system", "Neoplasms";

– we detected that chlorinated organic compounds occurred in drinking water due to chlorination of water taken from a drinking water supply source;

– we determined risk factors, chlorinated organic admixtures such as chloroform, carbon tetrachloride, dibromchloromethane, dichlorobrommethane, and 1,2-dichloroethane;

– we revealed that environmental health risks calculated on the basis of average instrumental data collected over a long period of time were 1.5-1.7

times higher than levels that were considered to be permissible (acceptable). Major contributions into health risks were made by chloroform (85-100%). The liver, kidneys, CNS, endocrine system, and blood system were critical damaged organs and systems;

– the exposure was proven by chemical admixtures detected in blood of exposed children who permanently consumed the examined drinking water; the admixtures were characteristic for oral introduction. The frequency of admixtures detection was high in the examined group (up to 91%); admixtures concentrations were authentically ($p<0.05$) higher than in the reference group that was not being exposed to the examined substances;

– we revealed that admixtures occurrence in blood authentically changed the system of homeostasis laboratory parameters; "contaminant in blood – a laboratory parameter" correlations detected with mathematical statistics techniques were biologically plausible, relevant to available scientific data, and stable;

– we proved that exposed children suffered from increased morbidity associated with risk factors and substantiated taking into account clinical, laboratory, and functional parameters that had authentic and biologically substantiated correlations with exposure (markers of exposure);

– the data taken from case histories and questioning results didn't reveal any other authentic factors that could cause detected health disorders.

We formed a personified evidence base for damage to health caused by activities performed by the examined economic entity in the sphere of water collection and purification as these activities made quality of drinking water supplied to population unsatisfactory as per chlorinated organic compounds. This base was created for each examined child and it allowed us to prove a correlation between damage to health and drinking water quality that deviated from standards as per chlorinated organic compounds contents for 31 out of 93 examined children. These 31 children suffered from 3.6 diagnosed diseases (35 diseases diagnosed in "Diseases of the nervous system" nosologic group (G00-G99); 41, "Endocrine, nutritional, and metabolic diseases" (E00-E90); 59, "Diseases of the digestive system" (K00-K93); 2 morbidity cases in "Genitourinary system diseases" nosologic group (N00-N39)).

31 children from the examined group had damage to their health proven but this proven damage differed as per its gravity; thus, in accordance with the scoring scale for proved damage gravity (realized individual risk), damage was estimated as mild (*Rv* was lower than 0.05 or low R) for 26 children; moderate (average gravity), for 5 children (*Rv* was within 0.05-0.35, moderate or average R).

At the population level, damage related to impacts exerted by excessive chlorinated organic compounds concentrations probably caused approximately 5,476 additional morbidity cases among children living on the examined territory as per above mentioned health disorders.

A system of parameterized models that described cause-and-effects relationships allowed us to detect a reference level for chloroform contents in blood; it was equal to 0.0031 mg/dm^3; reference level of this chemical contents in drinking water - its reference concentration amounted to 0.07 mg/dm^3; reference body burden amounted to 0.0095 mg/(kg*day). The obtained data coincide with safety criteria for chloroform contents in drinking water fixed in the RF (0.06 and 0.2 mg/l) and a reference dose under oral introduction, 0.01 mg/(kg*day).

The analysis of obtained results on proven individual and population health damage allowed us to detect total population damage taking into account gravity of consequences (in this case reduced to the gravest ones, or death) and it amounted to $3.88*10^{-5}$, that accounted for 6.5% of the calculated value of potential damage risk concerning children population.

We calculated economic losses caused by additional 5,476 morbidity cases among children that were associated with detected environmental factors and resulted from activities performed by only 1 economic entity in the sphere of water collection and purification with violation of Clause 19 of the Federal law No. 52. Our calculation revealed that only treatment of these cases would require 10.4 million rubles; 18.5 million rubles would be spent by social insurance funds on obligatory payments according to sick-leaves certificates; tax losses due to temporary disability of people who didn't go to work (including parents of sick children) would amount to 1.9 million rubles; economic losses that occurred due to products not being manufactured (GDP losses) would amount to 72.5 million rubles.

Certain activities were performed on a water supply source in order to clean it; after it average annual calculated number of additional morbidity cases among children associated with hyperchlorination products went down to 1.404 (but still, as per social and hygienic monitoring data, in 2016 chloroform concentration in a distribution network

amounted to 3.8 MPC; average annual concentration amounted to 1.2 MPC). As a result, total population health damage amounted to $9.8*10^{-6}$, that corresponded to 1.67% of potential health damage risk calculated for a water supplying organization. Decreased contamination of drinking water with chlorinated organic compounds in a distribution network allowed to move the examined economic entity from the 3rd risk category (considerable health damage, $R_V=3.88*10^{-5}$) to the 4th risk category (average health damage $R_V=9.8*10^{-6}$) as per realized health damage according to calculated data.

Conclusions.

1. Activities in the sphere of water collection and purification take a leading place as per relative average potential health risk per one economic entity ($6.10*10^{-3}$) among priority activities performed in the RF in the sphere of healthcare, communal, social, and personal services (30.9%). 36% of economic entities that deal with water collection and purification (41.00.1) belong to the 1st risk category (extremely high risk) and the 2nd risk category (high risk).

2. When obligatory requirements fixed in Clause 19 of the Federal Law No. 52 passed on March 30, 1999 "On sanitary-epidemiologic welfare of the population" are violated in the sphere of water collection and purification, it causes a potential health risk in relation to such health disorders as "Genitourinary system diseases", "Endocrine, nutritional, and metabolic diseases", "Diseases of the nervous system", "Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism" , "Diseases of the digestive system", and "Neoplasms". People who consume services are a basic population contingent influenced by activities performed in the sphere of water collection and purification. As per data taken from the Register, a number of population under exposure caused by economic entities in the sphere with the extremely high and high risk categories as per potential health risks is within 0.0066 – 0.84 and 0.00066 – 0.0064 million people correspondingly.

3. Economic entities that deal with water collection and purification and belong to the categories with extremely high and high risks are large water supplying organizations located in all the RF regions in settlements where a number of population consuming their services amounts to more than 6.5 thousand and 660 people correspondingly. The greatest quantity of economic entities with the 1st and 2nd risk categories as per potential health damage was detected in Privolzhskiy Federal District, Central Federal District, and Sibirskiy Federal District.

4. Quality of drinking water supplied to population as a result of activities in the sphere of water collection and purification doesn't conform to hygienic standards as per chemical, microbiological, and parasitic parameters in 13.5%, 2.9% and 0.07% cases correspondingly (2017), and as per data collected in 2015-2017 it annually causes approximately 16-19 thousand additional death cases and 1.5-2.0 million additional morbidity cases among population.

5. The examined economic entity (a representative one for the sphere) with the 1st risk category ($R^I=2.98*10^{-3}$) deals with water collection and purification and provides water with such a quality that doesn't conform to the requirements fixed in SER 2.1.4.1074-01 and HS 2.1.5.1315-03 as per chloroform contents (up to 12.3 MPC), and dichlorobrommethane contents (up to 4.3 MPC), a share of samples deviating from the standards as per concentrations of these chemicals amounted to 78.6-100.0%.

6. Results of the environmental risks assessment validate calculated data on potential health risk. Oral introduction of chlorinated organic compounds and their additive effects cause increased non-carcinogenic risk described with hazard indexes for possible disorders in the liver (HI 1.74), kidneys (HI 1.72), neuroendocrine system (HI 1.56), CNS (HI 1.55), and circulatory system (HI 1.48). A major contribution into hazard indexes values is made by chloroform (up to 99.75%).

7. We assessed conditions under which health could be damaged and created an evidence base with a set of medical and biological examinations; it allowed us to prove there was an individual health risk (for 33% of examined children) and population health risk (more than 5,400 additional morbidity cases) that was realized as diseases of the digestive organs, nervous, endocrine, and urinary excretion systems. Individual damage to health was assessed as mild in 84% cases and as moderate in 16% cases.

8. Damage to health was realized at a level of 6.5% of the calculated value of potential health damage risk R^I for children.

9. There were more than 100 million rubles of economic losses caused by additional 5,476 morbidity cases among children that were associated with detected drinking water quality and resulted from activities performed by only 1 economic entity that violated Clause 19 of the Federal law No. 52

10. Basing on the system of parameterized models describing cause-and-effect relationships, we fixed the following reference levels of chloroform con-

tents for children: in blood, 0.0031 mg/dm^3; in drinking water, 0.07 mg/dm^3; reference body burden, 0.0095 mg/(kg*day).

11. The existing situation requires development and implementation of operational and scheduled activities; these activities should be of sanitary-hygienic, legal, technological, organizational, and medical and preventive nature.

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References

1. Global health risks: mortality and burden of disease attributable to selected major risks. *World Health Organization*. Available at: http://apps.who.int/iris/handle/10665/44203 (05.05.2018) (in Russian).

2. Ambient (outdoor) air quality and health. *World Health Organization*. 2016 Available at: http://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health (09.03.2018) (in Russian).

3. Review of evidence on health aspects of air pollution – REVIHAAP project: final technical report. *World Health Organization*. 2013. Available at: http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2013/review-of-evidence-on-health-aspects-of-air-pollution-revihaap-project-final-technical-report (08.02.2018) (in Russian).

4. Human biomonitoring: facts and figures. Copenhagen, WHO Regional Office for Europe, 2015, 104 p.

5. Popova N.V., Zaitseva N.V., May I.V. Opyt metodicheskoi podderzhki i prakticheskoi realizatsii risk-orientirovannoi modeli sanitarno-epidemiologicheskogo nadzora: 2014–2017 gg. [Experience of methodological support and practical implementation of the risk-oriented model of sanitary-epidemiological surveillance in 2014–2017]. *Gigiena i sanitariya*, 2018, vol. 97, no. 1, pp. 5–9 (in Russian).

6. Kleyn S.V., Vekovshinina S.A., Sboev A.S. Prioritetnye faktory riska pit'evoi vody i svyazannyi s etim ekonomicheskii ushcherb [Priority risk factors of drinking water and the related with it economical loss]. *Gigiena i sanitariya*, 2016, vol. 95, no. 1, pp. 10–14 (in Russian).

7. Zaitseva N.V., May I.V., Kleyn S.V., Khankhareev S.S., Boloshinova A.A. Nauchno-metodicheskie aspekty i prakticheskii opyt formirovaniya dokazatel'noi bazy prichineniya vreda zdorov'yu naseleniya v zone vliyaniya otkhodov proshloi ekonomicheskoi deyatel'nosti [Scientific and methodological aspects and practical experience for the formation of the evidential base of hazard to health in the population in the zone of influence of waste from the past economic activity]. *Gigiena i sanitariya*, 2017, vol. 96, no. 11, pp. 1038–1044 (in Russian).

8. Bremya boleznei i otsenka effektivnosti zatrat [Diseases burden and cost effectiveness estimate]. *World Health Organization*. Available at: http://www.who.int/water_sanitation_health/diseases/burden/ru/ (08.05.2018) (in Russian).

9. Rukovodstvo po obespecheniyu kachestva pit'evoi vody. 3-e izdanie. [Guidelines for drinking water quality. The 3rd edition]. *World Health Organization*. Available at: http://www.who.int/water_sanitation_health/dwq/gdwq3rev/ru/ (09.04.2018) (in Russian).

10. Hill A.B. The Environment and Disease: Association or Causation? *Proceedings of the Royal Society of Medicine*, 1965, vol. 58, pp. 295–300.

11. Identifying the environmental cause of disease: how should we decide what to believe and when to take action? London: Academy of Medical Sciences, 2017, 147 p. Available at: http://www.acmedsci.ac.uk/index.php (16.04.2018).

12. Rosenberg D. The Causal Connection in Mass Exposure Cases: «A public Law» Vision of the Tort System. *Harvard Law Review*, 1984, vol. 97, pp. 849–919.

13. Volker S., Schreiber C., Kistemann T. Drinking water quality in household supply infrastructure – A survey of the current situation in Germany. *Int. J. Hyg Environ Health*, 2010, vol. 213, no. 3, pp. 204–209.

14. Fletcher R., Fletcher S., Vagner E. Klinicheskaya epidemiologiya. Osnovy dokazatel'noi meditsiny [Clinical epidemiology. Basics of evidence-based medicine]. Moscow, Media Sfera Publ., 1998, 352 p. (in Russian).

15. Chashchin V.P. Osobennosti primeneniya printsipov dokazatel'nosti pri provedenii gigienicheskikh issledovanii, ekspertiz i otsenok [The specific features of using the evidencebased principles during hygienic studies, examinations, and evaluations]. *Zdravookhranenie Rossiiskoi Federatsii*, 2008, no. 1, pp. 17–18 (in Russian).

16. Gorbanev S.A., Chashchin V.P., Fridman K.B., Gudkov A.B. Primenenie printsipov dokazatel'nosti pri otsenke prichinnoi svyazi narushenii zdorov'ya naseleniya s vozdeistviem vrednykh khimicheskikh veshchestv v okruzhayushchei srede [Operation of evidence-based principles in assessment of causal link between health condition and environmental hazardous substance exposure]. *Ekologiya cheloveka*, 2017, no. 11, pp. 10–17 (in Russian).

17. Vasil'eva M.I. Pravovye problemy vozmeshcheniya vreda, prichinyaemogo zdorov'yu grazhdan neblagopriyatnym vozdeistviem okruzhayushchei sredy [Legal issues related to compensation of damage to citizens' health caused by adverse impacts of the environment]. *Gosudarstvo i pravo*, 2008, no. 10, pp. 26–36 (in Russian).

18. Krasovskii G.N., Egorova N.A. Khlorirovanie vody kak faktor povyshennoi opasnosti dlya zdorov'ya naseleniya [Chlorination of water as a high hazard to human health]. *Gigiena i sanitariya*, 2003, no. 1, pp. 17–21 (in Russian).

19. Shelton D. Human Right & Environmental. Protection: Linkages in Law & Practice: A Background Paper for the WHO. Health and Human Rights Working Series No1. London, 2002, 24 p.

20. The GRADE approach and Bradford Hill's criteria for causation / Schünemann H., Hill S., Guyatt G., E.A. Akl, F. Ahmed. *Journal of Epidemiology & Community Health*, 2011, vol. 65, no. 5, pp. 392–395.

21. Lucas R.M, Mcmichael A.J. Association or Causation: evaluating links between «environment and disease». *Bulletin of the World Health Organization: the International Journal of Public Health*, 2005, vol. 83, no. 10, pp. 792–795.

Zaitseva N.V., Kleyn S.V. On assessing potential risk of damage to health when dealing with water collection and purification and probability of its occurrence. Health Risk Analysis, 2018, no. 3, pp. 40–53. DOI: 10.21668/health.risk/2018.3.05.eng

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FACTORS AND POPULATION HEALTH RISKS UNDER EXPOSURE TO COMPONENTS DETECTED IN DRINKING WATER WITHIN NATURAL HYDROGEOCHEMICAL PROVINCES IN PERM REGION

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Our research goal was to assess health risks for population who consumed drinking water with specific chemical structure systematically and for a long time. Drinking water quality is determined by conditions existing in hydrogeochemical provinces where rocks and soils contain increased concentrations of such hazardous metals as chromium, nickel, lead, manganese, and iron. We showed that low frequency or even absence of non-conformity to hygienic standards for admixtures in drinking water doesn't fully guarantee its safety in complicated hydrogeochemical conditions.

When certain carcinogenic admixtures (cadmium, chromium, nickel, arsenic, and lead) occur together in drinking water even in low concentrations, it can cause unacceptable population health risks. Drinking water taken in examined geochemical provinces in Perm region causes individual lifelong carcinogenic risk which is (under the worst exposure scenarios) equal to $4 \cdot 10^{-3}$. It can be ranked as De manifestis Risk and requires immediate measures to be taken by those responsible to reduce it. Unacceptable non-carcinogenic risks are caused by joint concentrations of arsenic, strontium, and some other compounds in drinking water. The highest risks existing on the examined territories were detected in relation to gastrointestinal tract diseases (HI up to 10.9, basic risk factor is chromium and its compounds), musculoskeletal system diseases (HI up to 11.8, strontium as a basic factor), and central nervous system diseases (HI up to 11.8, basic factors are arsenic, manganese, and lead). Contributions made by various elements into overall risks were different in different provinces.

In some cases, when a certain element occurs in the crust in hazardous concentrations, its contents in drinking water are not observed. We recommend organizations that deal with water supply and sanitary surveillance bodies to take into account peculiarities of a geochemical province and to include admixtures that are contained in the environment in high quantities into monitoring programs and laboratory research.

Key words: *geochemical province, drinking water, chemical structure, safety, health risk.*

The supreme governmental bodies in our country rank provision of population with qualitative and, consequently, safe drinking water among top priorities of the state[1]. The task is not simple as quality of water which is supplied to consumers depends on multiple factors, such as natural composure of water taken from this or that water source, anthropogenic influence (primarily, vol-

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[1] On national goals and strategic tasks in the development of the Russian Federation up to 2024: The RF President Order. *President of Russia: official web-site*. Available at: http://www.kremlin.ru/events/president/news/57425 (access date 20.06.2018).

umes and composure of sewage water discharged into surface water sources or pumped into underground water horizons), water treatment technologies and reactants applied in the process, state of infrastructure etc. [1–3]. Anthropogenic pollution, technical and technological equipment of water treatment systems are manageable factors, while it is practically impossible to change natural chemical structure of a water objects by means that are contemporarily available to us. The situation becomes even more complicated in such cases when a water source that doesn't fully correspond to hygienic requirements has no alternatives or all the water objects located on a specific territory are very similar in their chemical structure due to its natural geochemical peculiarities. The latter is quite typical of hydrogeochemical provinces and it is quite often a very complicated task to supply qualitative and safe drinking water to people who live there. For example, experts detected natural arsenous anomalies in such countries as Argentina, Nepal, Cambodia, Ghana, China, Bangladesh, and Iran; these anomalies exerted substantial impacts on quality of natural and drinking water [4, 5]. One-shot examinations allowed to obtain data on As concentrations in water reaching 2,500 mg/l and it means such water was unsafe for people's health [6].

Experts from Turkey mention problems related to natural increased concentrations of Pb in drinking water sources [7]. Hazardous concentrations of U, As, and Se in underground waters consumed by population were described in works by Mongolian experts [8]. High concentrations of fluorides cause unacceptable health risks for people living in Mastung, Mangochar, and Pringabad regions of Baluchistan province in Pakistan [9, 10] etc.

As per data provided by some experts, there are large regions in Russia where underground drinking water contains increased concentrations of toxic elements and causes health disorders among population [11]. Thus, quality of underground water in the Republic of Dagestan was studied, and, given the basic geochemical preconditions, it allowed to reveal that natural processes that occurred in the north part of the Republic caused formation of a regional hydrogeochemical province where underground water contained increased As concentration, up to 20 MPC [12]. Voteiko highlights functional disorders in the kidneys that occur in Zabaikalsaya biogeochemical province with increased Se concentrations [13]. As per data by A.V. Abramkin, a hyper-fluoric biogeochemical province that formed in the Republic of Mordovia causes endemic fluorosis in people who live there [14]. There are territories with increased natural Rn concentrations that cause risks of radiation exposure for population [15].

Overall, there are several basic factors that determine a possibility of high toxic elements concentration in surface and underground water taken from drinking water supply sources within boundaries of specific hydrogeochemical provinces. They are:

– rocks with relatively high concentrations of such substances;

– high leaching capability of water-containing rocks;

– variability of states in which elements occur in rocks, including easily soluble compounds;

– favorable hydrogeological and hydrochemical conditions determined by high speed of water exchange and chemical types of water;

– intense exploitation of underground water which is used for communal and household water supply; it makes for active interaction between different water-bearing horizons, makes water exchange faster, and enhances intensity of physical and chemical interactions within "water–rock" systems.

Perm region is a territory with a complicated geological structure and diverse chemical composure of its soil and subsoil. There are 14 geochemical provinces in the region and each of them has increased concentrations of specific non-organic compounds (Figure). Accordingly, peculiarities of underlying rocks and soils within these provinces exert their influence on chemical composure of water sources which are used to supply drinking water to population [16, 17]. And there are elements and compounds registered in the provinces and specific for this or that one with proven negative influence on population health even in insignificant concentrations. These elements and compounds are Pb, Cd, Ni, Cr, Mn, V and others (Table 1).

Our research goal was to assess risks of health disorders occurrence among people who permanently and for a long time consumed drinking water with chemical structure characteristic for some geochemical provinces in Perm region.

Data and methods. Boundaries of geochemical provinces were fixed as per data taken from the atlas drawn up by Geokarta-Perm Geological Party as vector layers of GIS ArcView format and scaled 1:1000000. Places were water intake points were located were determined as per data provided by the Perm Regional Office of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being. We connected water sources and spatial intersection of water intake points and geochemical provinces in GIS ArcView 3.2 (ESRI, the USA).

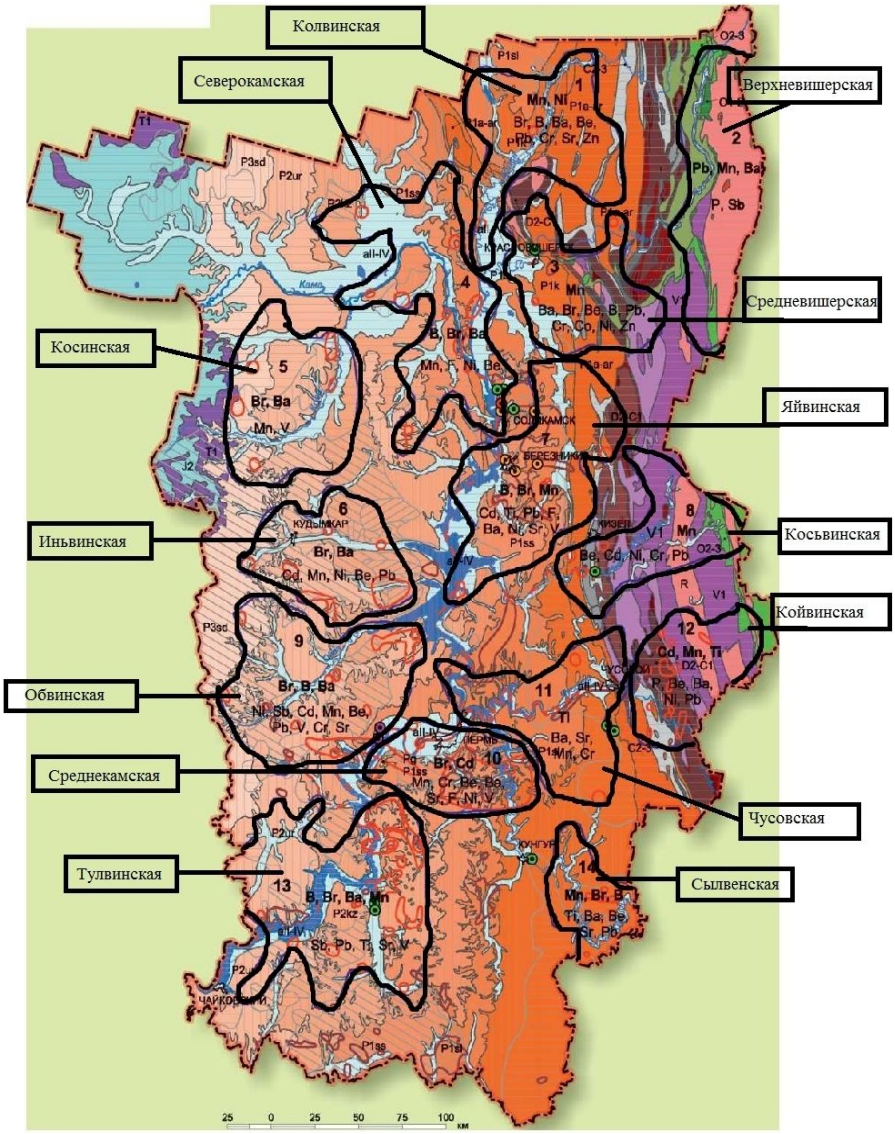

Figure. Geochemical provinces in Perm region [2]

Table 1

Environmental components in geochemical provinces located in Perm region: peculiarities of chemical structure

Geochemical province	Chemical structure and its peculiarities	
	Areal prevalence	Spotted prevalence
Kolvinskaya	Mn, Ni	B, Br, Ba, Be, Pb, Cr, Sr, Zn
Verkhnevisherskaya	Pb, Mn, Ba	P, Sb
Srednevisherskaya	Mn	Ba Br, Be B, Pb, Cr, Co, Ni, Zn
Yay'vinskaya	B, Br, Mn	Cd, Ti, Pb, F, Ba, Ni, Sr, V
Kosinskaya	Br, Ba	Mn, V
Koyvinskaya	Cd, Mn, Ti	P, Be, Ba, Ni, Pb, B, Br
Chusovskaya	Ti	Ba, Sr, Mn, Cr
Sylvenskaya	Mn, B, Br	Ti, Ba, Be, Sr, Pb
Tulvinskaya	B, Br, Ba, Mn	Sb, Pb, Ti, Sr, V
Srednekamskaya	Br, Cd.	Mn, Cr, Be, Ba, Sr, F, Ni, V
Obvinskaya	Br, B, Ba	Sb, Cd, Mn, Be, Pb, V, Cr, Sr
In'vinskaya	Br, Ba	Cd, Mn, Ni, Be, Pb
Kos'vinskaya	Mn	Be, Cd, Ni, Cr, Pb
Severokamskaya	Br, B, Ba	Mn, F, Ni, Be

To assess risks, we chose 3 geochemical provinces where large water intakes were located; they were used to supply water into centralized drinking water supply systems.

Sylvenskaya geochemical province. It is located on the south-east of Perm region and includes central and southern parts of Suksunskiy district and the north of Kishertskiy region. This province is characterized with increased concentrations of B, Ba, Sr (clarke[2] is about 3.1), Pb (clarke is 1.3), Mn (clarke is 15.5). There are water intakes located in the province on Sylva river near Suksun settlement; they supply water to more than 8.3 thousand people.

Koyvinskaya geochemical province. It is located in the east of the region and includes the central part of Gornozavodskiy district, the east of Chusovskoy district and the north of Lys'venskiy district. This province is characterized with increased concentrations of Cd, Mn, Pb, and Ni, Cd clarke reaches 25 and Mn, 15.4, and it is substantially higher than in other parts of the region. There are large water intake in the province located on Pashiyka river (Pashya settlement, 4.1 thousand people) in the central part of Gornozavodskiy district, and on Chusovaya river near Voronovka settlement (about 2.000 people) in the south of Gornozavodskiy district.

Chusovskaya geochemical province. It is located in the central part of Perm region and includes the central part of Chusovskoy district, a small part of Dobryanskiy district in the east, Gremyachnskiy district in the south, and Lys'venskiy district in the north-west. It has the most variable chemical structure as per various metals that can be found there; there are increased concentrations of Mn (clarke is 23.0), Cu (clarke is 3.0), Fe (clarke is 10.0), and Mo (clarke is 11.0). There are some large water intakes located in this province, including those on Chusovaya river in Chusovoy town (48,521 people), on Lys'va river in Kalino settlement (2,425 people), Komarikhinskiy settlement, and some others. The province is characterized with increased concentrations of Mn, Cr. Fe, and Ni.

We assessed quality of drinking water taken from centralized drinking water supply systems as per data provided by the Center for Hygiene and Epidemiology in Perm region; the data were obtained during control and surveillance activities and social and hygienic monitoring; some data were submitted by laboratories of water supplying organizations (results of industrial control performed with conventional techniques). When analyzing quality of drinking and natural water, we examined results of profound chemical and sanitary analysis obtained for an observation period from 2011 to 2016. Heavy metals were examined with atomic absorption analysis that allowed to indentify smallest concentrations, up to 0.0001 mg/sample. We analyzed more than 12,000 results of tests performed on water intakes in Gornozavodskiy district (Pahiyka river, Chusovaya river), Chusovskoy district (Chusovaya river, Lys'va river), Kungurskiy district (Kama river, Yug river), and Suksunskiy district (Sylva river) and others.

Risk assessment methodology was chosen as an efficient instrument for preliminary analysis of the situation; this analysis didn't require substantial financial and organizational costs and simultaneously allowed us to obtain information for further managerial actions [18]. We assessed risks in conformity with the "Guidelines on assessment of population health risks..."[3], and considered adverse effects on health described in the document (Table 2). Lifelong carcinogenic risk equal to 1*10-4 was considered to be acceptable. Hazard index value equal to 1.0 was considered to be acceptable non-carcinogenic risk.

We preset the following exposure scenario: daily water consumption for 350 days per year, with water quality being the same as it was determined at the moment of the research; the period for calculation of carcinogenic risks was equal to 30 years, and non-carcinogenic risks, 70 years. Bearing the precautionary principle in mind, we examined concentrations of admixtures in drinking water at 95% percentile level over the whole observation period.

We took standard parameters of drinking

[2] Clarke value (or clarkes of elements, more often, just clarke) are values that describe average concentration of chemical elements in earth crust, hydrosphere, the Earth, cosmic bodies, geochemical or cosmochemical systems etc., against the overall mass of this system. they are usually given in % or g/kg.

[3] P 2.1.10.1920-04. Guidelines on assessment of population health risks under exposure to chemicals that pollute environment. Moscow, Federal Center for state sanitary and epidemiologic surveillance of the RF Public Healthcare Ministry, 2004, 143 p.

Table 2

Parameters applied in assessing health risks under exposure to chemical admixtures consumed with drinking water

Element	*RfD*, mg/kg-day	Critical organs and systems	*SFo**
Ba	0,07	Kidneys, cardiovascular system	–
B	0,2	Reproductive system, gastrointestinal tract	–
Fe	0,30	Mucous tunics, skin, blood, immune system	–
Cd	0,0005	Kidneys, endocrine system	0,38
Mn	0,14	Central nervous system, blood	–
Cu	0,019	Gastrointestinal tract	–
Mo	0,005	Kidneys	–
As	0,0003	Skin, central nervous system, cardiovascular immune, and endocrine systems, gastrointestinal tract	1,5
Ni	0,02	Liver, cardiovascular system, gastrointestinal tract, blood, body weight	1,7
Pb	0,0035	Central nervous system, peripheral nervous system, blood, development, reproductive system, endocrine system	0,047
Sr	0,6	Kidneys, cardiovascular system	–
Ti	4,00	Reproductive system, gastrointestinal tract	–
Cr	0,005	Mucous tunics, skin, blood, immune system	0,42

Note: * – Carcinogenic potential factor for carcinogens

water consumption and body weight to calculate daily doses [2].

Basic results. Results collected over a long period of time, including those obtained via comprehensive sanitary analysis of examined drinking water, revealed that research structure was similar for different water supply sources. Control programs (both industrial and state one) pay little attention to hydrogeochemical peculiarities of territories. B and Br are admixtures that are characteristic for some geochemical provinces and it is well proven that they produce adverse effects under oral exposure. However, these admixtures are not controlled either by water supplying organizations or sanitary surveillance bodies. Sanitary analysis of drinking water from water intakes located in Chusovskaya province didn't include Sr concentrations although the element is specific for geological rocks that form natural waters there.

Metals, including heavy and amphoteric ones, cause the most serious population health risks as a results of long-term consumption of drinking water in the examined geochemical provinces. Such metals were registered in water practically everywhere (Table 3).

Table 3

Average long-term daily concentrations of priority chemical admixtures in drinking water supplied to population, M±m, mg/dm^3

Chemical element	Geochemical province		
	Sylvenskaya	Koyvinskaya	Chusovskaya
Mn	0,005 ± 0,0008	0,05 ± 0,0075	0,01 ± 0,0015
Cd	0,0002 ± 0,0001	0,0002 ± 0,0001	Not measured
Fe	0,0500 ± 0,0075	0,31 ± 0,05	1,1 ± 0,13
Pb	0,0012 ± 0,0003	0,0001 ± 0,0001	Not measured
Ni	0,0065 ± 0,0012	0,0071 ± 0,015	0,0075 ± 0,015
Cr	0,010 ± 0,006	0,012 ± 0,007	0,018 ± 0,003
Mo	Not measured	0,003 ± 0,0004	0,003 ± 0,0001
Cu	0,005 ± 0,001	0,004 ± 0,001	0,02 ± 0,003
Ba	Ltdl*	Ltdl	Not measured
As	0,0025 ± 0,0005	0,001 ± 0,0003	0,0005 ± 0,0001
Sr	7,30 ± 1,22	Not measured	Not measured

Note: * – means lower than detection limit

Hygienic standards for specific admixtures contents were violated extremely rarely (less than 1% of the overall number of examined samples). Assessment of lifelong carcinogenic risk revealed that the overall situation with drinking water safety was rather alarming. Levels of lifelong carcinogenic risk calculated as per maximum contamination varied from 2.99*10-4 to $4.01*10^{-3}$ and were considered unacceptable (Table 4).

Recalculation of carcinogenic risk per average lifelong va[1]ue allowed to assess risks as substantially less significant however they still were above the upper permissible limit of acceptable risk (1.9*10-4 in Sylvenskaya province; $2.3*10^{-4}$ in Koyvinskaya province, and $2.99*10^{-4}$ in Chusovskaya province). Basic contribution into carcinogenic health risks for population was made by Ni in all three provinces. Concentration of this component in natural water sources is to be analyzed more profoundly. It is necessary to estimate a determination procedure in terms of validity and precision of its results. It also seems vital to examine seasonal fluctuations in admixtures contained in drinking water and to detect primary sources of Ni introduction into it.

Unacceptable non-carcinogenic health risks for population who permanently consume drinking water with quality outlined above occur as regards a number of organs and systems (Table 5).

Table 4

Average long-term concentration of certain chemical elements in drinking water from water intakes located within geochemical provinces

Element	Average long-term concentration, 95% percentile, mg/dm3	Dose, mg/kg-day	Carcinogenic risk	Factor contribution into risk, %
Sylvvenskaya province				
Cd	0,00025	6,85E-06	2,60E-06	0,5
Pb	0,0015	4,11E-05	1,93E-06	0,4
Ni	0,0075	2,05E-04	**3,49E-04**	71,7
Cr	0,0180	2,44E-05	8.89E-05	18,3
As	0,0030	2.94E-05	4,40E-05	9,0
Overall carcinogenic risk			**3,98E-04** (unacceptable)	
Koyvinskaya province				
Cd	0,00057	2,00E-05	5,93E-06	0,10
Pb	0,0001	1,00E-06	1,29E-07	0,0
Ni	0,0080	2,19E-03	**3,73E-03**	93,1
Cr	0,0200	5,50E-04	**2,30E-04**	5,75
As	0,0010	3,00E-05	4,11E-05	1,03
Overall carcinogenic risk			**4,01E-03** (unacceptable)	
Chusovskaya province				
Ni	0,0082	9,63E-05	**1,64E-04**	54,7
Cr	0,0250	2,94E-04	**1,23E-04**	41,2
As	0,0007	8,22E-06	1,25E-05	4,12
Overall carcinogenic risk			**2,99-04** (unacceptable)	

Table 5

Admixtures with carcinogenic effects – Cd, Pb, and Ni compounds

Target organs (systems)	*HI*	Priority risk factors	*HI*	Priority risk factors	*HI*	Priority risk factors
	Sylvenskaya province		Koyvinskaya province		Chusovskaya province	
Kidneys	1,4	Cr	3,4	Cr, Mo	4,2	Cr
Gastrointestinal tract	10,9	Cr, As	6,3	Cr, As	6,7	Cr, As, Cu
Central nervous system	11,8	As, Pb	3,7	As, Mn	1,7	As
Cardiovascular system	8,7	As	3,7	As	2,0	As
Blood	4,0	Pb	1,8	Mn, Fe, Pb	4,1	Ni, Fe
Immune system	8,5	As	4,3	As	5,4	As
Bones	11.8	Sr	–	–	–	–

High risks of functional damage (HI>5.0[4]) are predicted as regards digestive organs, the central nervous system, and the immune system for people living in all the examined geochemical provinces. There were moderate risks (3.0<HI≤5.0) of damage to the immune system and kidneys (for Koyvinskaya and Chusovskaya provinces), and blood (for Sylvenskaya and Chusovskaya provinces) [19].

High risks of damage to bones are characteristic for Sylvenskaya province due to high natural Sr concentrations in drinking water.

We didn't set a task to compare risk levels with actual population morbidity in this work. But still, research performed by some experts is well in line with our results. Thus, O. Yu. Ustinova et al. performed profound clinical and laboratory research and confirmed adverse effects produced by Mn contained in drinking water on children's health; these effects became obvious through neuro-vegetative dysfunctions [20]. There are data on increased Sr concentration registered in blood of people who consumed water with high Sr concentration. Biological aged of exposed people didn't correspond to proper one and musculoskeletal system pathology (posture disorders, deformation of the spinal column and feet) were registered among such people 2.5-10 times more frequently than in the reference group [21].

Conclusion. Our research revealed that geochemical provinces are characterized with different concentrations of such hazardous metals as Cr, Ni, Pb. Mn, Fe, and others, in rocks and soils; it can exert substantial influence on quality of drinking water supplied to population who live within these geochemical provinces.

Absence or rare violations of hygienic standards don't guarantee complete safety of drinking water when its structure is formed under complicated hydrogeochemical conditions.

When some carcinogenic admixtures (Cd, Cr, Ni, As, and Pb) jointly occur in natural and drinking water, it can cause unacceptable population health risks. Carcinogenic risk in the examined provinces of Perm region amounts to 4*10-3(in the worst exposure scenario) which is ranked as De manifestis Risk. Such risk level requires immediate actions aimed at its reduction from decision makers. Unacceptable non-carcinogenic risks are caused by joint occurrence of As, Mn, Sr, and some other compounds in drinking water. The highest risks occurred on the examined territories in relation to gastrointestinal tract diseases (HI is up to 10.9; basic risk factors are Cr and its compounds); musculoskeletal system diseases (HI is up to 11.8; basic factor is Sr in water), and central nervous system diseases (HI is up to 11.8, basic factors are as, Mn, and Pb; contributions made by the elements into the overall risk were different in different provinces). Obviously, it is necessary to work out and implement a system of activities aimed at reducing health risks and at informing all the concerned parties about these risks, including water supplying organizations, population, and local authorities.

We didn't reveal any authentic relationships between average concentrations of elements in the earth crust in a geochemical province and concentrations of admixtures in drinking water in our research. But still, the highest Cd and Pb concentrations were detected exactly in drinking water in those provinces where their concentrations in rocks and soils were the highest. In some cases, when a hazardous element is contained in the earth crust in high concentrations, its content is not measured in drinking water. In relation to that we recommend water supplying organizations and sanitary surveillance bodies to take into account specific features of a geochemical province and include admixtures that occur in high concentrations in the environment into monitoring and laboratory research programs.

As reference concentrations of metals are very low, it seems advisable to improve procedures for quantitative determination of elements in drinking water.

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[4] Criteria are given as per authors' expert opinion

References

1. Ivleva I.A., Alekseev L.S., Boldin A.V. Bar'ernye funktsii tekhnologii podgotovki podzemnykh vod dlya khozyaistvenno-pit'evykh tselei [Barrier Functions of Ground Water Treatment Technologies for Domestic Purposes]. *Vodosnabzhenie i sanitarnaya tekhnika*, 2007, no. 9–2, pp. 33–40 (in Russian).

2. Chudnovskii S.M., Likhacheva O.I., Odintsov V.V. Optimizatsiya protsessov upravleniya traditsionnymi tekhnologiyami podgotovki pit'evoi vody [Conventional technologies of drinking water treatment: managerial processes optimization]. *Evraziiskii soyuz uchenykh*, 2015, vol. 14, no. 5–3, pp. 14–16 (in Russian).

3. Chernikov V.A., Yunusov Kh.B. Otsenka ekologicheskogo sostoyaniya presnykh vod i sovremennye effektivnye metody ee ochistki ot zagryaznenii [Assessment of ecological situation with fresh water and up-to-date efficient techniques for its purification from admixtures]. *AgroEkoInfo*, 2017, vol. 27, no. 1, pp. 7 (in Russian).

4. Nordstrom D.K. Worldwide occurrences of arsenic in ground water. *Public health. Science*, 2002, vol. 296, no. 5576, pp. 2143–2145.

5. Khorasanipour M., Esmaeilzadeh E. Geo-genic arsenic contamination in the Kerman Cenozoic Magmatic Arc, Kerman, Iran: Implications for the source identification and regional analysis. *Applied Geochemistry*, 2015, vol. 63, pp. 610–622.

6. Mukherjee A., Bhattacharya P., Savage K., Foster A., Bundschuh J. Distribution of geogenic arsenic in hydrologic systems: controls and challenges. *Journal of Contaminant Hydrology*, 2008, vol. 99, no. 1–4, pp. 1–7.

7. Duz M.Z., Sagirdag M., Çelik K.S., Hasan M.A., Kilinç E. Geochemical multi-element ICP-OES analysis of borehole waters from SE Anatolia. *Atomic Spectroscopy*, 2016, vol. 37, no. 2, pp. 43–49.

8. S Ariunbileg., Gaskova O., Vladimirov A., Battushig A., Moroz E. Spatial distribution of uranium and metalloids in groundwater near sandstone-type uranium deposits, Southern Mongolia. *Geochemical Journal*, 2016, vol. 50, no. 5, pp. 393–401.

9. Chandio T.A., Khan M.N., Sarwar A. Fluoride estimation and its correlation with other physicochemical parameters in drinking water of some areas of Balochistan, Pakistan. *Environmental Monitoring and Assessment*, 2015, vol. 187, no. 8, pp. 531.

10. Zakutin V.P., Golitsin M.S., Shvets V.M. Aktual'ny problemy izucheniya i otsenki kachestva podzemnykh pit'evykh vod [Current issues in the study and quality assessment of drinking groundwater]. *Vodnye resursy*, 2012, vol. 39, no. 5, pp. 485–495 (in Russian).

11. Krainov S.R., Ryzhenko B.N., Shvets V.M. Geokhimiya podzemnykh vod. Teoreticheskie, prakticheskie i ekologicheskie aspekty [Geochemistry of underground waters. Theoretical, practical, and ecological aspects]. Moscow, TsentrLitNefteGekh Publ., 2012, 672 p. (in Russian).

12. Abdulmutalimova T.O., Kurbanova L.M., Guseinova A.Sh., Ramazanov O.M., Mammaev B.O. Otsenka vliyaniya prirodnykh gidrogeokhimicheskikh provintsii na kachestvo pit'evykh vod i zdorov'e naseleniya (na primere Respubliki Dagestan) [Assessment of influence exerted by hydrogeochemical provinces on drinking water quality and population health (on the example of Dagestan)]. *Trudy Instituta geologii Dagestanskogo nauchnogo tsentra RAN*, 2016, no. 66, pp. 231–235 (in Russian).

13. Voteiko L.G. Selenovyi status i narusheniya funktsii pochek v usloviyakh Zabaikal'skoi biogeokhimicheskoi provintsii [Selenium status and kidney function disorders in conditions of Zabaikalje biogeochemical provinces]. *Ekologiya cheloveka*, 2007, no. 1, pp. 12–15 (in Russian).

14. Abramkin A.V. K voprosu o biogeokhimicheskikh provintsiyakh i gigienicheskoi otsenke kachestva pit'evoi vody [The question of biogeochemical provinces and hygienic drinking water quality assessment]. *Sciences of Europe*, 2016, vol. 8, no. 8–1, pp. 18–22 (in Russian).

15. Chaslavsky M., Danikhelka P., Krzhizh L., Pashkovskii I.S., Sukhankova Ya. Radon v podzemnykh vodakh kak istochnik riska dlya zdorov'ya naseleniya [Radon in ground water as a factor of risk for human health]. *Geoekologiya, inzhenernaya geologiya, gidrogeologiya, geokriologiya*, 2010, no. 3, pp. 270–275 (in Russian).

16. Atlas Permskogo kraya [Perm region atlas]. In: A.M. Tartakovskii, ed. Perm', Perm. gos. nats. issled. un-t Publ., 2012, 124 p. (in Russian).

17. Shiryaeva I.A., Popova E.V. Tyazhelye metally v pit'evykh vodakh razlichnykh prirodnykh geokhimicheskikh provintsii Permskogo kraya kak faktory kantserogennogo riska dlya zdorov'ya naseleniya [Heavy metals in drinking water on geochemical provinces in the Perm region as factors of carcinogenic risk to protect public health]. *Vestnik Permskogo universiteta. Seriya: Biologiya*, 2014, no. 4, pp. 89–96 (in Russian).

18. Zaitseva N.V., Popova A.Yu., Onishchenko G.G., May I.V. Aktual'nye problemy pravovoi i nauchno-metodicheskoi podderzhki obespecheniya sanitarno-epidemiologicheskogo blagopoluchiya naseleniya Rossiiskoi Federatsii kak strategicheskoi gosudarstvennoi zadachi [Current problems of regulatory and scientific-medical support for the assurance of the sanitary and epidemiological welfare of population in the Russian Federation as the strategic government task]. *Gigiena i sanitariya*, 2016, vol. 95, no. 1, pp. 5–9 (in Russian).

19. Shvets V.M., Krainov S.R. Regional'nye gidrogeokhimicheskie provintsii normiruemykh komponentov presnykh pit'evykh podzemnykh vod [Regional hydrogeochemical provinces of the normalized components of the fresh drinking groundwater]. *Izvestiya vysshikh uchebnykh zavedenii. Geologiya i razvedka*, 2014, no. 5, pp. 33–37 (in Russian).

20. O Maklakova.A., Ustinova O.Yu., Luzhetskii K.P., Baidina A.S., Mazunina D.L., Permyakov I.A., Osheva L.V. Neirovegetativnye disfunktsii u detei, prozhivayushchikh na territorii s povyshennym urovnem margantsa v pit'evoi vode [Neurovegetative dysfunctions at children, living in the territory with the raised level of manganese in drinking water]. *Izvestiya Samarskogo nauchnogo tsentra Rossiiskoi akademii nauk*, 2013, vol. 15, no. 3–6, pp. 1845–1849 (in Russian).

21. Vandysheva A.Yu., Luzhetsky K.P., Ustinova O.Yu., Shcherbakov A.A. Tempy biologicheskogo sozrevaniya i osobennosti narushenii kostno-myshechnoi sistemy u detei v usloviyakh peroral'noi ekspozitsii strontsiya s pit'evoi vodoi [Rates of the biological maturation and particularities of violation of the locomotor system in children under conditions of oral exposure to strontium in drinking water]. *Zdorov'e naseleniya i sreda obitaniya*, 2015, vol. 273, no. 12, pp. 45–47 (in Russian).

Fomenko A.N., Aristov V.A., Maklakova O.A., Khoroshavin V.A. Factors and population health risks under exposure to components detected in drinking water within natural hydrogeochemical provinces in Perm region. Health Risk Analysis, 2018, no. 3, pp. 54–62. DOI: 10.21668/health.risk/2018.3.06.eng

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APPLICATION OF BABY WALKERS IN RUSSIA: EPIDEMIOLOGICAL ASPECTS

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As per various research data, from 42 to 90 % families all over the world use baby walkers. There are some data implying that baby walkers prevent motor skills from their natural development and are to a certain extent dangerous for infants' health. Prevalence of damages associated with baby walkers varies from 7 to 50 % according to different estimations. Our research goals were to determine reasons for application of baby walkers in Russia and their prevalence in Russian families; to assess levels and structure of children injuries caused by baby walkers and their influence on motor development and on walking pattern formation.

We performed three cohort pieces of research with pseudo-retrospective design. The overall sampling included 749 children; "baby-walker" groups consisted of 363 infants. We also performed an anamnestic questioning of parents with specially designed anonymous questionnaires. The research was accomplished on typical Russian territories (Rzhev and Rzhev district in Tver' region, population amounts to approximately 60.3 thousand people).

We detected that frequency with which baby walkers were applied among children on the examined territories was similar to average frequency detected worldwide and amounted to 62.11 ± 18.5 %. Parents think that basic advantages and reasons for application of baby walkers are as follows: they make a child to develop faster; they keep a baby busy and help to keep it safe; they entertain a baby; it is a tradition. The detected level of injuries caused by baby walkers was relatively low (15.4 %). There were no injuries that require medical aid. Our research didn't reveal any statistically authentic influence exerted by baby walkers on formation of acquired static deformations in infancy. There is also no statistically authentic discrepancy between children from "baby walkers" group and "without baby walkers" group in the examined sampling when they reach the following stages in their development: "standing with a support" and "moving with a support". But on average, children who grew with baby walkers started to walk on their own with a 13-day delay. We detected a statistically authentic strong correlation ($p<0.01$) between application of baby walkers and risk of tiptoe walking (RR=3.56; CI 2.56–4.99 for 95 % provision). A longer period of tiptoe walking in "baby walkers" group confirms that baby walkers exert long-term negative influence on walking pattern structure. We detected the following additional (attributable) population risk (PAR): absence of walking on one's own, PAR=4.45–5.3 %; tiptoe walking, PAR=19.6–23.4 %. Application of baby walkers in families from the examined population decreased from 52.03 to 43.66 % and it means that active informative campaigns aimed at explaining baby walkers dangers to parents and guardians were quite efficient. It is advisable to perform further research on the matter.

Key words: *baby walkers, children injuries, stages in motor development, delay in onset of walking, tiptoe walking, idiopathic toe-walking.*

Any parents want their baby to develop as fast and actively as possible and they are ready to do anything to help in the process. It's an integral part of our biological program, an instinct that makes us take care of our offspring. Baby walkers were initially invented as a toll for providing this help;

but they turned out to be a rather controversial device. As per data obtained in various research [1–8], including domestic one [9,10], baby walkers prevent motor skills from their natural development and even cause a certain threat for health, primarily related to additional traumatism.

Examinations of baby walkers[1] as a phenomenon that influences health have been accomplished in various research all over the world since late 80ties last century. These

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[1] *Baby walkers* is a technical device. It has a base made of hard plastic sitting on top of wheels with additional appliances that help to keep a baby in a vertical position.

examinations can be divided into three basic groups epidemiological ones, examinations of injuries associated with baby walkers, and assessment of their effects on motor skills development.

Epidemiological aspects related to application of baby walkers have been examined since early 90ties last century. The first examination on the issue was performed in Denia (Spain) in 1992-1993. S.L. Santos et al. conducted a questioning that lasted from November 1, 1992 to January 31, 1993 and included parents of 207 children aged from 3 to 24 months [11]

The authors revealed that 42% children aged from 4.3 to 13.4 months were at least once put into baby walkers, and parents of 46.7% out of this number applied them every day. They also revealed a statistically significant inverse correlation (r>–0,6) between frequency and duration with which baby walkers were applied and a mother's education. It was shown that parents reported on the following presumable advantages of baby walkers: 34.2% stated it was comfortable for parents; 10.9% said baby walkers entertained their babies; 12.9% believed baby walkers helped their children to develop[; 46.3% respondents didn't mention any advantages.

Also parents stated there were some hazards caused by application of baby walkers; thus, 33.5% mentioned deformation of lower extremities; 43.0%, accidents, including 33.5% mentioning injuries, and 12%, falling off the stairs; 27.2% said there were no any hazards. As per data collected by the authors, 24.9% children who spent some time in baby walkers were injured (76.2% fell; 14.3% had ambulatory injuries, and 4.8% were taken to hospitals to be treated after an injury). Injuries much more frequently occurred among boys.

The next research was performed in Baltimore in 1993 by Doctor A. Trinkoff and Doctor P.L. Parks [12]. They questioned parents who had children aged 3-12 months and revealed that baby walkers were used quite frequently, in 66% cases (n=77). It is remarkable that this frequency was even higher among low-educated parents. Parents mentioned the following reasons for application of baby walkers: to entertain a baby, to limit its movements, to help it to develop locomotor skills.

Data were collected via individual questioning performed among parents; the total number of participants were 158 people, and 55% respondents stated they applied baby walkers. The basic reasons for that were the following: baby walkers brought positive emotions to babies; application of such devices started with the eldest child in a family (a tradition). No respondents in a "baby walkers" group thought that safety issues could make them abandon baby walkers; 48% respondents in a "without baby walkers" group stated that thinking about safety would persuade them to stop using the device. 12.5% children who spent some time in baby walkers had at least one injury during this period.

In 1998 American scientists conducted standard interviews among 254 people (parents or guardians) who applied for medical aid to a clinic within a month in which the research took place [14]. Parents of 77% (n-119) firstborns and 85% of the second and consequent child applied baby walkers. The researchers didn't reveal any statistically authentic discrepancies between children from "baby walkers" and "without baby walkers" groups as regards a child's sex, being the eldest or not in a family, parents' race or education, or a type of guardianship. There were also no discrepancies between the groups related to information given by a pediatrician as regards hazards caused by baby walkers application. 97% parents in a "baby walkers" group heard about such devices prior to a childbirth but 65% didn't start using them after a child was born. 61% of those who applied the device stated there was no external influence that made them buy it; 75% bought the device on their own. These decisions didn't correlate with parents' education or seniority of a child in a family. Finally, 78% parents thought baby walkers were useful, and 72% parents stated the device fastened the development of an independent walking skill[2].

The research conducted by two British scientists D. Kendrick and P. Marsh in 1998 contains data obtained via questioning of parents with children aged 3-12 months; the parents were registered in each of 36 ambulances for primary reception in Nottingham, Great Britain (n=2,152) [15]. The number of answers amounted to 74%. 50% families applied baby walkers.

[2] ***Independent walking*** is walking on two feet on one's own, without any support, making more than 5 steps, with further progress.

It was detected that application of baby walkers wasn't authentically correlated with either living on hardship allowance (*OR* = 1,42; 95 % *CI* = 1,02–1,99), or renting a housing (*OR* = 1,46; 95 % *CI* = 1,04–2,04), dwelling in a poor district (*OR* = 1,42; 95 % *CI* = 1,06–1,91), parents being unemployed (*OR* = 0,64; 95 % *CI* = 0,41–0,99). Families that applied baby walkers installed smaller number of gates that lock the staircases (χ^2 = 4,36, 1*DF*, *p* = 0,037) and fire control systems (χ^2 = 6,80, 1*DF*, *p* = 0,009). in their houses. There were a lot of probable home hazards in their houses (Mann-Whitney test *U*, *Z* = –2,90, *p* = 0,004). However, there were no differences detected between risks of injuries and risks related to home hazards when such risks were assessed for a group of parents who bought and applied baby walkers.

In 1999 D. DiLillo, A. Damashek, and L. Peterson performed a retrospect phone questioning that comprised 329 mothers; they gave information on application of baby walkers and stationary playpens for their 463 children born in Columbia, Missouri, from January 1994 to April 1999 [16]. It was revealed that a share of families who applied baby walkers dropped steadily from 1994 to 1999 while application of playpens grew over the same period. 48.9% out of 329 questioned mothers stated they put at least one baby in their family into baby walkers. Frequency of application was distributed as follows: 14.1% applied the device only once or twice; 16.5%, "from time to time"; 15.5%, "several times a month"; 5.3%, every week; 48.5%, every day. Overall, 88% mothers were aware of risks related to injuries and it was the most frequent reason for abandoning baby walkers. But still, 38% of respondents applied the device.

Parents mentioned various reasons that made them buy baby walkers, including "to entertain a baby", "to make it develop faster", the device was easy to buy and quite affordable; some parents mentioned also that stationary playpens were safer.

In 2003 in Singapore N.C.Tan and his colleagues selected parents of 445 children who were brought to clinics when they were 4-6 months old for scheduled immunization [17] These parents were questioned, and standardized questionnaires were applied in the process. The research revealed that 71.2% (311 out of 437 parents) applied baby walkers when their child was 9 months old. 66.7% parents didn't know about injuries related to baby walkers and only 37.5% were aware of some alternative devices. Besides, 48.3% respondents believed baby walkers helped their children to develop, although even at that time (*2003, author's note*) there were assumptions that the device actually postponed independent walking. In addition, it was detected that 20.1% parents took safety precautions when applying such devices. The researchers determined factors that statistically authentically increased application of baby walkers in families. They were parents' education; overall incomes of a family; housing; availability of baby walkers; an opinion that baby walkers made for early independent walking. Such factors as awareness of hazards, alternative devices, and total number of children in a family, didn't have any statistically authentic influence on decisions made by parents on the issue.

The research also revealed 24 "baby walkers-related" injuries and it accounted for 7% out of all the respondents (n=311). Prevailing injuries were falls on plane surface (5.5%), and falling off the stairs(14.9%).

In 2007–2008 in Iran Doctors F. Shiva, F. Ghotbi, and S.F. Yavari examined families who visited medical clinics in Teheran with their children aged from 6 months to 2 years [18]. They applied a standard questionnaire to conduct questioning among parents. The results were assessed via comparing between two groups, "baby walkers" one and "without baby walkers" one. 414 (54.5%) children (216 girls and 198 boys) spent some time in baby walkers. Baby walkers were much more frequently applied in families with just one child (p-value is 0.009) and in families where parents were better educated (p-value<0.001).

76.8% parents of children from "baby walkers" group thought the device promoted early walking (against 8.2% parents of children from "without baby walkers" group). 44.7% parents who applied baby walkers and 22.3% who didn't do it knew about hazards related to the device. 136 parents (60.17%) stated they applied baby walkers "to teach a child to walk earlier"; 57 (25.2%) wanted "to entertain a baby"; 23 (10.17%) said "it was a tradition"; 10 (4.4%) stated it was "just their wish" or there was "no reason at all".

The research didn't reveal any serious injuries among babies put into baby walkers, but still 14.1% babies had insignificant injuries of soft tissues while being in baby walkers.

As per data obtained by D.G. Dogan et al. [19] parents of 495 children aged from 2 months to 5 years who visited consultative clinics for child care at Fatih University Hospital in Ankara (Turkey) applied baby walkers in 75.4% cases. Female sex (OR 1.82, 95% CI 1.19–2.78) and

lower education of a mother (OR 0.37, 95% CI 1.18-0.74) were parameters that statistically authentically increased application of such devices. Injuries were rare (7.8%). Only 18.6% (n=92) families received relevant consultations from their pediatricians.

In 2015 in the UAE Doctor M. Grivna et al. [20] questioned 696 female 12th grade students who attended four state schools, 55% (n=385) out of them being the UAE citizens. Girls from three "scientific" classes and three "art" classes gave their answers to questions and stated that 90% (n = 619) families used to apply or still applied baby walkers. As for reasons for application of the device, 92% respondents mentioned safety of baby walkers, 11% thinking the device was completely safe, and 74%, that it was moderately safe. Only 16% noted that application of baby walkers could cause injuries.

Overall, a share of children who grew in families where baby walkers were applied varies from 42% to 90% in various populations (Figure 1), average value being 62.11 %±18.5= 43.61;80.61(CI=99%).

Parents mention the following basic advantages and reasons for application of baby walkers: faster development of a baby (8 out of 10 examinations); babies being occupied with something and being safe (8 out of 10 examinations); entertainment for babies (3 out of 10 examinations); traditions or absence of reasons (3 out of 9 examinations).

Data on additional factors that influence baby walkers application in samplings are rather controversial: parents' education was detected to exert statistically authentic influence in 4 examinations [4, 8, 11, 12], but the correlation was inverse in 3 of them [4, 8, 12], and direct in the remaining one [11], and there was an unreliable correlation detected in one more examination [6]. Income level was detected to be significant in one examination [8], and insignificant in another [14]. Therefore, it is difficult to authentically spot out an additional risk group in relation to the examined problem.

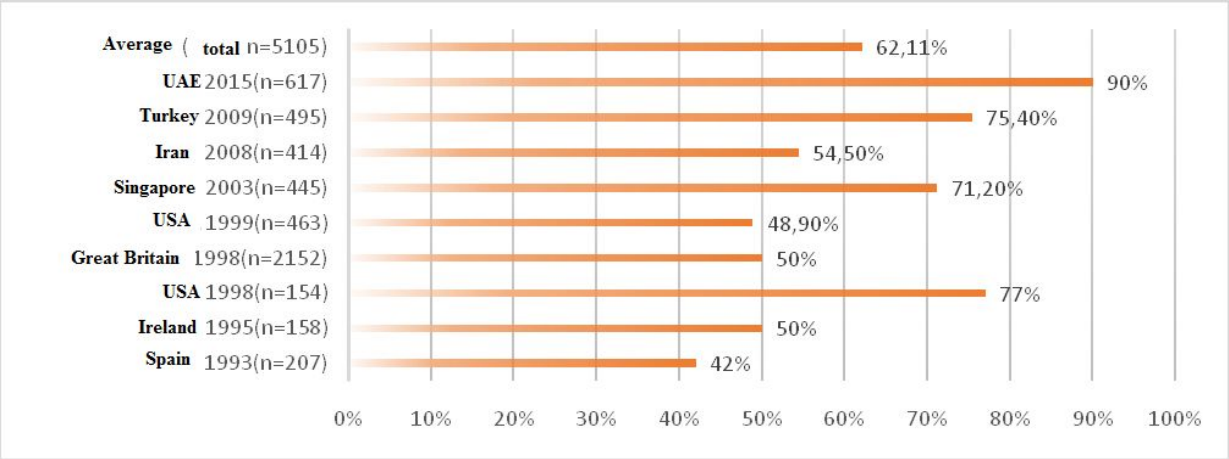

Figure 1. A share of children who were put in baby walkers in various samplings. As per data taken from foreign research [11, 13–20].

Various injuries, as well as gravity of traumas, up to deaths [21] are naturally considered by world scientists to be the basic problem related to baby walkers. As per results obtained in the examinations described above, as well as some other research, prevalence of injuries related to baby walkers various from 7% (Singapore, 2003) [17] to 50% (Italy, 1981) [22]; as per the biggest sampling, n-57500 (the USA 1987), injuries accounted for 35% [23]. The structure of traumatism is most profoundly described in a work that occupies the core place in studies on "baby walkers" traumatism; the work was published by scientists from Ohio (the USA) who analyzed 197,200 (sic!) injuries related to baby walkers that occurred over a period from 1990 to 2001. The following distribution of injuries as per various groups was detected among infants younger than 15 months [24]: surface soft tissue traumas (53,0%); closed craniocerebral injuries (25.1%); lacerations and bruises (10.1%); damages to bones and joints, fractures/dislocations (5.2%); burns (2.2%); other injuries (4.4%).

As per data taken from some research, falling off the stairs causes the gravest "baby walkers"-related injuries [24–27]. Such falls are authentically related to skull fracture risks: RR=3.28 (95% CI 1.35–7.98) [27] and OR 3.74 (p<0,01; 95% CI 3.42–4.09) [24]. Injuries that are not caused by falling off the stairs are predominantly ambulatory, or they don't even require any medical aid [24–31].

There has been a lot of research performed in various countries in different years on assessing influence exerted by baby walkers on motor skills [1–3,5,6,8], and the results are rather controversial. For example, reviews by M.C. Mancini et al. contain the following conclusion: "from a critical point of view, we can't make any precise judgment on actual effects produced by baby walkers when motor skills develop typically due to insufficient evidence base" [32]. Patricia Burrows and Peter Griffiths (2002) came to a conclusions that "results of two examinations considered in the review didn't reveal any significant influence exerted by baby walkers on a start of independent walking. Cohort research revealed that application of baby walkers delayed it, as generalized analysis of four cohort examinations revealed delays within an interval from 11 to 26 days" [33].

Tiptoe walking [3] occurs from the very beginning of independent walking, as per data by foreign authors [34–39]. This walking pattern is thought to be a pathologic one at 2-3 years, but prior to this age it is considered to be a part of a normal walking formation [40]. As regards influence exerted by baby walkers on motor skills, there is an assumption that the device can possibly change locomotor pattern and lead to tiptoe walking (Martín-Casas P et al.) [41]). Our empirical observations also allow us to make similar assumptions.

Data and methods. Data for the work were obtained via three cohort examinations which were pseudo-retrospective; the examinations were performed in a children clinic at Rzhevskaya Central District Hospital, and four pre-school children facilities in Rzhev, Tver' region. The overall number of children in sampling was equal to 749; 363 children were in "baby walkers" group.

The first examination (No. 1) entitled "Epidemiologic aspects related to application of baby walkers and correlation with talipes valgus" was performed in February – September 2016 among children born from January – September 2015 In Rzhev, Tver' region. We excluded patients whose parents couldn't give exact necessary data, as well as patients with grave congenital pathologies (16 children totally). The sampling included 268 babies aged 11-18 months. We performed our research via anamnestic questioning among parents with a standardized, specially designed, and anonymous questionnaire; we also conducted an objective assessment of heel bone angle. The results were then collected in Table 1

Table 1

Examination results registration

No.	1	2	…	10
Period of application				
Daily application				
Age				
Sex				
Reasons for application				
Talipes valgus, other pathologies				

We initially grouped the data regarding application of baby walkers; additional grouping was made as per sex, reasons for application of such devices, "baby-walkers"-related injuries, and talipes valgus. We calculated and analyzed relative values (extensive parameters) for separate groups and then designed a fourfold table to assess influence exerted by application of baby walkers on occurrence of acquired statistical talipes valgus. We also calculated Chi-square criterion.

The second examination (No. 2) entitled "Influence exerted by baby walkers on motor skills development in infants" was conducted from September 2014 to September 2015. The sampling included all infants who were healthy at the moment of prophylaxis inspection by a traumatologist-orthopedist; all of them were born in period from September 2013 to September 2014 in Rzhev, Tver' region. We excluded patients with delays in motor development caused by diseases in the locomotor or nervous system, with congenital or acquired hypotrophy, as well as children whose parents couldn't provide us with all necessary data. Children weren't divided as per sex. The sampling included 11-15 month old infants. Totally 514 children were born in the period, and we questioned parents of 408 children (79.3%), and only 358 (69.6%) babies were included into research sampling. We performed our research via anamnestic questioning among parents with a standardized, specially designed, and anonymous

[3] *Tiptoe walking* is a manner in which a baby moves on two feet without stepping on its heels, making more than 5 consequent steps, and repeats it for at least a week when starting to walk independently. Periods when a baby was lifted on tiptoes without moving were not taken into account.

questionnaire. The data were then collected in Table 2 by a medical expert (Table 2).

Table 2

Examination results registration

Parameter	1	2	…	10
Age (months)				
Diagnosis at 1-3- months.				
Standing with support[4] from …(months)				
Walking with support from…(months)				
Independent walking from…(months)				
Tiptoe walking (yes/no)				
Application of baby walkers (yes/no)				
Minutes per day (in baby walkers)				
Total number of days (in baby walkers)				

We performed an interval (as per baby-walkers/day index)[5] grouping of children who walked on tiptoes.

We initially grouped our sampling taking into account a stage and a factor for application of baby walkers as well as period of their application (Figure 2).

Data obtained for specific groups were statistically processed and extensive values were calculated for each group. We designed weighted leveled-off series for development stages. Leveling-off was accomplished via upsizing an interval. We determined series variations and analyzed average values. Mean weighted value of the general sampling was calculated as per Student's technique (taking into account t-distribution of the samplings) for 99% confidence intervals. Obtained general average stages were compared with data taken from the WHO Motor Development Study [42], via calculating pair Student's t-test (p-value ≤ 0.01 and ≤ 0.05).

A discrete series for baby-walkers/day index was divided into intervals and variation series were drawn up for bay-walkers/day intervals <1 bw/d and ≥1 bw/d; mean values were calculated and compared with previously obtained data. These intervals were selected as the most representative ones for assessing discrepancies.

At the next stage we assessed significance of discrepancies in mean group values for different ages that corresponded to various stages in a child's development. To detect the most representative statistical technique, we calculated normalcy of distribution; asymmetry of distribution; Fischer's test (F) for assessing equality of general dispersions; and two-sample Kolmogorov-Smirnov test for assessing identity of distribution laws in pair groups. bearing all these calculations in mind, we chose Student's pair t-test and Mann-Whitney U-test. We calculated significance of discrepancies between mean group values (including those for specific bw/s intervals); discrepancies at p-value ≤ 0.01 and ≤ 0.05 were considered to be authentic. In addition, we drew up a box diagram and a summary table containing general mean values for all groups and stages allowing for 99% confidence interval.

At the next stage we tried to reveal a correlation between a period of time spent in baby-walkers a day (both for the whole series of values and for specific intervals) and age of various stages in development of locomotion. We applied correlation analysis to calculate the following coefficients: parametric Pierson's test and non-parametric ρ-Spearman test, τ(c)-Kendall test, and τ(b)-Kendall test. A statistic hypothesis was considered to be authentic at $p<0,05$. Within specific elements of one-factor regression analysis we built scattering diagrams, a regression straight as per the least square method with 95% confidence intervals, and calculated coefficients of determination (R2) for similar stages and intervals.

Then we examined a group of children who didn't walk on their own at the moment of our examination (n-61). Primarily we accomplished an

[4] ***Standing with support*** is a vertical position of a baby when it stands on two feet for more than 5 minutes on its own but supporting itself with some objects or an adult's hand.

[5] ***Baby walkers/day index (bw/d)*** is equal to a 1hour spent by a baby in baby walkers a day during 1 month. Example: 30 minutes per day during 1 months is 0.5 bw/d; 2 hours per day during 3 months is 6 bw/d; 6 hours per day during 5 months is 30 bw/d.

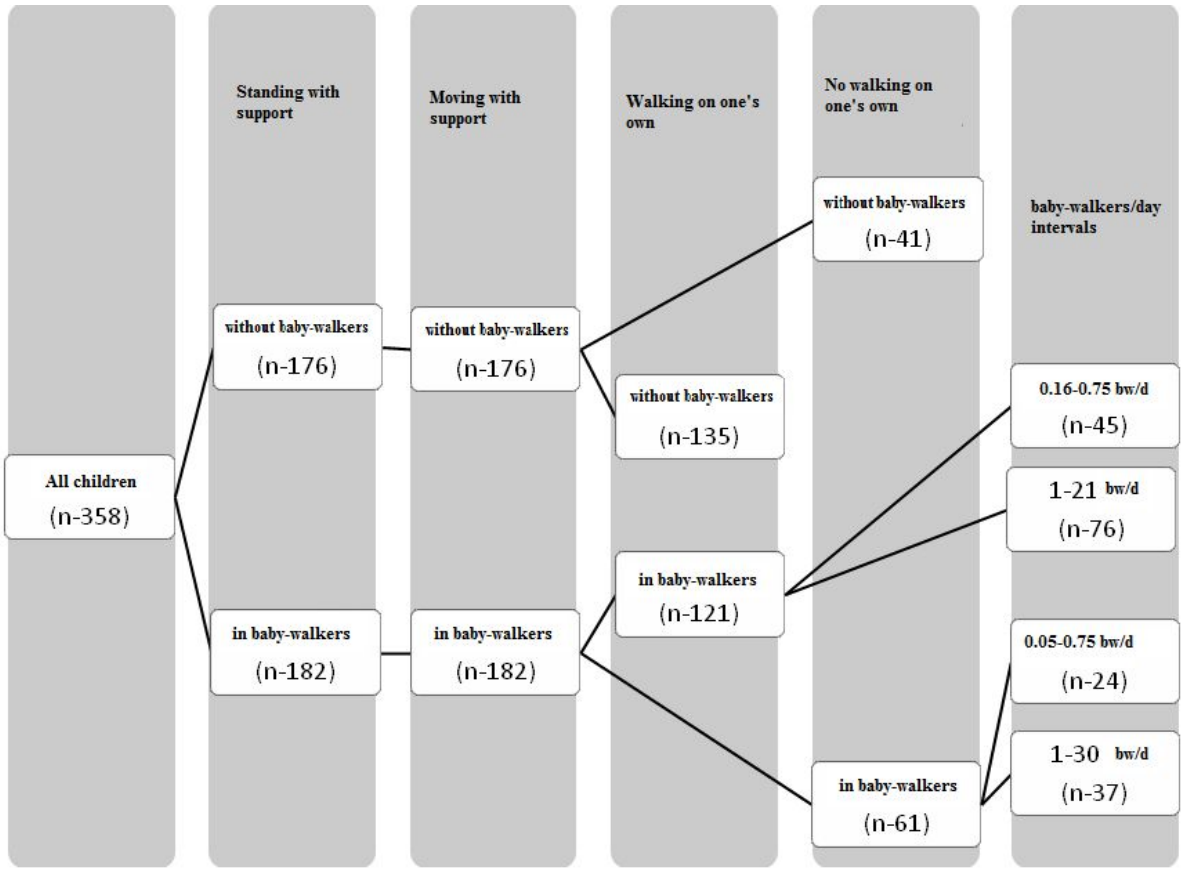

Figure 2. Research sampling grouping – influence exerted by baby walkers on motor skills development in children

interval grouping as regards bw/day index, and <1 bw/d and ≥1 bw/d intervals were selected as the most representative for assessing discrepancies. To assess this group, we applied correlation and regression analysis to reveal influence exerted by baby-walkers on this phenomenon similar to the previous stage in calculations. We calculated r-Pearson test, ρ-Spearman test, τ(c)-Kendall test, and τ(b)-Kendall test. A statistical hypothesis was considered to be authentic at $p<0.05$. Then we drew up scattering diagrams and regression straights as per least square method and calculated coefficients of determination (R2).

To assess influence exerted by baby-walkers as a factor that prevents a baby from walking and a factor that makes a baby walk on tiptoes, we analyzed fourfold tables, determined Chi-square criterion and Pearson's contingency coefficient. A statistical hypothesis was considered to be authentic at $p<0.05$. We also calculated relative risk (RR) and population attributive risk (PAR) with 95% confidence interval.

In addition, we accomplished interval (as per baby-walkers/day index) grouping of children who walked on tiptoes and calculated chi-square and Pearson's test for each interval. A statistical hypothesis was considered to be authentic at $p<0.01$. We again calculated relative risk (RR) and population attributive risk (PAR) at CI=95%.

Our third examination (No.3) was entitled "Baby walkers and tiptoe walking". Data were collected from April 2016 to July 2016 in four pre-school children facilities in Rhzev, Tver' region. We performed our research with an anamnestic questioning among parents with a standardized, specially designed and anonymous questionnaire. The results were then filled in the table by medical experts (Table 3).

We questioned 180 parents. If parents couldn't provide all the necessary data, their children were excluded from the examination. Precise data were given by 123 respondents; 64 infants (52.03%) were put into baby-walkers at least once; 59 (47.97%) were never put into the device. Our sampling had the following structure in terms of sex: 69 girls (54.31%) and 54 boys (45.69%). As for age, children were 18-41 months old.

Table 3

Questioning results

No	1	2	…	10
Date of birth and sex of a child				
A diagnosis by a surgeon (orthope-dist), if any				
Tiptoe walking (yes/no)				
If yes, than till what age				
Applied baby-walkers (yes/no)				
Additionally: Any anomalies related to walking and lower extremities mentioned by parents (for example, club-foot, "crossed legs" etc.) (if any)				

First, we divided our sampling into groups as per baby-walkers application and tiptoe walking. Then we calculated and analyzed relative values (extensive parameters) for groups in the sampling. We drew up a fourfold table to assess influence exerted by baby-walkers as a factor promoting a specific walking pattern, tiptoe walking. We analyzed this fourfold table and calculated Chi-square, φ criterion, Cramer's V test, Chuprov's coefficient, Pearson's contingency coefficient (C) (for p-value<0.05). Then we calculated risks of a child walking on its own but no toes with 95% confidence interval.

At the next stage, we calculated average values for an age at which babies stopped walking on tiptoes in "baby-walkers" group and "without baby-walkers" group with 95% CI and assessed how appropriate it was to further apply Student's pair t-test; to do it, we calculated normalcy and asymmetry of distribution; Fischer's test (F) (at p=0.01); two-sample Kolmogorov-Smirnov test. To estimate discrepancies between various ages at which babies from "baby-walkers" group and "without baby-walkers" group stopped tiptoe walking, we calculated Student's pair t-test (p<0.05) and Mann – Whitney U-test (p<0.01).

Then we again calculated additional population risk caused by baby-walkers as a pathological factor that promoted a higher tonus in extensor muscles of lower extremities taking into account all the results obtained in the 2nd and 3rd examination.

And finally, we assessed application of baby-walkers in samplings involved in all three examinations.

We performed all the calculations in all three examinations with the following software: Microsoft Excel®, IBM® SPSS® Statistics and online calculators at http://app.statca.com, http://medstatistic.ru and http://www.semestr.ru on a compatible IBM with installed Microsoft Windows 10®.

Two systematic errors were detected in all three examinations. The first one is a population bias as samplings include children belonging to Caucasian race but their exact ethnic structure is not defined (provisionally it was taken as similar to that of the Central Federal District in Russia). The second one is a recall bias and it is closely related to a structure of examinations, or, to be more exact, anamnestic questionings being their basic tool.

All parents or guardians gave their written informative consent to take part in the examinations.

Results of our own examinations. We started to assess our results with determining a volume and a structure of the phenomenon. The 1st examination chronologically was the last one; here we revealed the following distribution of baby-walkers application by parents in Rzhev: the overall sampling included 268 children; "baby-walkers" group was made up of 117 children (43.6%), "without baby-walkers" group was made up of 151 children (56.4%). As regards sex, the groups had the following structure: 70 girls (46.4%) and 81 boys (53.6%) in "without baby-walkers" group, totally 151; 63 girls (53.9%) and 54 boys (46.1%) in "baby-walkers" group, totally 117. A distribution peculiarity was a bit higher number of girls in "baby-walkers" group.

Parents in Rzhev mentioned similar reasons that made them apply baby-walkers as their foreign counterparts. A priority motive was parents' desire to teach their baby to walk (40.17%) and/or entertain it thus finding some free time for their own (57.26%). Family traditions as a reason were mentioned by a very small number of respondents (2.56%). However, while making a baby develop faster was chosen as a primary reason for application of baby-walkers as per data obtained in foreign research, more than a half parents in Russia (57.26%) apply baby-walkers not to teach (help) a child to walk, but see it as a safe mean to limit a baby's freedom of movement; when a baby is in baby-walkers, parents can "stop looking after it and do something else".

We detected relative low number of damages among baby-walkers users in Russia (15.35%). Falling on a plane surface or overturning was a prevailing cause of injuries, 17 out of 18 cases, and one child fell down due to hooking over a threshold. We didn't detect any falling off the stairs. All injuries were solely superficial, to be

more exact, they were surface soft tissue traumas (bruises, sprains, and graze wounds). There were no applications for medical aid. Three respondents recalled having two or three injuries. In our opinion, children had such mild traumas due to their families living in one-floor flats and houses without any stairs inside. And injuries made parents abandon baby-walkers only in 5 cases.

Our attempt to reveal any possible early pathological outcomes of baby-walkers, such as acquired static deformations in infant age, was not successful in this research. We didn't detect any statistically authentic correlation between baby-walkers and talipes valgus (Chi-square 3.743, $p>0.05$).

In our 2nd examination, we didn't detect any statistically authentic discrepancies in age at which various development stages began in comparison with data obtained in WHO Motor Development Study [42] (Table 4).

Table 4

Average weighted age at which development stages began in "without baby-walkers" groups in comparison with average world ones

Stage	Weighted mean (M) of the general sampling
Standing with support	7.33±0.17; 7.16-7.5months (99% CI), Rzhev
	7.6±1.4; 6.2 – 9.0 months (95% CI) worldwide
Moving with support [6]	8.99±0.16; 8.83-9.15 months (99% CI), Rzhev
	9.2±1.5; 7.7- 10.7 months (95% CI) worldwide
Walking on one's own	10.57±0.26; 10.31-10.83 months (99% CI),* Rzhev
	12.1±1.8; 10.3 – 13.8 months (95% CI) * worldwide

*Note : ***** – confidence interval of the data obtained in WHO Motor Development Study overlaps values obtained in our research; it is confirmed by comparing average values with Student's pair t-test $t=1.65(p>0.05)$, therefore, discrepancies are not statistically significant. The detected discrepancy is a systematic error of selection (selection bias).*

Similarly, there is no statistically authentic age discrepancy between "baby-walkers" and "without baby-walkers" groups as regards their age at which they start sanding with support and moving with support (Table 5).

We detected a delay in walking on one's own among "baby-walkers" children and it is well in line with data obtained in foreign research [4, 5], especially the work by Doctors Garrett M. et al. which was very close to ours as per its design and sampling structure (Northern Ireland, 2002) [6].

Table 5

Assessment of development stages age: standing with support and moving with support in "baby-walkers" and "without baby-walkers" group

Stage	Test	Discrepancies (p-value)
Standing with support	Student's t= 0.67	No discrepancies ($p \leq 0.01$)
	Mann-Whitney U=15425	No discrepancies (p=0.5316)
Moving with support	Student's t= 0.63	No discrepancies ($p \leq 0.01$)
	Mann-Whitney U=16868	No discrepancies (p=0.4797)

Overall delay in walking on one's own for all the children in families where baby-walkers were applied and with "baby-walkers/day" indexes being ≥1 bw/d amounted to:

– 10.57 months (M without baby-walkers) - 10.9 months (M with baby-walkers, all children) = **- 0.33 months** (**10.04 days**);

– months (M without baby-walkers) -11 months (M in baby-walkers ≥1 bw/d) = - **0.43 months** (**13.08 days**).

We confirmed co-variation of bw/d index (for ≥1 bw/d with authenticity p=0.035) and delays in walking on one's own; we also revealed a trend of increasing influence at high values of "baby-walkers/day" index.

We detected that more children in "baby-walkers" group didn't walk on their own than in "without baby-walkers" one.

This point is confirmed by our analysis of the fourfold table and calculation of risks. We revealed a statistically authentic ($p<0.05$) weak correlation and relative risk (RR)=1.439. The latter is the evidence there is a delay in motor development.

The 2nd and the 3rd examinations confirmed there was a correlation between baby-walkers and

[6] ***Moving with support*** is when a baby moves on two feet, on its own, and supports itself with objects or a parent's hand, making more than 5 steps, with a progress.

tiptoe walking. The results are given in Table 6.

Table 6

Parameters of correlation between baby-walkers and a child walking on tiptoes

Parameter	Examination No. 2	Examination No. 3*
Correlation strength, *p-value*	Relatively strong, $p<0,01$	average, $p<0,01$
Risk ratio (*RR*)	3,56 (2,54 – 4,99; *CI* 95 %)	2,77 (1,18 – 6,49; *CI* 95 %)
Risk discrepancy (*RD*)	0,45	0,18

Note : * The sampling is less representative (wider CI, smaller sampling n-123, anamnestic data are less precise)

In our third examination we revealed a longer period of tiptoe walking in "baby-walkers" group. General mean values amounted to 14.58 ± 3.49 months (95% CI=11.09–18.07 months) in "baby-walkers' group; 13.00 ± 2.1 months (95% CI 10.09–15.1 months) in "without baby-walkers" group. Discrepancies were statistically authentic (t= 2.61; p<0.05; U= 58 p<0.01).

As for the 2nd examination, when we calculated chi-square and Pearson's contingency coefficient for specific intervals of bw/d index, we naturally revealed a greater influence exerted on patterns of walking under longer periods of baby-walkers applications.

Nowadays some examinations are being performed in order to get better insights into possible influence exerted by baby-walkers on development on idiopathic tiptoe walking [10, 41] and on static deformations occurrence [43].

We revealed a relatively high additional population risk of tiptoe walking and absence of walking on one's own in all the samplings in all three examinations (Table 7).

Table 7

Assessment of population attributable risk, PAR, in the examinations

Indicator	Examination No. 1 baby-walkers group amounted to 117 children (43.66%)	Examination No. 2 walkers group amounted to 182 children (50.84%)	Examination No. 3 walkers group amounted to 64 children (52.03%)
Absence of walking	*PAR* = 4,45	*PAR* = 5,18	*PAR* = 5,3
Tiptoe walking RD 0.425*, %	*PAR* = 19,647	*PAR* = 22,878	*PAR* = 23,4135
Tiptoe walking RD 0,18*, %	*PAR* = 7,86	*PAR* = 9,15	*PAR* = 9,36

Note: *The 2nd and the 3rd examination respectively, see Table 6.

When assessing discrepancies in risks, it is advisable to rely on the results obtain in the second examination as the third sampling is less representative, and, consequently, all the data are less precise.

When we compared all the data on the phenomenon obtained in all three examinations described above, we revealed a decrease in application of baby-walkers over from 52.03% in 2013 to 43.66% in 2015.

In our opinion, it has happened due to substantial educational work performed over recent years by pediatricians and their efforts aimed at raising awareness among parents and guardians about threats caused by such devices.

Basically, all the obtained results allowed to come to several conclusions:

1. Frequency of baby-walkers application among children in Rzhev and Rzhev district as a representative Russian region is close to average world frequency 62.11%±18.5=43.61-80.61(CI=99%), but still a bit lower: 43.66%; 50.84% and 52.03% in all three samplings.

2. Parents in Rzhev gave the same reasons for application of baby-walkers as their foreign counterparts:

¨ to entertain a baby/to give a baby something to do (57.26%);

¨ to teach a baby to walk/to develop a baby (40.17%);

¨ family tradition (2.56%)

3. Damages and traumas caused by baby-walkers are relatively rare in Russian families (15.35%, n-18). We didn't register any injuries that required medical aid in our examinations; all the injuries were insignificant;

4. We didn't reveal any statistically authentic influence exerted by baby-walkers on formation of acquired static deformations in infant age. Such negative consequences possibly occur

at an older age; however, this assumptions requires further investigation.

Naturally there is no statistically authentic discrepancy in ages at which various development stages begin in "without baby-walkers" groups in comparison with average data obtained worldwide in WHO Motor Development Study [Onis M., 2004].

5. There is no statistically authentic discrepancy between "baby-walkers" group and "without baby-walkers" one as regards an age at which such development stages as "standing with support" and "moving with support" begin; therefore, it confirms an assumption that there is no influence exerted by baby-walkers on children development at these stages.

6. A delay in walking on one's one among children who were put into baby-walkers is confirmed; it amounts to 10-13 days depending on frequency and time spent in baby-walkers a day.

7. We revealed a statistically authentic relatively strong correlation between application of baby-walkers and relative risk of tiptoe walking (RR= 3.6 (2.5-5.0 for 95% CI) in the most representative sampling. A longer period of tiptoe walking in "baby-walkers" group proves that baby-walkers exert negative influence on walking patterns. Population attributable risk, or PAR, amounted to PAR=4.45% - PAR=5.3% for the absence of walking on one's own; and PAR=19.647% - 23.4135% for tiptoe walking.

8. Application of baby-walkers among children on the examined territories decreased from 52.03% to 43.66% and we think it proves that active campaigns and informing parents and guardians about threats cause by baby-walkers are truly effective.

Given all the above stated, we can be sure that baby-walkers are a real influence factor for the population. However, structure and significance of this influence require further investigation; therefore, we hope that our examinations will continue.

As we join the world scientific society dealing with issues related to baby-walkers application, we urge every expert in the field to cover negative outcomes of their application as profoundly as its only possible.

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References

1. Kauffman I.B., Ridenour M. Influence of an infant walker on onset and quality of walking pattern of locomotion: an electromyographic investigation. *Perceptual and motor skills*, 1977, vol. 45, no. 3f, pp. 1323–1329. DOI: 10.2466/pms.1977.45.3f.1323

2. Ridenour M.V. Infant walkers: developmental tool or inherent danger. *Perceptual and motor skills*, 1982, vol. 55, no. 3f, pp. 1201–1202. doi: 10.2466/pms.1982.55.3f.1201

3. Crouchman M. The effects of baby walkers on early locomotor development. *Developmental Medicine & Child Neurology*, 1986, vol. 28, no. 6, pp. 757–761. DOI: 10.1111/j.1469-8749. 1986.tb03929.x

4. Thein M.M., Lee J., Tay V., Ling S.L. Infant walker use, injuries, and motor development. *Injury Prevention*, 1997, vol. 3, no. 1, pp. 63–66. DOI: 10.1136/ip.3.1.63

5. Siegel A.C., Burton R.V. Effects of baby walkers on motor and mental development in human infants. *Journal of Developmental & Behavioral Pediatrics*, 1999, vol. 20, no. 5, pp. 355–360. DOI: 10.1097/00004703-199910000-00010

6. Garrett M., McElroyet A.M., Staines A. Locomotor milestones and baby walkers: cross sectional study. *BMJ*, 2002, vol. 324, no. 7352, pp. 1494. DOI: 10.1136/bmj.324.7352.1494

7. Shiva F., Ghotbi F., Yavari S.F. The use of baby walkers in Iranian infants. *Singapore medical journal*, 2010, vol. 51, no. 8, pp. 645–649.

8. Engelbert R.H.H., Van Empelen R., Scheurer N.D., Helders P.J.M., Van Nieuwenhuizenl O. Influence of infant-walkers on motor development: mimicking spastic diplegia? *European Journal of Pediatric Neurology*, 1999, vol. 3, no. 6, pp. 273–275. DOI: 10.1016/s1090-3798 (99) 90982-0

9. Sharov A.N., Krivova A.V. Vliyanie detskikh khodunkov na razvitie dvigatel'nykh navykov u mladentsev [Effect of Baby Walkers on the Development of Locomotor Skills in Infants]. *Vestnik travmatologii i ortopedii imeni N.N. Priorova*, 2016, no. 3, pp. 40–46 (in Russian).

10. Krivova A.V., Sharov A.N. Baby walkers and the phenomenon of toe-walking. *Pediatric Traumatology, Orthopaedics and Reconstructive Surgery*, 2018, vol. 6, no. 1, pp. 23–32. DOI: 10.17816/ptors6123-32

11. Santos S.L. Paricio Talayero J.M., Salom Pérez A., Grieco Burucúa M., Martín Ruano J., Benlloch Muncharaz M.J., Llobat Estellés T., Beseler Soto B. Patterns of use, popular beliefs and proneness to accidents of a baby walker (go-cart). Bases for a health information campaign. *Anales espanoles de pediatria*, 1996, vol. 44, no. 4, pp. 337–340.

12. Trinkoff A., Parks P.L. Prevention strategies for infant walker-related injuries. *Public Health Reports*, 1993, vol. 108, no. 6, pp. 784.

13. Laffoy M., Fitzpatrick P., Jordan M., Dowdall D. Attitudes to and use of baby walkers in Dublin. *Injury prevention*, 1995, vol. 1, no. 2, pp. 109–111. DOI: 10.1136/ip.1.2.109

14. Bar-on M. E., Boyle R. M., Endriss E. K. Parental decisions to use infant walkers. *Injury prevention*, 1998, vol. 4, no. 4, pp. 299–300. DOI: 10.1136/ip.4.4.299

15. Kendrick D., Marsh P. Babywalkers: prevalence of use and relationship with other safety practices. *Injury Prevention*, 1998, vol. 4, no. 4, pp. 295–298. DOI: 10.1136/ip.4.4.295

16. DiLillo D., Damashek A., Peterson L. Maternal use of baby walkers with young children: recent trends and possible alternatives. *Injury Prevention*, 2001, vol. 7, no. 3, pp. 223–227. DOI: 10.1136/ip.7.3.223

17. Tan N.C., Lim L.H., Gu K. Factors influencing caregiver's use of an infant walker.*Asia Pacific Family Medicine*, 2003, vol. 2, no. 1, pp. 16–22. DOI: 10.1046/j.1444-1683.2003.00045

18. Shiva F., Ghotbi F., Yavari S.F. The use of baby walkers in Iranian infants. *Singapore medical journal*, 2010, vol. 51, no. 8, pp. 645–649.

19. Dogan D.G., Bilici M., Yilmaz A.E., Catal F., Keles N. Baby walkers: a perspective from Turkey. *Acta paediatrica*, 2009, vol. 98, no. 10, pp. 1656–1660. DOI: 10.1111/j.1651-2227.2009.01397

20. Grivna M., Barss P., Al-Hanaee A., Al-Dhahab A., Al-Kaabi F., Al-Muhairi S. Baby walker injury awareness among grade-12 girls in a high-prevalence Arab country in the Middle East. *Asia-Pacific journal of public health*, 2015, vol. 27, no. 2, pp. NP1507–NP1516. DOI: 10.1177/1010539513498766

21. Committee on Injury and Poison Prevention. Injuries Associated With Infant Walkers. *Pediatrics*, 2001, vol. 108, no. 3, pp. 790–792. DOI: 10.1542/peds.108.3.790

22. Fazen L.E., Felizberto P.I. Baby walker injuries. *Pediatrics*, 1982, vol. 70, no. 1, pp. 106–109.

23. Wishon P.M., Huang A., Spangler R.S. Hazard Patterns and Injury Prevention with Infant Walkers and Strollers. 1989, 17 p.

24. Shields B.J., Smith G.A. Success in the Prevention of Infant Walker–Related Injuries: An Analysis of National Data, 1990–2001. *Pediatrics*, 2006, vol. 117, no. 3, pp. e452–e459. DOI: 10.1542/peds.2005-1916

25. Chiaviello C.T., Christoph R.A., Bond G.R. Infant walker-related injuries: a prospective study of severity and incidence. *Pediatrics*, 1994, vol. 93, no. 6, pp. 974–976.

26. Petridou E., Simou E., Skondras C., G Pistevos., Lagos P., Papoutsakis G. Hazards of baby walkers in a European context. *Injury Prevention*, 1996, vol. 2, no. 2, pp. 118–120. DOI: 10.1136/ip.2.2.118

27. Smith G.A., Jo Bowman M., Luria J.W., Shields B.J. Babywalker-related injuries continue despite warning labels and public education. *Pediatrics*, 1997, vol. 100, no. 2. Available at: http: //pediatrics.aappublications.org/content/100/2/e1 (18.04.2018).

28. Rieder M.J., Schwartz C., Newman J. Patterns of Walker Use and Walker Injury. *Pediatric Emergency Care*, 1987, vol. 3, no. 1, pp. 59. DOI: 10.1097/00006565-198703000-00022

29. Partington M.D., Swanson J.A., Meyer F.B. Head injury and the use of baby walkers: a continuing problem. *Annals of emergency medicine*, 1991, vol. 20, no. 6, pp. 652–654. DOI: 10.1016/s0196-0644 (05) 82386-8

30. Coats T.J., Allen M. Baby walker related injuries--a continuing problem. *Emergency Medicine Journal*, 1991, vol. 8, no. 1, pp. 52–55. DOI: 10.1136/emj.8.1.52

31. Walker J.M., Fagard R., Narkiewicz K., Redón J., Zanchetti A., Böhm M., Christiaens T., Cifkova R., De Backer G., Dominiczak A., Galderisi M., Grobbee D.E., Jaarsma T., Kirchhof P., Kjeldsen S.E., Laurent S., Manolis A.J., Nilsson P.M., Ruilope L.M., Schmieder R.E., Sirnes P.A., Sleight P., Viigimaa M., Waeber B., Zannad F.; Task Force Members. Hazardous baby walkers: a survey of use. *Pediatric Physical Therapy*, 1996, vol. 8, no. 1, pp. 25–30. DOI: 10.1097/00001577-199600810-00005

32. Mancini M.C., Magalhães L.C. Clinical Scenario. 2007.

33. Burrows P., Griffiths P. Do baby walkers delay onset of walking in young children? *British journal of community nursing*, 2002, vol. 7, no. 11, pp. 581–586.

34. Sala D.A., Shulman L.H., Kennedy R.F., Grant A.D., Y Chu M.L. Idiopathic toe-walking: A review. *Developmental medicine and child neurology*, 1999, vol. 41, no. 12, pp. 846–848. DOI: 10.1017/s0012162299001681

35. Shulman L.H., Sala D.A., Y Chu M.L., McCaul P.R., Sandler B.J. Developmental implications of idiopathic toe walking. *The Journal of pediatrics*, 1997, vol. 130, no. 4, pp. 541–546. DOI: 10.1016/s0022-3476 (97) 70236-1

36. Tidwell M. The child with tip-toe gait. *International Pediatrics*, 1999, vol. 14, pp. 235–238.

37. Brouwer B., Davidson L.K., Olney S.J. Serial casting in idiopathic toe-walkers and children with spastic cerebral palsy. *Journal of Pediatric Orthopaedics*, 2000, vol. 20, no. 2, pp. 221–225. DOI: 10.1097/01241398-200003000-00017

38. Fragniere B., Garoflid N., Dutoit M. Mon enfant marche sur la pointe des pieds. *Revue médicale de la Suisse romande*, 2000, vol. 120, no. 10, pp. 811–814.

39. Stricker S.J. Evaluation and treatment of the child with tiptoe gait. *International Pediatrics*, 2006, vol. 21, no. 2, pp. 91.

40. Sutherland D.H., Olshen R.A., Cooper L. The development of mature gait. *J. Bone. Joint. Surg. Am.*, 1980, vol. 62, no. 3, pp. 336–353. DOI: 10.2106/00004623-198062030-00004

41. Martín-Casas P., Ballestero-Pérez R., Meneses-Monroy A., Beneit-Montesinos J.V., Atín-Arratibel M.A., Portellano-Pérez J.A. Neurodevelopment in preschool idiopathic toe-walkers. *Neurología (English Edition)*, 2017, vol. 32, no. 7, pp. 446–454. DOI: 10.1016/j.nrleng.2016.02.006

42. Onis M. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. *Acta Paediatrica*, 2006, vol. 95, no. S450, pp. 86–95.

43. Shafeek M.M., El-Negmy E.H. Pilot Study: The Onto Ward Effect of Baby Walker Usage on Gait Pattern in Three Years Normal Children. *Med. J. Cairo Univ.*, 2016, vol. 84, no. 2, pp. 379–383.

Sharov A.N., Krivova A.V., Rodionova S.S. Application of baby walkers in Russia: epidemiological aspects. Health Risk Analysis, 2018, no. 3, pp. 63–75. DOI: 10.21668/health.risk/2018.3.07.eng

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INDICATORS WHICH ARE APPLIED WHEN ASSeSSING EFFECTS ON A BODY EXERTED BY NITRATES AND N-Nitrosodimethylamine INTRODUCED WITH DRINKING WATER

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The authors comparatively assessed N-Nitrosodimethylamine (N-NDMA) contents in blood samples taken from children who consumed drinking water with increased nitrates and N-NDMA concentrations and in blood samples taken from children who consumed drinking water which fully corresponded to the existing hygienic standards; the article dwells on the results of this comparative assessment. We detected authentic discrepancies ($p<0.005$) in N-NDMA contents between blood samples taken from children from the focus group (0.0045 ± 0.0009 mg/dm^3) and the reference one (0.003 ± 0.0006 mg/dm^3). We revealed that free-radical oxidation mechanisms were activated in children from the focus group who were exposed to N-NDMA. Lipids hydroperoxidation content in blood serum was proved to be 1.6 times higher in children from the focus group than in those from the reference one. When N-NDMA was detected in blood of children from the focus group, they ran 1.73 times higher risks of damages to their cells membranes.

Our assessment of antioxidant protection revealed that glutathione-S-transferase became less active, B12 vitamin content went down, and glutathione peroxidase increased in children from the focus group against those from the reference group; all these parameters were 1.2–1.7 times different between the groups ($p = 0.000–0.030$). The children from the focus group also ran 2.91 times higher risks of an increase in glutathione peroxidase content.

We detected an authentic cause-and effect relation between an increase in IgG to N-NDMA and growing N-NDMA concentrations in blood ($R^2 = 0.958$, at $p = 0.001$). Risk of changes occurring in this parameter of humoral immunity was 1.3 times higher in the focus group.

The results of the experimental research allowed us to reveal an increase in fetal proteins (S-CEA and CA 199) contents detected in blood serum of children from the focus group against those from the reference one; the contents were 2.7 and 3.9 times higher correspondingly ($p = 0.010–0.023$). This increase could be a sign of ongoing processes which characterized tissue proliferation; it could also become a mechanism of uncontrolled cellular proliferation.

The performed research allowed us to substantiate and fix the following biological markers of the effects: an increase in IgG to N-NDMA and in glutathione peroxidase, ASAT activity, and total bilirubin level which can be applied in risk assessment and in giving grounds for permissible concentrations of these toxic compounds in blood.

Key words: *nitrates, N-nitrosodimethylamine, drinking water, exposure indicator, indicator of an effect, odds ratio, specific sensitization.*

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Non-organic compounds are a significant chemical factor that causes population health risks in the RF due to contamination of drinking water supply sources. Thus, consumption of drinking water with high nitrates concentrations that constantly tend to increase[1] [1], is hazardous because when they penetrate a body, endogenous synthesis makes them turn into highly toxic N-nitrosoamines[2] [2]. N-nitrosoamines are widely used in industry; their synthesis in natural reservoirs as well as in a human body is quite possible. They are stable, dissolve easily, and can penetrate drinking water in multiple ways; all the above said means drinking water is one of the main sources of N-nitrosoamines introduction into a human body[3].

A vital aspect in any hygienic assessment is to reveal a relationship between effects produced by drinking water contamination and the consequent biological effects [3–5]. To detect hazardous effects produced on human health by chemical factors related to drinking water, experts apply epidemiologic, instrumental (laboratory), and clinical techniques that allow to assess exposure to chemical factors.

Biomarkers of effect and their determination is one of basic instruments applied to detect persistent cause-and-effect relationships between health disorders and exposure to environmental chemical factors [6]. Pathogenetic mechanisms related to negative effects produced by nitrogen-containing substances (nitrates and nitrosoamines) consumed with drinking water still remain an unsolved task of contemporary hygiene and human ecology.

Our research goal was to substantiate indicators of negative effects in children under chronic exposure to nitrates and N-nitrosodimethylamine (N-NDMA) consumed with drinking water. The substantiation was based on modeling and assessment of "exposure indicator – indicator of an effect" relationship.

Data and methods. To achieve our goals, we applied a set of sanitary-hygienic, epidemiologic, and statistical techniques. Hygienic assessment of drinking water quality on examined territories was performed on the basis of monitoring data obtained from "Center for Hygiene and Epidemiology" of Perm Center for Hydrometeorology and Environmental Monitoring and data provided by the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies.

Water samples were examined in respect of nitrates content[4] and N-NDMA content[5] on the examined territory and the reference one; the results were assessed with regard to maximum permissible concentrations according to the hygienic standard 2.1.5.1315-03[6].

To substantiate indicators of effects, we performed an in-depth examination of two groups of children who lived in the same region with the same social-economic and geochemical features. The focus group was made up of children exposed to nitrates and N-NDMA consumed with drinking water; the reference group included children who weren't exposed to these chemicals. Children were examined in full conformity with the obligatory compliance with the ethical standards fixed in Helsinki Declaration adopted in 1975 and supplemented in 1983.

Examinations of biological media taken from children included determination of N-NDMA in blood and nitrates in urine. Parameters detected in the reference group were applied as assessment criteria for nitrates content in urine and N-NDMA content in blood. We examined 153 children aged

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[1] Loginova E.V., Lopukh P.S. Hydroecology: course of lectures. Minsk, Belarus State University Publ., 2011, 300 p. (in Russian).

[2] Drinking water quality guidelines. *The World Health Organization*, 2004, Vol. 1. Available at: http://www.who.int/water_sanitation_health/dwq/gdwq3rev/ru/ (access date 01.06.2018).

[3] Arustamov E.A., Barkalova N.V., Levakova I.V. Ecological grounds for use of natural resources. The 5th edition., revised and complemented. Moscow, 2008, 320 p. (in Russian).

[4] State Standard 31867-2012. Drinking water. Determination of anions content with chromatography and capillary electrophoresis. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200097406 (access date 26.08.2018).

[5] MG 4.1.1871-04. Gas chromatography determination of N-nitrosodimethylamine (NDMA) in drinking water and water reservoirs. *GOSTRF.COM.* Available at: http://www.gostrf.com/normadata/1/4293855/4293855338.htm (access date 26.08.2018).

[6] HS 2.1.5.1315-03. Maximum permissible concentrations (MPC) of chemicals in water objects for communal and drinking water supplies. *KODEKS: an electronic fund of legal and reference documentation.* Available at: http://docs.cntd.ru/document/901862249 (access date 26.08.2018).

4-10 who attended schools and pre-school children facilities (53% were girls and 47% boys) and lived on territories with increased nitrates concentrations in drinking water (up to 1.2 MPC, 66.9±12.92 mg/dm^3, the focus group). To perform a comparative analysis, we examined 100 children of the same age (the reference group) who consumed drinking water without any excessive nitrates contents, their average concentration being 0.2 MPC (10.9±2.7 mg/dm^3).

Blood samples were analyzed with capillary gas chromatography technique on a gas chromatographer with N-nitrosoamines specific thermionic detector and analytical column of DB-624-30m*0,32mm*1,8μm series [7]. To prepare blood samples, we applied an automated solid phase extraction system (SPE) to concentrate and extract an analyte (N-NDMA) out of a biological medium matrix [8, 9]. Urine samples with respect of nitrates concentration were examined with capillary electrophoresis[7].

Chronic introduction of nitrates and N-NDMA with drinking water results in an increased N-NDMA concentration in blood. To perform criterial assessment of effects, we profoundly examined and assessed body reactions, namely deviations in biochemical and immunological parameters. Laboratory examinations of biological media taken from children included the following:

1. *Biochemical research* ((lipids hydroperoxides, superoxide dismutase (SOD), nitrogen oxide in blood serum; 8-hydroxi-2-deoxyguanosin in blood and urine, alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), albumin, cholesterol, conjugated bilirubin, crude bilirubin, malonic dialdehyde (MDA), AOA (anti-oxidant activity) in blood plasma, crude protein, dextrose, creatinine, urea, alkaline phosphatase, gamma-glutamyl transferase (GGT), calcium, phosphor, iron, ratio of apolipoprotein A1 to B100 (Apo A1/Apo B100); methemoglobin in whole blood; B12).

2. *General clinical research* ((erythrocytes, hemoglobin, thrombocytes, leucocytes, lymphocytes, reticulocytes, eosinophils, neutrophils, and color index).

3. *Immunologic research* (IgG to nitrosoamines, cancer antigen 199 (CA 199) and carcinoembryonic antigen (S-CEA) in blood serum).

Immunologic and biochemical parameters were examined with unified procedures in Immune Biological Techniques Department (headed by O.V. Dolgikh, Doctor of Medical Sciences) and in Biochemical and Cytogenetic Techniques Department (headed by the M.A. Zemlyanova, Doctor of Medical Sciences) of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies[8, 9] [10–12].

Laboratory research was performed with an automated hematologic analyzer, biochemical automated analyzer, immunoassay analyzer, photoelectric photometer, and flow cytofluorimeter.

Indicators of effects were substantiated as per odds ratio (OR) calculation; this parameter characterized a correlation between N-NDMA concentration in blood and biochemical parameters of a response. OR>1 condition was considered to be a criterion showing the correlation existed [13].

We determined parameters of OR dependence on N-NDMA concentration in blood with building up a regression model in a form of an exponential function OR=ea0-a1x, where OR is odds ratio; x is N-NDMA concentration in blood, mg/dm3; a0, a1 are parameters of a model determined with regression analysis.

We assessed validity of an obtained model on the basis of one-factor dispersion analysis as per Fischer test (F>3.63). Discrepancies in the results were considered to be statistically significant at $p \leq 0.05$.

We processed data obtained during the research and assessed parameters of the models with Statistica 6.0 applied software and specific software products [14].

Results and discussion. Results of our research on determining nitrates and N-NDMA concentrations in water on the examined territories allowed us to reveal that nitrates concentration was 4.7 times higher, and N-NDMA concentration, 2.5 times higher, than in water consumed by children from the reference group (Table 1).

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[7]Organizational Standard M 26-2017. A procedure for measuring mass concentrations of nitrate-ions in urine with capillary electrophoresis / A certificate of accreditation given to a measuring procedure No. 88-16207-030-RA.RU.310657-2018

[8]Kamyishnikov V.S. A reference book on clinical–biochemical research and laboratory diagnostics. Moscow, MEDPress-inform Publ., 2004, 920 p. (in Russian).

[9] Tkachuk V.A, Clinical biochemistry. Edited by academician V.A. Tkachuk, – the 3rd edition, amended and supplemented. Moscow, GEOTAR-Media Publ., 2008, 462 p. (in Russian).

Table 1

Nitrates concentration in water and urine, N-NDMA concentration in blood of children from the focus and the reference group

Drinking water, mg/dm^3, ($p \leq 0.005$)			
Nitrates concentration		N-NDMA concentration	
Reference group	Focus group	Reference group	Focus group
10,9 ± 2,7	66,9 ± 12,9	0,0065 ± 0,0013	0,016 ± 0,003
Biological media, mg/dm^3			
Nitrates concentration in urine		N-NDMA concentration in blood	
Reference group (n=100)	Focus group (n = 153)	Reference group (n = 100)	Focus group (n =153)
43,7 ± 8,74	78,3 ± 15,66	0,003 ± 0,0006	0,0045 ± 0,0009

Table 2

Comparative analysis of biochemical and immunological parameters ($p<0.05$)

Parameter	Focus group			Reference group			Discrepancies between groups as per averages (p)
	M ± *m*	Frequency of samples deviating from the physiological standards, %		*M* ± *m*	Frequency of samples deviating from the physiological standards, %		
		higher	*lower*		*higher*	*lower*	
Lipid hydroperoxides, µmol/dm^3	259,8 ± 51,3	68,8	6,2	163,8 ± 39,1	0,0	73,7	0,010
B12, pmol/dm^3	116,6 ± 12,4	8,3	75,7	139,0 ± 12,5	38,6	12,6	0,030
Glutathione-S-transferase, ng/ml	103,7 ± 22,5	0,0	85,7	170,7 ± 28,8	81,0	9,5	0,000
Glutathione peroxidase,ng/ml	43,4 ± 3,8	50,0	25,7	40,2 ± 2,4	0,0	46,7	0,010
ASAT, E/dm^3	29,9 ± 1,5	50,9	35,7	27,3 ± 0,87	23,1	57,5	0,002
Alkaline phosphatase, E/dm^3	447,0 ± 41,4	50,0	25,0	382,5 ± 23,2	10,7	57,3	0,010
Crude bilirubin, µmol/dm^3	11,4 ± 1,2	41,1	47,3	9,7 ± 0,7	22,4	60,8	0,005
IgG to N-NDMA, g/dm^3	0,29 ± 0,09	51,7	41,4	0,16 ± 0,03	12,1	67,3	0,010
S-CEA, ng/ cm^3	1,2 ± 0,5	11,0	32,0	0,5 ± 0,04	0,0	30,2	0,010
CA-199, units/ml	15,3 ± 5,2	38,9	33,3	8,2 ± 3,5	3,0	85,1	0,023

Our research revealed that long-term exposure to nitrates and N-NDMA consumed with drinking water caused increased N-NDMA concentration (1.5 times higher) in blood of children from the focus group against children from the reference group ($p \leq 0.005$). Performed chemical and analytical research allowed us to reveal increased nitrates concentrations in urine of children from the focus group (1.5 times higher against the reference group).

Increased N-NDMA concentration in blood substantiates indicators of negative effects in a body. Comparative analysis of biochemical and immunological parameters in children from the focus group and the reference group was the next stage in our research on cause-and-effect relationship. The results are given in Table 2.

Increased lipids hydroperoxides concentration in blood plasma is known to be a signal that oxidation processes are activated at cellular membranes level. The performed research revealed that lipids hydroperoxides level in blood serum of children from the focus group (259.8±51.3 µmol/dm^3) was authentically 1.6 times higher than the same parameter in children from the reference group (p=0.01). Increased lipids peroxides concentration was detected in 68.8% of samples taken in the focus group. There were no similar samples in the reference group (p=0.01).

We assessed antioxidant protection in children from the focus group and revealed a 1.2 times decrease in glutathione-S-transferase concentration and a 1.7 times lower vitamin B12 level than in the reference group (p=0.000–0.030). We also detected that decreased levels of glutathione-S-transferase and vitamin B12 were registered in 75% and 85% of samples; as for the reference group, the share of such samples amounted to 12.6% and 9.5% correspondingly. Children from the focus group had 1.2 times higher glutathione peroxidase concentration than children

from the reference group. Increased glutathione peroxidase concentration was registered in 50% of samples taken in the focus group but there were no such samples in the reference group (p=0.01).

An increase in free radical oxidation processes leads to disorders in penetrability and functional properties of cellular membranes, in particular, hepatocytes [6]. It is also proved by an increase in ASAT and alkaline phosphatase activity in blood serum of children from the focus group (the parameter was up to 1.2 times higher than in the reference group, p=0.002–0.01). A number of samples with increased activity of these enzymes amounted to 51% and it was 2.21 times higher than in the reference group (23 %) (p=0.002–0.01).

We assessed excretory function of the bile-excreting tracts and detected a 1.2 times increase in crude bilirubin level in blood serum of children from the focus group against the same parameter in the reference group (p=0.005).

We examined immune regulation parameters and detected an authentic 1.8 times increase in level of IgG specific to N-NDMA against the same parameter in the reference group (p=0.01). Increased IgG to N-NDMA level was detected in 51% of samples taken in the focus group and it was 4.2 times higher than in the reference group (12 %, p=0.01).

Increased S-CEA concentration was detected in blood serum of 11% children from the focus group. We detected authentic deviations in fetal proteins concentrations from the same parameter in the reference group: S-CEA level was 2.4 times higher (p=0.01); CA-199, 1.9 times higher (p=0.023).

Detected cause-and-effect relationships within "N-NDMA concentration in blood – immunologic and biochemical parameters" system allowed us to determine regularities related to changes in immunologic and biochemical parameters of blood; these regularities confirmed that the toxicant exerted specific and non-specific impacts on the immune and digestive system [15]. Models and parameters that describe "N-NDMA concentration in blood – IgG to N-NDMA concentration in blood" are given in Table 3.

Assessment of a correlation between specific sensitization to N-NDMA as per IgG criterion revealed that increased N-NDMA concentration in blood of children from the focus group led to increased level of IgG to N-NDMA and was a linear relationship (Figure 1).

Table 3

Parameters and criteria of the model for "N-NDMA concentration in blood – IgG to N-NDMA concentration in blood" relationship

Model equation	Model parameters		Fischer test, F	Validity of model, p	Determination coefficient, R^2
	b_0	b_1			
y = 0,0094+10,76x	0,00944	10,76	1202,19	0,001	0,958

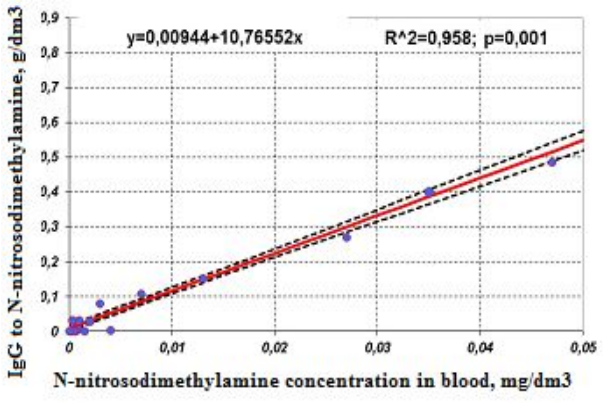

Figure 1. Model of linear "N-NDMA concentration in blood – IgG to N-NDMA concentration in blood" relationship

As we detected an increase in average group N-NDMA concentration in blood of the examined children from the focus group, we also detected an authentic (p=0.001) increase in concentration of IgG specific to N-NDMA that was confirmed by the obtained model of linear "N-NDMA concentration in blood – IgG to N-NDMA concentration in blood" relationship described with the following equation: y=0.0094+10.76x (Table 3, Figure 1).

Concentration of IgG specific to N-NDMA deviated from average values; a share of explained dispersion of these deviations was related to a factor parameter of N-NDMA concentration and amounted to 96%.

Models and parameters that described "N-NDMA concentration in blood – CA-199 concentration" relationship and "N-NDMA concentration in blood – S-CEA concentration" relationship are given in Table 4.

Table 4

Parameters and criteria of the model for "N-NDMA concentration in blood – CA-199, S-CEA concentration in blood" relationship

Model equation	Model parameters		Fischer test, F	Validity of model, p	Determination coefficient, R^2
	b_0	b_1			
y = 1,072+34,92x	0,611	3,090	12,170	0,0008	0,135
y = 0,611+3,09x	1,072	34,915	21,137	0,0001	0,203

Mathematical modeling allowed us to obtain authentic relationships for "N-NDMA concentration in blood – CA-199, S-CEA concentration in blood" that were described with the following equations: y=0.611+3.09x and y=1.072+34.92x accordingly (p=0.0001–0.0008). The detected linear relationships showed that an increase in average group concentrations of fetal proteins (CA-199 an S-CEA) in blood of the examined children from the focus group was related to N-NDMA concentration in blood. These linear relationships are shown on Figures 2 and 3.

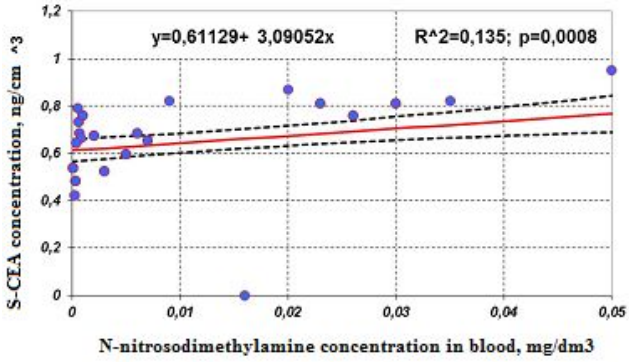

Figure 2. Model of linear "N-NDMA concentration in blood – S-CEA concentration in blood" relationship

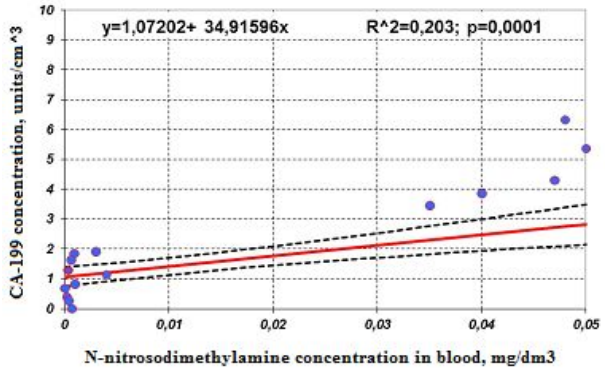

Figure 3. Model of linear "N-NDMA concentration in blood – CA-199 concentration in blood" relationship

Concentrations of CA-199 and S-CEA in blood deviated from average values; shares of explained dispersion of these deviations related to N-NDMA factor parameter amounted to 14% and 20% correspondingly, the determination coefficient being authentic.

Basing on the obtained regularities, we detected that if N-NDMA concentration in blood increased by 1 mg, CA-199 and S-CEA concentration increased on average by 0.2 units/ml and 0.002 units/ml correspondingly. This correlation can be considered a signal parameter showing a proliferation process occurs under such level of exposure to nitrates and N-NDMA in drinking water. When concentrations of nitrates and N-NDMA in drinking water increase, fetal proteins concentrations in blood will go up too.

Indicators of an effect and parameters of models that describe dependences of deviations in biochemical blood parameters on N-NDMA concentration in blood and characterize occurrence of negative effects in children are given in Table 5.

Assessment of parameters that characterize oxidation processes activity reveals that free radical damage to cellular membranes is intensified. An authentic correlation between increased lipids hydroperoxides concentration in blood serum and N-NDMA content (R^2=0.73; F=27.97; p=0.000) was an evidence that free-radical oxidation processes became more active.

Our research revealed that if N-NDMA concentration in children's blood increased, glutathione peroxidase, an intra-cellular enzyme, authentically (p=0.000) became more active (R^2=0.93; F=39.99).

Statistically authentic cause-and-effect relationships between a decrease in glutathione-S-transferase (R^2=0.49; F=88.99; p=0.000) and increased N-NDMA concentration in blood also proves there was strain in a body antioxidant protection as a response to more active free-radical processes. Liver enzymes, ASAT and alkaline phosphatase, probably became more active due to lytic impacts exerted by highly toxic N-NDMA on

Table 5

Parameters and criteria of models for "N-NDMA concentration in blood – biochemical blood parameters" relationship

Indicator of an effect	A change in a trend	Model parameters		Fischer test (F)	Validity (p<0,05)	Determination coefficient (R^2)
		a_0	a_1			
Lipid hydroperoxides	Increase	–1,80	8089,90	27,96	0,000	0,73
Glutathione-S-transferase	Decrease	0,28	4138,70	88,99	0,000	0,49
Glutathione peroxidase	Increase	–1,21	7927,64	39,99	0,000	**0,93**
ASAT	Increase	–0,38	81,89	85,66	0,000	**0,81**
Alkaline phosphatase	Increase	–1,39	1610,25	28,98	0,000	0,58
Crude bilirubin	Increase	–0,15	136,649	38,433	0,000	**0,84**
IgG to N-NDMA	Increase	–0,832	–24,497	85,465	0	**0,95**

Table 6

Results of research on cause-and-effect relationships between increased N-NDMA concentration in blood and biochemical blood parameters

Indicator	Response to an impact	Number of children		*OR*	95 % *DI*	Risk (R)	OR
		Risk factors occurrence	Absence of risk factors				
More active glutathione peroxidase	yes	18	13	8,92	3,28–24,25	0,49	2,91
	no	9	58				
More active ASAT	yes	70	43	4,67	2,67–8,19	0,50	1,78
	no	30	86				
Increased crude bilirubin	yes	93	58	11,55	5,52–24,16	0,59	1,65
	no	10	72				
Increased IgG to N-NDMA	yes	44	12	5,36	2,38–12,05	0,63	1,30
	no	26	38				

hepatocytes membranes and it could cause a risk of cytolysis syndrome. It was also proved by a detected statistically authentic dependence of an increase in activity of ASAT and alkaline phosphatase in blood serum on increased N-NDMA concentration in blood (R^2=0.58–0.81; 28.98≤F≤85.66; p=0.000).

We assessed excretory function of the bile-excreting tracts and proved that increased crude bilirubin level authentically depended on increased N-NDMA concentration in blood (R^2=0.84; F=38.43, p=0.000).

Results of our research on cause-and-effect relationships as per odds ratio (OR)[10] parameter are given in Table 6.

We verified a relationship between N-NDMA concentration in blood and glutathione peroxidase concentration (OR=8.92, DI=3.28–4.25) and it causes 2.91 times higher risk of greater strain in functional state of a body antioxidant protection system.

We also proved there was a correlation between increased penetrability of liver cells membranes (more active ASAT in blood serum) and increased N-NDMA concentration in blood (OR=4.67, DI is from 2.67 to 10.97). Accordingly, risk of increased liver enzymes levels is 1.78 times higher.

We assessed excretory-concentration function of the bile-excreting tracts and detected an authentic cause-and-effect correlation between increased crude bilirubin in blood serum and increased N-NDMA concentration in blood (OR=11.55, DI is from 5.52 to 24.16) (Table 6). Risk of a decrease in excretory function of the liver is 1.65 times higher.

We proved that concentration of IgG to N-NDMA depended on N-NDMA concentration in

[10] Chetyirkin E.M. Statistical forecasting techniques. Moscow, Statistices Publ., 1977, 356 p. (in Russian).

blood (OR=5.36, DI is from 2.38 to 12.05). Risk of changes in humoral immunity is 1.3 times higher.

Therefore, hygienic indication and criterial assessment of effects produced by chronic exposure to nitrates and N-NDMA consumed with drinking water allowed us to prove that changes in some biological regulation parameters (biochemical and immunologic ones) depended on increased N-NDMA concentration in blood. We substantiated indicators of effects produced by nitrates and N-NDMA consumed with drinking water on the basis of OR calculation and determination of cause-and-effect relationships between N-NDMA concentration in blood and indicators of responses. The substantiated indicators of effects are increased activity of glutathione peroxidase, increased ASAT activity, and higher levels of IgG to N-NDMA and crude bilirubin. These indicators of effects can be applied to assess risks of impacts on human health exerted by non-organic nitrogen-containing compounds consumed with drinking water; they can also be quite useful for prevention activities development.

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References

1. Rakhmanin Yu.A., Stekhin A.A., Yakovleva G.V. Strukturno-energeticheskie izmeneniya vody i ee biologicheskaya aktivnost' [Structural and energy changes in water and its biological activity]. *Gigiena i sanitariya*, 2007, no. 5, pp. 34–36 (in Russian).

2. Bastrakov S.I., Nikolaev A.P. Otsenka riska kachestva pit'evoi vody dlya zdorov'ya naseleniya [Assessment of population health risks related to drinking water quality]. *Sanitarnyi vrach*, 2013, no. 3, pp. 9–10.

3. Zaki A., Ait Chaoui A., Talibi A., Derouiche A.F., Aboussaouira T., Zarrouck K., Chait A., Himmi T. Impact of nitrate intake in drinking water on the thyroid gland activity in male rat. *Toxicol Lett*., 2004, vol. 147, no 1, pp. 27–33.

4. Til H.P., Falke H.E., Kuper C.F., Willems M.I. Evaluation of the oral toxicity of potassium nitrite in a 13-week drinking-water study in rats. *Food Chem Toxicol*., 1988, vol. 26, no. 10, pp. 851–859.

5. Biomarkers and human biomonitoring. Children's Health and the Environment WHO Training Package for the Health Sector. *World Health Organization*, 2011. Available at: www.who.int/ceh (19.03.2018).

6. Onishchenko G.G., Zaitseva N.V., Zemlyanova M.A. Gigienicheskaya indikatsiya posledstvii dlya zdorov'ya pri vneshnesredovoi ekspozitsii khimicheskikh faktorov [Indication and Assessment of Health Effects Caused by Environmental Chemical Exposure]. In: G.G. Onishchenko ed. Perm', Knizhnyi format Publ., 2011, 532 p. (in Russian).

7. Nurislamova T.V., Ulanova T.S., Popova N.A., Mal'tseva O.A. Sovremennye analiticheskie tekhnologii pri opredelenii vysokotoksichnykh N-nitrozoaminov v krovi [Modern analytical techniques in the determination of highly n-nitrosamines in biological fluids (blood)]. *Gigiena i sanitariya*, 2017, vol. 96, no. 1, pp. 84–89 (in Russian).

8. Yaroshenko D.V., Kartsova L.A. Matrichnyi effekt i sposoby ego ustraneniya v bioanaliticheskikh metodikakh, ispol'zuyushchikh khromato-mass-spektrometriyu [Matrix effect and methods for its elimination in bioanalytical methods using chromatography-mass spectrometry]. *Zhurnal analiticheskoi khimii*, 2014, vol. 69, no. 4, pp. 351 (in Russian).

9. Krupina N.A., Gushchenko A.V., R Pashovkina.N., Krasnova R.R., Kaletina N.I. Primenenie tverdofaznoi ekstraktsii pri issledovanii proizvodnykh benzodiazepina v biologicheskikh ob"ektakh na primere fenazepama [Application of solid phase extraction in research performed on benzodiazepine derivatives in biological objects (on the example of phenazepam)]. *Perspektivy razvitiya i sovershenstvovaniya sudebno- meditsinskoi nauki i praktiki: Materialy VI Vserossiiskogo s"ezda*

sudebnykh medikov [Development prospects of forensic theory and practice: Materials collected at the 6th Russian conference of forensic pathologists]. Moscow, Tyumen', 2005, pp. 175–178 (in Russian).

10. Glants S. Mediko-biologicheskaya statistika / pod red. N.E. Buzikashvili i soavt [Medical-biological statistics]. Moscow, Praktika Publ., 1998, 459 p. (in Russian).

11. Zaitseva N.V., Dolgikh O.V., Tyrykina T.I., M.A. Zemlyanova Diagnostika sensebilizatsii k formal'degidu [Diagnostics of sensitization to formaldehyde]. *Gigiena i sanitariya*, 2000, no. 6, pp. 44–46 (in Russian).

12. Kamilov R.F., Khanov T.V., Kudryavtsev V.P., Shakirov D.F. Svobodnoradikal'noe okislenie i antioksidantnaya zashchita pri vozdeistvii organicheskikh rastvoritelei v proizvodstve [Free radical oxidation and antioxidant defense upon exposure to organic solvents during production]. *Klinicheskaya laboratornaya diagnostika*, 2009, no. 1, pp. 9–13 (in Russian).

13. Fletcher R., Fletcher S., Vagner E. Klinicheskaya epidemiologiya. Osnovy dokazatel'noi meditsiny [Clinical epidemiology. Basics of evidence-based medicine]. Moscow, Media Sfera Publ., 1998, 352 p. (in Russian).

14. Aycicek A., Iscan A., Erel O., Akcali M., Ocak A.R. Oxidant and antioxidant parameters in the treatment of meningitis. *Pediatr. Neurol*., 2007, vol. 37, no. 2, pp. 117–120.

15. The Ethical aspects of Nanomedicine, Proc. of Roundtable Debate. Brussels, EGE Publ., 2006, 118 p.

Nurislamova T.V., Sinitsyna O.O., Mal'tseva O.A. Indicators which are applied when assessing effects on a body exerted by nitrates and N-nitrosodimethylamine introduced with drinking water. Health Risk Analysis, 2018, no. 3, pp. 76–84. DOI: 10.21668/health.risk/2018.3.08.eng

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ON DETERMINATION OF REFERENCE CHLOROFORM CONTENT IN CHILDREN'S BLOOD

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The author showed that consumption of chlorinated drinking water from centralized water supply systems with chloroform concentration being equal to 0.49 mg/l caused unacceptable non-carcinogenic risk (HI being up to 3.13) of functional disorders in the liver, kidneys, central nervous system, hormonal system, as well as the circulatory system. Assessment of carcinogenic health risk born by children revealed that individual carcinogenic risk was equal to $1.64 \cdot 10^{-5}$ under such concentration; this value corresponds to the upper limit of acceptable risk. Morbidity analysis revealed that children who consumed chlorinated drinking water from water supply systems suffered from pathologies in the nervous system, digestive organs, urogenital and endocrine systems authentically more frequently. The results coincided with those obtained in non-carcinogenic health risk assessment. Epidemiologic assessment of children morbidity revealed an authentic cause-and-effect relationship between oral exposure to chloroform introduced with drinking water and diseases in critical organs and systems (according to Guide P. 2.1.10.1920-04). The calculations showed that if population consumed drinking water with chloroform, morbidity among then could possibly grow by 10.41 times against population who didn't consume chlorinated water. The author performed in-depth research on population health via examining changes in clinical and laboratory markers that described functional disorders in critical organs and systems caused by oral introduction of chloroform. Basing on the obtained data, the author modeled 34 mathematical relationships "chloroform contents in blood – clinical and laboratory marker of a response" and chose 3 most relevant models that reflected changes in clinical and laboratory markers in accordance with chloroform contents in blood. They were an increase in alanine aminotransferase and aspartate aminotransferase which meant there were functional disorders in the liver, and a decrease in hemoglobin contents that was a sign of circulatory system disorders. Reference chloroform content in blood was fixed as per limiting hazard index principle and was equal to 0.0004 mg/dm^3 that corresponded to aspartate aminotransferase marker and confirmed that the liver was a critical organ under oral introduction of chloroform.

Key words: *chloroform, concentration, blood, drinking water, communal drinking water supply, children, reference level, critical organs, marker of exposure.*

Quality of drinking water consumed by people every day is a significant factor that determines health and life quality of any person. Drinking water is to conform to safety requirements as per its sanitary-chemical, microbiological, and parasitological parameters. But when safety is provided as per a certain parameter, it can lead to greater contamination as per another one; thus, to provide population with drinking water which conforms to all the microbiological safety parameters, it is necessary to apply disinfection [1]. Application of chlorine and chlorine-containing compounds (CCCs) as disinfectants is the most efficient and widely spread technique for water disinfection [2–4]. However, the technique has a serious drawback as it results in synthesis of highly toxic chlorinated organic compounds (COCs) due to a chemical reaction between chlorine ions and organic compounds that occur in initial water [1,5,6]. The most widely spread COCs are chloroform, tetrachloromethane (TCM), dibromchloromethane (DBCM), bromdichloromethane (BDCM) and others [7–9].

C.F. Tumasonis et al. (1987) [10], L.W. Condie et al. (1983) [11], De Salva et al. (1975) [12], F.J.C. Roe et al. (1979) [13], and A.E. Munsonetal. (1982) [14] detected in their research that chlorinated organic compounds (chloroform, tetrachloromethane, BDCM, and others) exert adverse impacts on the digestive organs, urinary excretion organs, the circulatory, nervous, and hormonal systems under oral exposure. Some COCs are carcinogenic [15–19]. When entering a body, chlorinated organic compounds are ab-

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sorbed in the gastrointestinal tract, then penetrate blood and are distributed all over a body with it (primarily damaging the parenchymal organs); they are also partially deposited in adipose tissue [20,21].

Damaging effects produced by chlorinated organic compounds are mostly determined by their metabolic transformations; as a result, highly toxic compounds occur and they can activate lipid peroxidation. It causes damage to cellular membranes and induces cells death. As a result, dystrophic and necrotic changes occur in the parenchymal organs; hemolytic disorders develop in blood cells, the nervous system suffers as neurons cellular membranes are damaged and, consequently, disorders in neural transmission occur. It confirms that impacts exerted by chlorinated organic compounds on human health are significant and it is vital to explore the subject more profoundly. Taking into account that COCs contents in water are by 70-90% determined by chloroform, its concentration in water is considered to be an indicator of chlorination products contents [22]. At the same time, M.A. Zemlyanova (2015) and D.M.Desiderio et al. (2010) state in their works that chloroform content in blood is a marker of exposure to chloroform consumed with drinking water [23,24].

Given all the above mentioned, the author chose the following **research goal:** to detect impacts exerted by chloroform in drinking water taken from centralized water supply systems (CWSS) on health of children in order to determine a reference level of chloroform content in their blood.

Data and methods. We performed hygienic assessment of water quality on territories in Perm region where drinking water was distributed and supplied to consumers via centralized water supply systems. Test and control groups were made up as per a criterion of specific chlorination techniques applied at water treatment stations prior to it being supplied to population. We examined data collected during monitoring research performed by the Center for Hygiene and Epidemiology in Perm region.

Quality of water taken from centralized water supply systems was analyzed over a period of 2012-2016. Water samples were taken at 5 different points in a water supply network: a reservoir with purified water, a pumping station of the 2nd hoist, a station for additional pumping, a stand-pipe, and a water tap. There were no authentic discrepancies in chloroform contents in water taken at all the examined points in a water supplying network ($p>0.05$). 345 samples of drinking water taken from centralized water supply systems were analyzed for the test group over 2012-2016; 387 ones, for the control group. Chloroform concentration in drinking water was determined in accordance with State Standard (GOST) 31951-2012[1]. Analysis of drinking water contamination included calculation of average parameters (upper 95% confidence limit) and their conformity with the maximum permissible concentrations fixed in Sanitary-Epidemiologic Requirements 2.1.4.1074-01[2].

We assessed population health risks that occurred under chronic oral exposure in accordance with the Guide 2.1.10.1920-04[3]. At exposure assessment stage, we calculated average daily doses of chloroform consumed with drinking water, hazard quotients (HQ), and individual carcinogenic risk (CR). To analyze carcinogenic properties, we generalized both domestic and foreign data on validity of carcinogenic effects. We took data on carcinogenic properties of chloroform primarily from the SER 1.2.2353-08[4], materials by the U.S.EPA, and databases of the IARC (Table 1).

[1] State Standard 31951-2012. Drinking water. Determination of volatile halogen-organic compounds contents with gas liquid chromatography. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200097813 (access date 11.09.2018) (in Russian).

[2] SER 2.1.4.1074-01. Drinking water. Hygienic requirements to quality of water from centralized drinking water supply systems. Quality control. Hygienic requirements to providing safety of hot water supply systems. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/901798042 (access date 11.09.2018) (in Russian).

[3] G 2.2.1.10.1920-04. Guide for assessing population health risks under exposure to chemicals that pollute environment. Moscow, The Federal Center for State Sanitary and Epidemiologic Surveillance of the RF Public Healthcare Ministry Publ., 2004, 143 p. (in Russian).

[4] SER 1.2.2353-08. Carcinogenic factors and basic requirements to prevention of carcinogenic hazards. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/902101545 (access date 11.09.2018) (in Russian).

Table 1

Data on hazards of carcinogenic and non-carcinogenic effects under oral exposure to chloroform

Chemical	CAS	Carcinogenic effects				Non-carcinogenic effects	
		U.S.EPA	IARC	Russia	SFo	RfD, μg/kg	Critical organs and systems
Chloroform	67-66-3	B2	2B	–	0,0061	0,01	Liver, kidneys, CNS, hormonal system, blood

We analyzed morbidity among children applying data taken from the Report Form 12 "Data on a number of morbid events registered in patients living on a territory served by a medical organization" issued in 2016 as per nosologic categories (according to ICD-10) which corresponded to critical organs and systems mentioned in the Guide 2.1.10.1920-04 for oral exposure to chloroform.

We compared maximum morbidity levels detected on various territories. We analyzed health of children aged 3-12 profoundly; the analysis examining biochemical blood parameters that reflected impacts exerted by chloroform on state and functions of critical organs and systems:

¨ liver and bile-excreting system (activity of alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), and alkaline phosphatase; content of highly sensitive C-reactive protein (CRP), total protein, albumin, total and direct bilirubin);

¨ kidneys (creatinine and b_2-microglobulin content);

¨ central nervous system (contents of glutamate, γ-aminobutyric acid (GABA), serotonin, and hydrocortisone);

¨ blood (contents of erythrocytes, thrombocytes, and hemoglobin in whole blood, mean corpuscular hemoglobin concentration (MCHC), ratio of erythrocytes to blood plasma volume, anisocytosis erythrocytes);

¨ oxidation processes (lipid hydroperoxides, malonic dialdehyde (MDA) in blood serum), antioxidation processes (activity of glutathione peroxidase (GPO), Cu/Zn-superoxide dismutase (Cu/Zn-SOD), glutathione-S-transferase (GST), glutathione peroxidase and antioxidant activity), cytolytic, inflammatory, and dysmetabolic processes (contents of leucocytes, dextrose, eosinophils, plasma cells, and erythrocytes sedimentation rate in whole blood); cellular immunity (lymphocytes and monocytes contents in whole blood).

We detected chloroform concentration in children's blood taking into account State Standard GOST R 8.563-96[5] via analyzing equilibrium vapor phase on "Kristall-5000" gas chromatographer with DB-624 capillary column and selective electron-capture detector (ECD) in accordance with Methodical Guidelines 4.1.2115-06[6]. All the examinations were performed in full conformity with Helsinki Declaration issued in 1975 and supplemented in 1983 and the RF National Standard GOST R 52379-2005 "Good Clinical Practice" (ICH E6 GCP).

We performed epidemiologic assessment of population morbidity via calculating odds ratio (OR) and 95% confidence interval (CI). If there was a correlation (OR>1), we considered it to be authentic in case the bottom limit of the confidence interval was higher than 1. We calculated risk parameters (R) for those nosologies for which we detected a statistically authentic relationship [25].

В качестве модели исследования использована зависимость содержания хлороформа в крови от концентрации хлороформа в питьевой воде $y = 0{,}00188 + 0{,}01782X$ ($R^2 = 0{,}263$ $p < 0{,}05$) [22].

We applied a dependence of chloroform content in blood on chloroform concentration in drinking water y=0.00188+0.01782X (R^2=0.263 p<0.05) as our research model [22].

The obtained results were statistically processed with Statistica 6.0 software and Microsoft Excel applied packages.

[5] State Standard GOST R 8.563-96. Amendment No. 2 to GOST R 8.563-96. State System for Ensuring the Uniformity of Measurements. Procedures of Measurements. *KODEKS: an electronic fund of legal and reference documentation.* Available at: http://docs.cntd.ru/document/1200030346 (access date 11.09.2018) (in Russian).

[6] Methodical Guidelines 4.1.2115-06. Determination of mass concentrations of chloroform, 1,2-dichloroethane, and tetrachloromethane in biological media (blood) via gas chromatographic analysis of equilibrium vapor. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200065247 (access date 11.09.2018) (in Russian).

If distribution of values was normal, we determined mean value (M) and a standard error of the mean (m) and assessed validity of discrepancy between them with Student's test (t). In case there was no normal distribution law, we applied Mann-Whitney test (U). Discrepancies were considered to be authentic at $p<0.05$.

Results and discussion. We detected that there were authentic discrepancies in chloroform concentrations in drinking waters between territories where chlorination was applied to treat water and territories where chlorine-containing compounds (CCCs) were not used as disinfectants (Table 2).

We detected that average annual chloroform concentrations in drinking water amounted up to 1.15 MPC on territories where drinking water was chlorinated.

Morbidity as per all the nosologies, excluding diseases of the blood, was authentically higher in children who consumed chlorinated drinking water (Table 3).

Epidemiologic assessment of morbidity among children confirmed the validity of discrepancies between the test and control groups, including diseases of the blood (Table 4).

Consumption of drinking water that contains chloroform leads to 10.41 times higher risk of the diseases of the blood; 2.94 times higher risks of diseases in the kidneys; 2.67 times higher risk of the nervous system diseases; 1.49 times higher risk of the digestive organs diseases; 1.25 times higher risk of the hormonal system diseases against people who consume non-chlorinated drinking water.

We determined unacceptable non-carcinogenic risk (HQ>1) under exposure to drinking water contaminated with chloroform; it was up to 3.13 HQ in the test group (Table 5).

Table 2

Average annual concentrations and values of 95-th quantile of chloroform drinking water samples (on territories with and without chlorination), 2012–2016

Year	Average annual chloroform concentration in water, mg/l				Validity of discrepancy (p)
	Test group (drinking water is chlorinated)	95% quantile	Control group (drinking water is not chlorinated)	95% quantile	
2012	0,013 ± 0,02	0,38	0,0158 ± 0,0020	0,030	<0,05
2013	0,20 ± 0,03	0,41	0,0113 ± 0,0018	0,024	<0,05
2014	0,23 ± 0,03	0,49	0,0091 ± 0,0020	0,019	<0,05
2015	0,20 ± 0,03	0,38	0,0043 ± 0,0015	0,020	<0,05
2016	0,087 ± 0,01	0,17	0,0031 ± 0,0012	0,010	<0,05
2012–2016	0,172 ± 0,01	0,39	0,0068 ± 0,0007	0,024	<0,05

Table 3

Morbidity among children who live on territories where drinking water is chlorinated (test group) and where it is not chlorinated (control group) in 2016 (per 1,000 people)

Code as per ICD-10	Nosology as per ICD-10	group		Validity of discrepancy (*p*)
		Test	Control	
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	35,13	33,26	0,19
E00-E90	Endocrine, nutritional, and metabolic diseases	41,0	13,75	<0,05
G00-G99	Diseases of the nervous system	64,82	23,76	<0,05
K00-K93	Diseases of the digestive organs	111,36	73,43	<0,05
N00-N99	Diseases of the genitourinary system	36,0	28,70	<0,05

Table 4

Epidemiologic assessment of morbidity among children who live on territories where drinking water is chlorinated (test group) and where it is not chlorinated (control group) in 2016

Code	Nosology as per ICD-10	Group	Response to exposure		*OR*	95% CI	Risk ratio
			yes	no			
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	test	6520	179 089	10,93	8,45–14,13	10,41
		control	59	17 708			
N00-N99	Diseases of the genitourinary system	test	7610	177 999	3,07	2,34–4,02	2,94
		control	53	3801			
G00-G99	Diseases of the nervous system	test	943	13 605	2,85	2,48–3,26	2,67
		control	276	11 339			
K00-K93	Diseases of the digestive organs	test	20 669	164 940	1,58	1,40–1,79	1,49
		control	283	3571			
E00-E90	Endocrine, nutritional, and metabolic diseases	test	6682	178 927	1,26	1,15–1,38	1,25
		control	510	17 257			

Table 5

Assessment of non-carcinogenic risk for children's health under oral exposure to chloroform consumed with drinking water

Year	Concentration, mg/l	*HQ*	95-th quantile	*HQ*	RfD, mg/kg	Critical organs and systems
Test group (consume chlorinated drinking water)						
2012	0,013 ± 0,02	0,08	0,38	2,43	0,01	Liver, kidneys, CNS, hormonal system, blood
2013	0,20 ± 0,03	1,28	0,41	2,62		
2014	0,23 ± 0,03	1,47	0,49	3,13		
2015	0,20 ± 0,03	1,28	0,38	2,43		
2016	0,087 ± 0,01	0,56	0,17	1,09		
2012–16	0,172 ± 0,01	1,10	0,39	2,49		
Control group (consume drinking water that is not chlorinated)						
2012	0,0158 ± 0,0020	0,1	0,030	0,19	0,01	Liver, kidneys, CNS, hormonal system, blood
2013	0,0113 ± 0,0018	0,07	0,024	0,15		
2014	0,0091 ± 0,0020	0,06	0,019	0,12		
2015	0,0043 ± 0,0015	0,03	0,020	0,13		
2016	0,0031 ± 0,0012	0,02	0,010	0,06		
2012–2016	0,0068 ± 0,0007	0,04	0,024	0,15		

When chloroform concentration in drinking water is equal to 0.49 mg/l, carcinogenic risk amounts to 1.64×10^{-5}, and it is the upper limit of acceptable risk so no activities aimed at its reduction are required.

We analyzed blood samples taken from children and detected chloroform in blood of 342 children, its concentrations varying from 0 to 0.02 mg/dm^3 (Table 6). Chloroform contents were authentically higher in children from the test group than in those from the control one.

We applied mathematical modeling to describe a relationship between changes in laboratory parameters of health and chloroform concentration in blood and obtained 8 biologically plausible mathematical models (Table 7).

The obtain results correlate well with scientific research data taken from various literature sources; according to them, chronic oral exposure to chloroform leads to disorders in enzymatic activity of the liver and blood system disorders. Basing on the designed models, we determined reference levels for chloroform contents in blood; the lowest one was detected at an increase in aspartate aminotransferase contents in blood (Figure).

Table 6

Average concentrations and values of 95-th quantile of chloroform contents in children's blood (test group)

Year	Average chloroform concentration in blood, mg/dm^3				Validity of discrepancies (p)
	Test group (consume chlorinated drinking water)	95% quantile	Control group (consume drinking water that is not chlorinated)	95% quantile	
2013	0,0035 ± 0,0009	0,009	–		–
2014	0,0007 ± 0,00008	0,002	0,00039 ± 0,0001	0,00019	<0,05
2015	0,0009 ± 0,0002	0,004	0,00020 ± 0,0001	0,0007	<0,05
2013–2015	0,0011 ± 0,0001	0,004	0,00027 ± 0,0002	0,0007	<0,05

Table 7

Parameters of models that describe a relationship between changes in clinical-laboratory indexes and chloroform concentration in blood

Direction of change	Index in blood	Laboratory index	Reference level of chloroform contents in blood, mg/dm^3	Validity of discrepancies, p	Coefficient of determination (R2)
Higher	Chloroform in blood	ALAT	0,00465	<0,05	0,02
Higher	Chloroform in blood	ASAT	0,00042	<0,05	0,90
Lower	Chloroform in blood	Hemoglobin	0,00075	<0,05	0,35
Higher	Chloroform in blood	Dextrose	0,00101	<0,05	0,39
Higher	Chloroform in blood	Glutathione peroxidase	0,00134	<0,05	0,51
Lower	Chloroform in blood	Total protein	0,07782	<0,05	0,07
Higher	Chloroform in blood	Lymphocytes	0,1355	<0,05	0,13
Higher	Chloroform in blood	Leukocytes	0,0834	<0,05	0,08

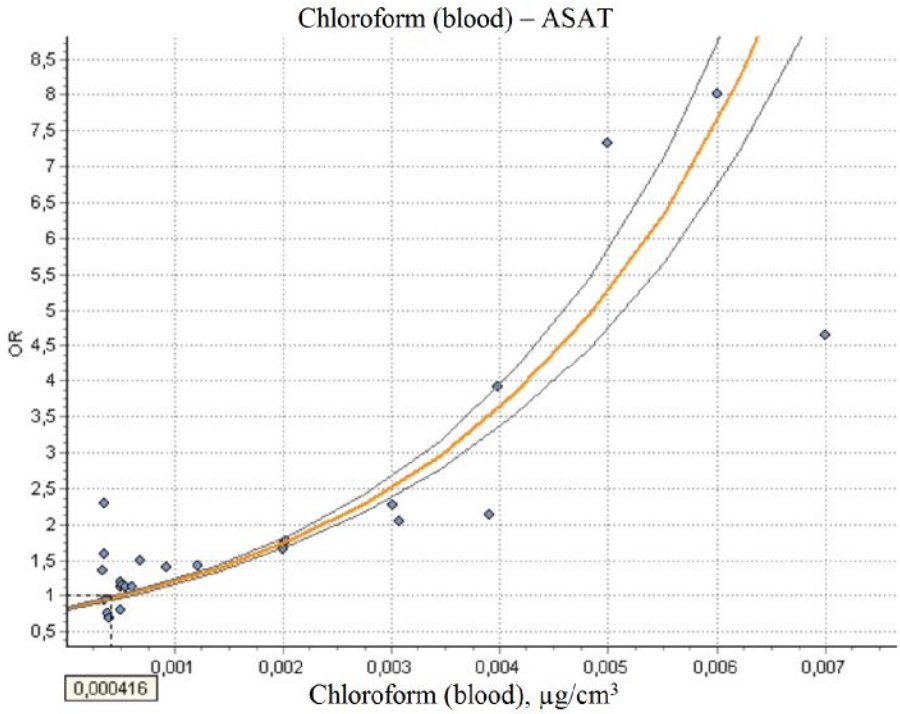

Figure 1. A model showing a dependence of odds ratio (OR) for an increase in aspartate aminotransferase contents on chloroform concentration in blood

Therefore, taking into account application of limiting hazard parameter, we can suggest to consider 0.0004 mg/dm^3 to be a reference level of chloroform contents in blood. This value corresponds to ASAT index that characterizes functioning of the liver and it confirms that the liver is a critical organ under oral exposure to chloroform.

Conclusion.

We detected an authentic discrepancy related to contamination of drinking water taken from centralized water supply systems; water was contaminated with chloroform on territories where it was disinfected with chlorine-containing compounds but there was no or insignificant chloroform contamination on territories where chlorination was not applied.

Morbidity among children assessed as per data on patients who applied for medical health due to diseases of the genitourinary system, nervous system, endocrine system, and the digestive organs was authentically higher on territories where population consumed chlorinated drinking water. Epidemiologic data are well in line with assessment of health risks among children (HQ being up to 3.13). Average long-term contamination of drinking water with chloroform that is equal to 0.172 mg/l causes unacceptable risk of diseases in the liver, kidneys, nervous system, endocrine system, and blood; it can result in higher morbidity on territories where drinking water is chlorinated. It can grow by 1.25 to 10.41 times.

We found out that contamination of drinking water taken from centralized water supply systems with chloroform that doesn't exceed 0.49 mg/l doesn't cause unacceptable carcinogenic risks (CR is not higher than 1.64×10^{-5}).

We determined a reference level of chloroform contents in blood (0.0004 mg/dm^3) as per an increase in aspartate aminotransferase contents in blood; it confirms that the liver is a critical organ under chronic oral exposure to chloroform. In future this parameter can be applied in solving tasks on fixing standards for safe chloroform concentrations in drinking water.

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References

1. Tul'skaya E.A., Rakhmanin Yu.A., Zholdakova Z.I. Obosnovanie pokazatelei bezopasnosti dlya kontrolya za primeneniem khimicheskikh sredstv obezzarazhivaniya vody i neobkhodimosti garmonizatsii ikh s mezhdunarodnymi trebovaniyami [Justification of both safety indices for control over the use of chemicals for water disinfection and need to harmonize them with international requirements]. *Gigiena i sanitariya*, 2012, no. 6, pp. 88–91 (in Russian).

2. Miftakhova K.R., P'yankova O.G., Rudakova L.V., Glushankova I.S. Khlorirovanie kak osnovnoi metod obezzarazhivaniya pit'evoi vody [Chlorination is the main method of disinfection of drinking water]. *Ekologiya i nauchno-tekhnicheskii progress. Urbanistika*, 2015, vol. 1, pp. 233–242 (in Russian).

3. Malkova M.A. Nekotorye problemy obrazovaniya trigalogenmetanov pri khlorirovanii pit'evoi vody [Some problems of formation of trigalogenmetans in chlorinated drinking water].*Vestnik molodogo uchenogo UGNTU*, 2016, no. 3, pp. 68–74 (in Russian).

4. Bahir V.M. Dezinfektsiya pit'evoi vody: problemy i reshen [Disinfection of drinking water: problems and solutions]. *Pit'evaya voda*, 2003, no. 1, pp. 13–20 (in Russian).

5. Onishhenko G.G., Zaitseva N.V., May I.V. [et al.]. Health risk analysis in the strategy of state social and economical development. In: G.G. Onishhenko, N.V. Zaitseva eds. Perm', Publishing house of the Perm National Research Polytechnic University, 2014, 738 p. (in Russian).

6. P'yankova O.G., Kuchukbaeva A.V., Glushankova I.S., Rudakova L.V. Analiz faktorov, vliyayushchikh na obrazovanie khloroforma v protsesse vodopodgotovki [Analysis of factors that influence formation of chloroform during water treatment]. *Modernizatsiya i nauchnye issledovaniya v transportnom komplekse*, 2015, no. 1, pp. 283–287 (in Russian).

7. Vozhdaeva M.YU., Cypysheva L.G., Kantor L.I., Kantor E.A. Vliyanie hlorirovaniya na sostav ogranichenno-letuchih organicheskih zagryaznitelej vody [Influence of chlorination on the composition

of partly volatile organic contaminants of water]. *Zhurnal prikladnoi khimii*, 2004, vol. 77, no. 6, pp. 952–955 (in Russian).

8. Mazaev V.T., Korolev A.A., Shlepnika T.G. Kommunal'naya gigiena [Communal Hygiene]. In: V.T. Mazaeva ed. The 2rd ed. Moscow, GEOTARMedia Publ., 2005, 304 p. (in Russian).

9. Rakhmanin Yu.A., Mikhailova R.I., Kir'yanova L.F., Sevost'yanova E.M., Ryzhova I.N., Savronskii A.Yu. Aktual'nye problemy obespecheniya naseleniya dobrokachestvennoi pit'evoi vodoi i puti ikh resheniya [Important problems of high quality drinking water supply, and the ways of their solution]. *Vestnik Rossiiskoi akademii meditsinskikh nauk*, 2006, no. 4, pp. 9–17 (in Russian).

10. Tumasonis C.F., McMartin D.N., Bush B. Toxicity of chloroform and bromodichloromethane when administered over a lifetime in rats. *Journal of Environmental Pathology, Toxicology and Oncology*, 1987, vol. 7, no. 4, pp. 55–64.

11. Condie L.W., Smallwood C.L., Laurie R.D. Comparative renal and hepatotoxicity of halomethanes: Bromodichloromethane, bromoform, chloroform, dibromochloromethane and methylene chloride. *Drug Chemical Toxicology*, 1983, vol. 6, no. 6, pp. 563–578.

12. De Salva S., Volpe A., Leigh G. [et al.]. Long-term safety studies of a chloroform-containing dentifrice and mouth-rinse in man. *Food and Cosmetics Toxicology*, 1975, vol. 13, no. 5, pp. 529–532. DOI: 1016/0015-6264(75)90007-3

13. Roe F.J.C., Palmer A.K., Worden A.N. Safety evaluation of toothpaste containing chloroform. I. Long-term studies in mice. *Journal of Environmental Pathology, Toxicology and Oncology*, 1979, vol. 2, pp. 799–819.

14. Munson A.E., Sain L.E., Sanders V.M. [et al.]. Toxicology of organic drinking water contaminants: Trichloromethane, bromodichloromethane, dibromochloromethane, and tribromomethane. *Environmental Health Perspectives*, 1982, vol. 46, pp. 117–126. DOI: 10.1289/ehp.8246117

15. Iksanova T.I., Malysheva A.G., Rastyannikov E.G., Egorova N.A., Krasovskii G.N., Nikolaev M.G. Gigienicheskaya otsenka kompleksnogo deistviya khloroforma pit'evoi vody [Hygienic evaluation of the combined effect of portable water chloroform]. *Gigiena i sanitariya*, 2006, no. 2, pp. 8–12 (in Russian).

16. Chernichenko I.A., Balenko N.V., Litvichenko O.N. Kantserogennaya opasnost' khloroforma i drugikh pobochnykh produktov khlorirovaniya pit'evoi vody [Carcinogenic hazard of chloroform and other drinking water chlorination by-products]. *Gigiena i sanitariya*, 2009, no. 3, pp. 28–33 (in Russian).

17. Sankpal U.T., Pius H., Khan M. [et al.]. Environmental factors in causing human cancers: emphasis on tumorigenesis. *Tumor Biology*, 2012, vol. 33, pp. 1265–1274. DOI: 10.1007/s13277-012-0413-4

18. Sciacca S., Conti G.O. Mutagens and carcinogens in drinking water. *Mediterranean Journal of Nutrition and Metabolism*, 2009, vol. 2, pp. 157–162.

19. Prokopov V.A., Gulenko S.V. Rol' khlorirovannoi pit'evoi vody v razvitii onkologicheskoi patologii [Role of chlorinated drinking water quality in cancer pathology development]. *Zdorov'e i okruzhayushchaya sreda*, 2013, no. 22, pp. 85–59 (in Russian).

20. Mikhailova D.L., Kol'dibekova Yu.V. Otsenka vozdeistviya khloroforma pri postuplenii v organizm s pit'evoi vodoi na sostoyanie zdorov'ya detei [Children health assessement from effect of chloroform entering in the organism with potable water]. *Vestnik Permskogo universiteta. Seriya: Biologiya*, 2012, no. 2, pp. 85–88 (in Russian).

21. U.S. EPA. Health Risk Assessment/Characterization Of The Drinking Water Disinfection Byproduct Chloroform. Prepared by Toxicology Excellence for Risk Assessment, Cincinnati, OH, under Purchase Order No. 8W-0767-NTLX. Washington, 1998, 52 p. Available at: https://www.tera.org/Publications/Chloroform.PDF (05.06.2018).

22. Dushkin S.S., Blagodarnaya G.I. Razrabotka nauchnykh osnov resursosberegayushchikh tekhnologii podgotovki ekologicheski chistoi pit'evoi vody: monografiya [Scientific substantiation for resource-saving technologies that are applied to obtain ecologically clean drinking water: Monograph]. Khar'kov, KhNAGKh Publ., 2009, 94 p. (in Russian).

23. Zemlyanova M.A., Peskova E.V. Otsenka narushenii biokhimicheskikh pokazatelei funktsii TsNS i pecheni u detei, potreblyayushchikh vodu s povyshennym soderzhaniem khlororganicheskikh soedinenii [As-

sessment of violations of biochemical indicators of central nervous system and liver in children consuming water with high content of organochlorine compounds]. *Vestnik Permskogo universiteta. Seriya: Biologiya*, 2015, no. 3, pp. 259–263 (in Russian).

24. Desiderio D.M., Nibbering N.M. White's Handbook of Chlorination and Alternative Disinfectants: Fifth Edition. New Jersey, John Wiley & Sons, Inc., 2010, 36 p. DOI:10.1002/9780470561331

25. Charles P. On the Origin of Risk Relativism. *Epidemiology*, 2010, vol. 21, no. 1, pp. 3–9. DOI: 10.1097/EDE.0b013e3181c30eba

Chetverkina K.V. On determination of reference chloroform content in children's blood. Health Risk Analysis, 2018, no. 3, pp. 85–93. DOI: 10.21668/health.risk/2018.3.09.eng

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ASSESSMENT OF CARDIOVASCULAR PATHOLOGY RISK IN MINERS EMPLOYED AT DEEP CHROME MINES

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Deep mining is widely spread in Russia; therefore, preservation of labor resources employed in the sphere is a vital task. Workers who are employed at deep chrome mines are exposed to combined effects exerted by adverse occupational factors. These factors can either be common for deep mining, or they can be related to specific natural resources. Adverse risk factors cause higher risks that not only occupational, but also production-related diseases can emerge in miners. The authors performed a complex hygienic assessment of working conditions which exist in deep chrome mines. We detected that working conditions in mines could be characterized as "hazardous" and they belonged to 3–4 hazard category due to combined negative effects exerted by physical and chemical factors of the labor process. We also performed clinical and functional examination of 135 workers employed at a chrome mine. Our focus group was made up of 88 miners; the reference group included 47 workers employed at this mine who weren't exposed to adverse factors related to chrome ores mining. All the examined workers were males, aged 30–49, with their working experience ranging from 10 to 25 years. We revealed a failure in functional activity of the endothelium in half of miners whose working experience was shorter than 10 years; and relative risk of such failure was almost 8 times higher than for workers who didn't deal with deep chrome mining. 10 % miners who had been working at the mine for more than 10 years had a substantial decrease in functional reserves of their cardio-respiratory system. Relative risk of atherosclerotic changes in vascular walls, morphological changes in the cardiac muscle and the valve apparatus was from 3.5 to 12 times higher for miners than for workers who didn't deal with deep chrome mining. We detected a direct correlation between a decrease in functional activity of the endothelium and adaptation reserves of the cardio-respiratory system and increased chrome contents in miners' blood. Periodical medical examinations of workers should include functional and morphologic research performed on the cardiovascular system as it will help to reduce morbidity with cardiovascular-pathology among miners employed at deep chrome mines and to properly implement an overall set of preventive measures.

Key words: *risk assessment, chrome mining, production-related diseases, morphofunctional changes in the vessels, the cardiac muscle and the valve apparatus of the heart.*

Working population in the Russian Federation will go down by 3 million people by 2020 as per forecasts made by the RF Ministry for Economic Development. Given that, public healthcare faces an urgent task to develop a set of activities aimed at preserving health and long occupational life of

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employable people [1, 2, 3]. But at the same time, data obtained in multi-focus research prove that more than 40% cases of temporary disability are caused by diseases related to unsatisfactory working conditions [1, 4–8].

Mining industry is one of the most successful industrial branches in the RF and preservation of labor resources there plays a most significant role in providing high labor productivity, competitiveness, and financial stability of enterprises [9–11]. Chrome ores mining is a key activity in the branch [3, 4, 12, 13]. Chrome ores are a scarce raw material in Russia and they are usually mined underground via pinpoint explosions [12,13]. Adverse/hazardous working conditions which are characteristic for mining industry cause significant health risks for workers [1, 4, 5, 14]. Workers employed at deep chrome mines are exposed to combined effects produced by adverse occupational factors when they perform their work tasks. These adverse factors are both common for any mining (neuro-psychic stress, excessive muscular load, forced body posture, increased dustiness at a workplace, unfavorable microclimate, increased radioactive background and electromagnetic radiation, in-plant noise, vibration, etc.) and related to composition of ores that are mined [1,12–15]. As per data taken from literature, combined effects produced by occupational factors, including chemical ones, have the following negative outcomes: miners suffer from angiodystonia and microcirculation disorders together with hypercoagulation, changes occur in adhesive-aggregative properties of their thrombocytes, rheological properties and oxygen-transporting function of their blood deteriorate, circulatory hypoxia occurs, lipid peroxidation is activated, and antioxidant protection is depleted [1,9,12–14]. It was detected that long-term aerogenic exposure to chrome compounds leads to disorders in vascular tonus regulation and cardiac activity, occurrence of pathomorphologic and histochemical changes in vascular walls, dystrophy, and energetic imbalance of cardiac hystiocytes [6, 9, 12–14]. Results obtained via epidemiologic and clinical research prove that cardiovascular pathology occurs in miners at an earlier age than in population in general, and life-threatening situations and disability related to this pathology are detected among miners more frequently [9, 14]. Targeted programs for early diagnostics and prevention of these diseases are to be based on risk assessment and determination of morpho-functional pathogenetic peculiarities related to cardiovascular pathology development in miners employed at deep chrome mines. Implementation of such programs will allow to stabilize working teams and increase economic efficiency of the branch.

Our research goal was to assess risks and to determine morpho-functional peculiarities associated with cardiovascular pathology development in miners employed at deep chrome mines.

Data and methods. We performed sanitary-hygienic assessment of working conditions and clinical and functional examination of 135 workers employed at a deep chrome mine. Our focus group was made up of 88 miners (miners, drifters, drilling machine operators, timber-men, scraper winch operators, spur drillers, and mining foremen) who were exposed to synergetic influence exerted by adverse occupational factors during their work shift. The reference group included 47 workers employed at the same mine but they worked on the surface and didn't have any direct contact with adverse factors associated with chrome ore mining. All the examined workers were male. Average age of workers from the focus group was 43.7±8.5 (38.9±8.4 in the reference group, p>0,05), средний стаж работы – 19,6±6,1 лет (в группе сравнения –17,3±4,7, p>0.05). The groups were comparable as per socioeconomic status and basic lifestyle factors, such as nutrition, smoking, alcohol intake, and physical activity (p>0.05). The examination was prospective (2015–2017).

Sanitary-hygienic assessment of working conditions was based on the analysis of reports drawn as per results of special assessment of working conditions (SAWC) and data obtained via field observations over working area air in accordance with valid regulatory documents[1].

To determine fractional structure, we took

[1] R 2.2.2006-05. Guide on hygienic assessment of working area and labor process factors. Criteria and classification of working conditions / approved by the RF Chief Sanitary Inspector on July 29, 2005. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs. cntd.ru/document/1200040973 (access date 26.06.2018)

dust samples on AFA-VP-20-2 filters. Suspended substances were determined with gravimetric technique[2]. To measure mass chrome concentration in working area air (WAA), we took samples on AFA-HP-20 filters.

Samples were prepared for analysis via "dry" mineralization in a muffle furnace; ash that had formed there was then dissolved in nitric acid. Chrome concentration in samples was detected with atomic absorption spectrometry (Aanalyst-400 spectrophotometer, PerkinElmer, the USA) in "acetylene-air" flame as per a conventional procedure[3]. Chrome concentration in blood was detected with inductively coupled plasma mass spectrometry (ICP-MS)[4]. Chemical elements contents were measured with Agilent 7500cx mass spectrometer ("Agilent Technologies Inc.", the USA).

A priori occupational health risk for workers dealing with deep chrome mining was assessed on the basis of sanitary-hygienic assessment of working conditions in accordance with R 2.2.1766-03[5].

Our in-depth clinical examination included research on occupational routes, data taken from case histories with assessment of lifestyle factors (heredity, tobacco smoking, and physical activity), functional examination of workers from the focus and the reference group. Volumes of clinical and functional research were determined in conformity with the RF State Standard GOST-R 52379-2005 "Good Clinical Practice"[6], as well as valid documents and standards.

We performed comparative analysis of basic diseases prevalence among workers in two groups; the analysis was based on the results obtained during periodical medical examinations and in-depth clinical and functional examination. Cardiovascular pathology was among these basic diseases.

We calculated Skibinslaya Index (SI) as per the following formula:

$$SI=0.01*VCL*BH/HR,$$

where VCL is vital capacity of lungs (in ml), determined with "Schiller SP-10" spirograph; BH is breath-holding (in minutes) during a test; HR is heart rate (per minute) determined with "Schiller AT-10 plus" electrocardiograph.

We assessed vasomotor function of the brachial artery endothelium in endothelium-dependent vasodilatation test as per a modified procedure developed by D.S. Celermajer et al. (1992); we assessed the state of extracranial sections in brachiocephalic arteries as per a conventional procedure developed by J.H. Stein et al (2008). Both tests were performed with an expert ultrasound scanner "Vivid q" with a linear sensor (4.0–13.0 MHz) [6, 16]. Doppler cardiography was performed with an expert ultrasound scanner "Vivid q" with a sector phase sensor (1.5–3.5 MHz). Structural and Doppler parameters of the heart were measured as per a conventional procedure [17, 18].

The program of sanitary-hygienic and clinical-functional research was approved by the Ethics Committee of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies (minutes No. 2, 2015). Medical and

[2] Guidelines 4.1.2468-09 Measurement of mass concentrations of dust in working are air at mining and non-metallic enterprises 2005. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/898911988 (access date 26.06.2018) (in Russian).

[3] M-01V/2011. The procedure for measuring mass concentrations of metals in pollutants emissions into the atmosphere and in working area air at industrial enterprises. *MEGANORM: information system*. Available at: http://meganorm.ru/Data2/1/4293754/4293754051.htm (access date 26.06.2018) (in Russian).

[4] Determination of chemical compounds and elements in biological media: A collection of methodical guidelines MG 4.1.3056-13, 4.1.3057-13 MG 4.1.3158-4.1.3161-14 MG 4.1.3230-4.1.3233-14. *The Federal Service for Surveillance over Consumer Rights Protection and Human Well-being*. Available at: http://www.rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=5616 (access date 26.06.2018) (in Russian).

MG 4.1.3230–14. How to measure mass concentrations of chemical elements in biological media (blood and urine) with inductively coupled plasma mass spectrometry. *MEGANORM: information system MEGANORM: information system*. Available at: http://meganorm.ru/Index2/1/4293757/4293757318.htm (access date 26.06.2018) (in Russian).

[5] R 2.2.1766-03. The Guide on Assessment of occupational risks for workers' health. Organizational and methodical grounds, principles, and assessment criteria. *Labor protection in Russia: information portal*. Available at: https://ohranatruda.ru/ot_biblio/norma/246225/ (access date 26.06.2018) (in Russian).

[6] GOST R 52379-2005. Good Clinical Practice: The RF national Standard. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200041147 (access date 26.06.2018) (in Russian).

biological research was conducted in full conformity with ethical principles fixed in Helsinki Declaration (1983). All the examined patients gave their voluntary informative consent to take part in sociological, clinical-functional, and laboratory research.

Information was analyzed with Statistica 6 software program and specific software compatible with MS-Office applications. Normalcy of measured variables distribution was checked on the basis of Kolmogorov-Smirnov test. We applied mean value (M) and error of the mean (m) to obtain quantitative characteristics of the examined parameters. Validity of discrepancies in the examined parameters between groups under comparison (Mn ± mn against Mk ± mk) was determined as per Student test ($t>2.0$; $p\leq0.05$) [19, 20].

Results and discussion. Analysis of SAWC data for the focus group revealed that equivalent noise at miners' workplaces varied from 65.3–70.9 dB(A) (miners and mining foremen, the 2nd hazard class of working conditions) to 108.2-114.9 dB(A) (drifters, spur drillers, and drilling machine operators, 3.4 hazard class of working conditions). Local vibration existing at workplaces of drifters and spur drillers was higher than the MPL (126 dB) and reached 135 dB while overall vibration was equal to 127 dB (with MPL set at 115 dB, 3.3 hazard class). Local vibration at workplaces of scraper winch operators amounted to 127 dB, and overall vibration was equal to 116 dB (3.1 hazard class). Low air temperature (9^0C, 3.3 hazard class) was detected at workplaces of all the miners. Regional/overall physical load and frequent forced (uncomfortable) body posture made for working conditions to be ranked as having 3.3 hazard class for drifters, spur drillers, and scraper winch operators; as having 3.2 hazard class, for miners, timber-men, and drilling machine operators; as having 3.1 hazard class, for mining foremen. Overall, working conditions at workplaces for all major mining occupations were considered "adverse" and were ranked as having 3.3 and 3.4 hazard class (Table 1).

Field observations results revealed that suspended substances (dust) contents in working area air for drifters, spur drillers, drilling machine operators, and scraper winch operators corresponded to 3.1 hazard class while dustiness existing at workplaces of miners, timber-men, and mining foremen didn't exceed 2 hazard class (Table 2).

At the same time, chrome concentration at workplaces of workers from the focus group didn't exceed 0.002-0.012 mg/m^3 (average shift concentration was lower than 0.5 mg/m^3; MPL is fixed at 1.0 mg/m^3), and it also corresponded to 2 hazard class (Tables 2, 3).

Chrome concentration in blood of workers from the focus group reached 0.0061±0.0022 μg/cm^3, while it was substantially lower in the reference group and didn't exceed 0.0003±0.0001 μg/cm^3 ($p=0.006$). We should note that chrome concentration in blood detected in the focus group was substantially higher than the reference level (0.0001 μg/cm^3, $p<0.001$), which can be related to cumulative effect of chrome which is typical of most metals [12].

We examined contributions made by various adverse occupational factors existing at workplaces of miners in conformity with valid regulatory documents[1], the examination revealed that a leading role belonged to physical factors of labor process (in-plant noise, vibration together with low air temperature and labor process hardness).

Table 1

Overall assessment of working conditions for workers with basic occupations in deep chrome mining

Occupations	Working conditions class as per its hazard and (or) danger							
	Chemical factor	Noise (Lequiv.)	Vibration (overall)	Vibration (local)	Microclimate	Labor Hardness	Labor Intensity	Overall estimation
miners	2	2	–	–	3,3	3,2	1	***3.3***
drifters	2	3.4	3,2	3,3	3,3	3,3	1	***3.4***
timber-men	2	3.2	–	2	3,3	3,2	1	***3.3***
spur drillers	2	3,4	3,2	3,3	3,3	3,3	1	***3.4***
mining foremen	–	2	–	–	3,3	3,1	2	***3.3***
scraper winch operators	2	3,3	3,1	3,1	3,3	3,3	1	***3.4***
drilling machine operator	2	3,4	2	2	3,3	3,2	1	***3.4***

Table 2

Filed observation results showing contents of suspended substances and chrome in working are air at workplaces of workers with basic occupations in deep chrome mining

Sampling point	Suspended substances, mg/m^3	Chrome, mg/m	Comments
Workplaces of sour drillers, drifters, scraper winch operators, and drilling machine operators	4,007 ± 0,962	< 0,0015	Measurements were performed after basic work operations had been completed (drilling, drifting, and scraping)
Miners' workplaces	2,016 ± 0,484	0,012 ± 0,003	Measurements were performed after trucks had been loaded
Timber-men's workplaces	0,704 ± 0,169	0,0034 ± 0,0008	Measurements were performed during basic work operations
Mining foremen's workplaces	0,443 ± 0,106	0,0020 ± 0,0005	Measurements were performed during basic work operations

Table 3

Assessment of working conditions class as per hazard and (or) danger related to chemical factors for workers with basic occupations in deep chrome mining

Occupations	Average shift chrome concentrations at workplaces (mg/m^3)	MPL	Overall assessment of working conditions class as per hazard and(or) danger related to chemical factors
miners	Lower than 0.5	1,0	2
drifters	Lower than 0.5	1,0	2
timber-men	Lower than 0.5	1,0	2
spur drillers	Lower than 0.5	1,0	2
mining foremen	-	1,0	1
scraper winch operators	Lower than 0.5	1,0	2
drilling machine operator	Lower than 0.5	1,0	2

Exposure to dust combined with chrome compounds is an additional adverse factor of labor process that exists at workplaces of drifters, spur drillers, drilling machine and scraper winch operators; exposure to dust and chrome compounds leads to summation of negative effects in target organs.

Working class conditions at all the workplaces in the reference group were admissible and corresponded to 2 hazard class.

We performed dynamic analysis of morbidity among workers from the examined groups and revealed that miners ran 2.8-5 times higher relative risks of nervous system diseases (ICD10: G00-G99), diseases in hearing organs (ICD10: H60-H95), upper respiratory tract diseases (J30-J84), and endocrine pathology (ICD10: E00-E07) than workers from the reference group ($p<0.001$–0,02), and diagnosed diseases were often (53-72%) or even mostly (>80%) occupational (Table 4).

Diseases of the circulatory system (ICD10: I00-I99) diagnosed in 2015-2017 in 66 workers from the focus group had a special place in morbidity structure among miners; these diseases made for their further employment strictly on the surface. They were replaced in underground operations by young workers with minimal working experience and it led to a decrease in newly detected morbid events related to the circulatory system diseases, from 28.7% in 2015 to 18.9% in 2017 ($p=0.05$). At the same time, in 2015-2016 miners with basic occupations ran 2 times higher relative risks of circulatory system diseases than workers from the reference group ($p<0.001$), and diagnosed diseases were occupational ones in 48-49% cases (average causality) (Table 4).

We analyzed the results of functional examination performed on workers from the compared groups in order to get an insight into peculiarities of cardiovascular pathology development in miners dealing with deep chrome mining. Skabinskaya Index calculation revealed that only 86.5% workers from the focus group had functional state of their cardiovascular and respiratory system at physiological level (the integral parameter was equal to 30-60 arb. units and higher) while the same level was detected in 100% of workers from the reference group ($p=0.01$); this parameter didn't exceed 21.8±2.6 arb. units in 13.5% miners ($p=0.03$ against the physiological standard), and it proved there was a significant decrease in func-

tional reserves of the cardiovascular and respiratory system.

We compared Skibinskaya Index in miners with different work experience and revealed that workers who had been employed at deep chrome mines for less than 10 years had its value lower than the physiological standard (26.3±2.8 arb. units; p=0.05) in quite insignificant number of cases (2.4%); while miners with longer work experience had this value lower than the physiological standard in each tenth case (11.1%), and the value didn't exceed 17.3±3.1 arb. units (p=0.02 against the group with working experience less than 10 years). We detected that a decrease in Skibinskaya Index value depended on chrome concentration in blood (b0=-1.89, b1=1,402.55; R^2=0.55; p≤0.001).

Table 4

Analysis of basic nosologies prevalence among workers from the compared groups

Categories of diseases (ICD10)	Observation period	Group		Relative risk of pathology for workers from focus group(p≤0,05)	CI	An extent to which a pathology detected in workers from focus group is occupational		Validity of discrepancy in frequency of pathology in the compared groups (p<0,05)
		Focus group (%)	Reference group (%)			*EF* %	Qualitative estimation	
Diseases of the nervous system (G00-G99)	2015	19,5	10,6	1,84	0,61–5,52	45	Average	**<0,001**
	2016	28,7	10,6	2,70	1,11–6,60	62	High	
	2017	54,0	14,8	3,63	1,99–6,60	72	Extremely high	
	2015–2017	34,1 ± 4,4	12,0 ± 6,0	2,72 ± 2,22	2,91–7,14	59,2 ± 33,9	-	
Diseases of the circulatory system (I00-I99)	2015	28,7	14,8	1,93	0,85–4,36	48	Average	**<0,001**
	2016	37,9	19,1	1,98	1,03–3,82	49	Average	
	2017	18,9	13,6	0,72	0,26–1,95	47	Average	
	2015–2017	28,5 ± 9,5	15,8 ± 7,2	1,54 ± 0,71	1,20–2,18	48,0 ± 2,5	Average	
Diseases of the musculoskeletal system (M00-M99)	2015	13,7	10,6	1,30	0,17–9,8	22	Insignificant	0,18
	2016	16,0	10,4	1,51	0,40–5,79	33	Average	
	2017	19,5	10,5	1,84	0,61–5,52	45	Average	
	2015–2017	16,4 ± 7,3	10,5 ± 0,3	1,55 ± 0,68	0,95–2,51	33,3 ± 11,5	-	
Diseases of the hearing organs (H90)	2015	13,7	6,3	2,16	0,49–9,62	53	High	**0,015**
	2016	12,6	2,1	5,94	0,78–45,43	83	Almost complete	
	2017	16,1	2,1	7,56	1,21–47,44	86	Almost complete	
	2015–2017	14,1 ± 4,5	3,5 ± 2,4	5,22 ± 2,77	1,88–8,53	74,0 ± 45,3	-	
Endocrine diseases (E00-E07)	2015	13,6	4,4	2,97	0,55–6,22	66	High	**0,020**
	2016	14,9	4,2	3,51	0,74–16,53	71	Extremely high	
	2017	13,4	4,1	3,11	0,68–15,18	69	Extremely high	
	2015–2017	14,0 ± 2,0	4,2 ± 0,4	3,20 ± 0,70	1,44–9,21	68,7 ± 6,3	Extremely high	
Upper respiratory organs diseases (J30-J84)	2015	8,0	6,3	1,27	0,34–4,62	62	High	**0,024**
	2016	12,6	2,1	5,94	0,79–44,62	83	Almost complete	
	2017	6,8	2,1	3,24	0,40–26,13	69	Extremely high	
	2015–2017	9,1 ± 3,1	3,5 ± 2,4	3,48 ± 2,35	1,11–6,60	71,3 ± 26,6	-	

Table 5

Examination of endothelium-dependent vasodilatation in workers from the compared groups

Brachial artery reaction	Group		Validity of discrepancy (p<0,05)
	Focus group	Reference group	
Growth in diameter ≥10%	45,24	89,47	**<0,001**
Growth in diameter <10%	54,76	10,53	**0,001**
Relative growth in brachial artery diameter, %	9,9 ± 1,7	13,7 ± 1,3	**0,001**
Coefficient of brachial artery sensitivity, arb. units	0,08 ± 0,02	0,20 ± 0,06	**<0,001**

Table 6

Examination of endothelium-dependent vasodilatation in workers from the compared groups with different working experience

Brachial artery reaction	Less than 10 years		Validity of discrepancy between groups (p<0.05)	More than 10 years		Validity of discrepancy between groups (p<0.05)
	Group			Group		
	Focus group	Reference group		Focus group	Reference group	
Growth in diameter ≥10%	51,7	91,3	**0,002**	30,8	86,7	**0,003**
Growth in diameter <10%	48,3	8,7	**0,002**	69,2	13,3	**0,003**
Relative growth in brachial artery diameter, %	10,7 ± 2,0	14,9 ± 1,7	**0,002**	8,2 ± 3,2	11,9 ± 1,8	**0,04**
Coefficient of brachial artery sensitivity, arb. units	0,10 ± 0,02	0,20 ± 0,07	**0,01**	0,06 ± 0,04	0,22 ± 0,10	**0,004**

We applied ultrasound to examine functional state of the vessels endothelium and revealed that a number of miners with low vasodilatation of the peripheral arteries was 5 times higher in the focus group than in the reference one (54.8% against 10.5%, p<0.001), and an average group growth in the brachial artery diameter was 25% lower (9.9±1.7% against 13.7±1.3%, p=0.001), and the coefficient of arteries sensitivity was 2.5 times lower (0.08±0.02 arb. units and 0.20±0.06 arb. units respectively, p<0.001) (Table 5).

As we compared assessment results for functional state of the endothelium in miners with different working experience, we revealed similar trends; in particular, a number of people with unsatisfactory test results was higher in the focus group for any working experience (48.3% and 69.2% against 8.7% and 13.3%; p=0.002–0.003), and functional failure of the endothelium was higher (p=0.004-0.01) (Table 6). Besides, it was interesting to note that a number of people with unsatisfactory vasodilatation increased by more than 20% as their working experience grew (48.3% among those with working experience shorter than 10 years, and 69.2% among those with longer working experience, p=0.02); but it increased only by less than 5% in the reference group (8.7% among those with working experience shorter than 10 years, and 13.3% among those with longer working experience, p=0.22). On the whole, relative risk of functional failure in the endothelium among workers with working experience shorter than 10 years was more than 8 times higher in the focus group than in the reference one (OR=8.6; DI=4.69–11.32; p=0.02); but as underground working experience grew longer than 10 years, this risks practically doubled (OR=14.7; DI=8.13–21.71; p=0.04). We detected that a decrease in functional activity of the endothelium depended on chrome concentration in blood (b0=2.67–4.16; b1=894.33–1129.87; R^2=0.47–0.53; p≤0.001).

The research results prove that a decrease in endothelium-dependent mechanisms of the vascular tone regulation is more apparent in ⅔ miners after just 10 years of work and gives ground for unfavorable forecast for early remodeling of the vascular wall and the consequent cardiovascular pathology development [16, 21].

We performed ultrasound examination of extracranial brachiocephalic arteries and revealed that atherosclerotic changes in vascular walls were registered 2 times more frequently in workers from the focus group than from the reference one (46.5% against 23.7%, p=0.03), and intima-media complex thickness was authentically greater (0.74±0.05 mm against 0.63±0.05 mm, p=0.003) (Table 7).

Table 7

Ultrasound examination of extracranial brachiocephalic arteries in workers from the compared groups

State of extracranial brachiocephalic arteries	Group		Validity of discrepancy (p<0,05)
	Focus group	Reference group	
No signs of atherosclerosis (%)	53,5	76,3	**0,03**
Signs of atherosclerosis (%)	46,5	23,7	**0,03**
Intima-media complex thickness (mm)	0,74 ± 0,05	0,63 ± 0,05	**0,003**

Table 8

Ultrasound examination of extracranial brachiocephalic arteries in workers with different working experience

State of extracranial brachiocephalic arteries	Less than 10 years		Validity of discrepancy between groups (p<0,05)	More than 10 years		Validity of discrepancy between groups (p<0,05)
	Group			Group		
	Focus group	Reference group		Focus group	Reference group	
No signs of atherosclerosis (%)	54,8	82,6	**0,004**	48,8	76,7	**0,04**
Signs of atherosclerosis (%)	45,2	17,4	**0,02**	51,2	23,3	**0,04**
Intima-media complex thickness (mm)	0,75 ± 0,06	0,59 ± 0,04	**<0,001**	0,79 ± 0,09	0,61 ± 0,09	**0,01**

Table 9

Doppler cardiography performed on workers form the compared groups

Test data	Group		Validity of discrepancy between groups (p<0.05)
	Focus group	Reference group	
No US-signs of pathology (%)	12,0	61,1	**<0,001**
US-signs of pathologic changes in the heart detected (%)	88,0	38,9	**<0,001**
Thicker cusps of the aortic and mitral valves (%)	60,0	27,8	**<0,001**
Interventricular septum hypertrophy (%)	54,0	22,2	**<0,001**
Eccentric hypertrophy of the left ventricle (%)	40,0	16,7	**0,01**
Muscle mass of the left ventricle, (g)	227,1 ± 15,3	189,7 ± 23,6	**0,01**
Mass index of the left ventricle cardiac muscle, (g/m^2)	113,7 ± 7,2	100,1 ± 9,9	**0,03**

We should note that miners from the focus group, even with different working experience, ran 3.5-3.8 higher relative risk of atherosclerotic changes in vascular walls than their colleagues from the reference group (OR=3.5–3.8; DI=1.44–9.89; p=0.002–0.03) (Table 8).

We analyzed Doppler cardiography results and revealed that pathologic changes in the cardiac muscle and the valve apparatus were registered 2.3 times more frequently in miners from the focus group than from the reference one (88.0% against 38.9%; p<0.001); they were thicker cusps of the aortic and mitral valves (60.0% against 27.8%; p<0.001), interventricular septum hypertrophy (54.0% against 22.2%; p<0.001), and eccentric hypertrophy of the left ventricle (40.0% against 16.7%; p=0.01) (Table 9). Overall, workers from the focus group ran almost 12 times higher risk of morphological restructuring in the cardiac muscle and the valve apparatus than workers from the reference group (OR=11.7; DI=5.39–18.72; p=0.02). We should note that average age of miners who had these detected changes in the cardiac muscle and the valve apparatus amounted to 40.6±2.7 in the focus group, while it was substantially greater in the reference group and amounted to 48.9±1.4 (p<0.001).

Results obtained via Doppler cardiography prove that miners involved in deep chrome mining and exposed to combined effects produced by adverse physical and chemical occupational factors have morphologic changes in the cardiac muscle and valve apparatus authentically more frequently.

These changes determine an unfavorable forecast of early cardiovascular pathology development.

Conclusions:

1. Existing approaches to assessing working conditions for miners involved in deep chrome mining are predominantly based on examining physical factors of labor processes and pay little attention to chemical ones.

2. 50% miners with their working experience at chrome mines being less than 10 years have early failure of the endothelium functional activity, and it is a leading promoter of cardiovascular pathology; they run 8 times higher relative risks of such pathologies against workers employed on the surface. 10% miners involved in deep chrome mining with their work experience being longer than 10 years suffer from a substantial decrease in functional reserves of the cardiorespiratory system.

3. We detected a direct correlation between a decrease in functional activity of the endothelium and adaptation reserves of the cardiorespiratory system and increased chrome concentration in blood.

4. Miners involved in deep chrome mining run 3.5-12 times higher relative risks of atherosclerotic changes in vascular walls, morphologic changes in the cardiac muscle and valve apparatus than workers employed on the surface.

5. In order to decrease morbidity with cardiovascular pathologies among miners at chrome mines and to implement prevention activities in due time, it is necessary to revise programs for periodical medical examinations and to include the following tests into them: assessment of the vasomotor function of the brachial artery endothelium and Skibinskaya Index calculation for miners with working experience longer than 5 years; Doppler ultrasonography of the brachiocephalic arteries and Doppler cardiography for miners with working experience longer than 10 years.

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References

1. Afanasova O.E., Poteryaeva E.L., Vereshchagina G.N. Vliyanie uslovii truda na formirovanie arterial'noi gipertenzii u rabotayushchikh v usloviyakh vysokogo professional'nogo riska [Influence of work conditions on arterial hypertension formation in workers under high occupational risk]. *Meditsina truda i promyshlennaya ekologiya*, 2007, no. 1, pp. 16–22 (in Russian).

2. Global strategy on Occupational health for all. The way to health at work: Recommendation of the Second Meeting of theWHO Collaborating Centres in Occupational Health. Geneva, 1995, 72 p.

3. Stein J.H., Korcarz C.E., Hurst R.T., Lonn E., Kendall C.B., Mohler E.R., Najjar S.S., Rembold C.M., Post W.S. Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force Endorsed by the Society for Vascular Medicine. *Journal of the American Society of Echocardiography*, 2008, vol. 21, no. 3, pp. 93–111. DOI: 10.1016/j.echo.2007.11.011

4. Bakirov A.B., Mingazova S.R., Karimova L.K., Serebryakov P.V., Mukhammadieva G.F. Risk of dust bronchopulmonary pathology development in workers employed in various economic brunches under impacts exerted by occupational risk factors: clinical and hygienic aspects. Health risk Analysis, 2017, no. 3, pp. 83–91. DOI: 10.21668/health.risk/2017.3.10.eng (in Russian).

5. Bukhtiyarov I.V., Yushkova O.I., Kalinina S.A., Merkulova A.G. Problema otsenki nervno-psikhicheskikh peregruzok i perenapryazheniya v meditsine truda [The problem of evaluation of neuropsychic overloads and overstrain in occupational health]. *Zdorov'e i bezopasnost' na rabochem meste: materialy II Mezhdunarodnogo nauchnogo foruma*, 2018, pp. 45–48 (in Russian).

6. Onishchenko G.G., Zaitseva N.V., Zemlyanova M.A. Gigienicheskaya indikatsiya posledstvii dlya zdorov'ya pri vneshnesredovoi ekspozitsii khimicheskikh elementov [Hygienic indication of consequences for health under exposure to chemicals contained in the environment]. Perm', Knizhnyi format Publ., 2011, 532 pp. (in Russian).

7. Onishchenko G.G., Rakhmanin Yu.A., N Zaitseva.V., Zemlyanova M.A. [et al.]. Nauchno-metodicheskie aspekty obespecheniya gigienicheskoi bezopasnosti naseleniya v usloviyakh vozdeistviya khimicheskikh faktorov [Scientific and methodological aspects related to providing hygienic safety

for population under exposure to chemical factors]. Moscow, MIG «Meditsinskaya kniga», 2004, 368 p. (in Russian).

8. Synoda V.A. Hygenic estimation of the structure and level of the professional risk of main professions in production of railway coachs. *Health Risk Analysis*, 2015, no. 2, pp. 52–61. DOI: 10.21668/health.risk/2015.2.07.eng (in Russian).

9. Panev N.I., Korotenko O.Yu., Zakharenkov V.V., Shavtsova G.M., Matveeva O.V., Popova E.V., Paneva N.Ya., Evseeva N.A., Panev R.N. Chastota zabolevanii serdechno-sosudistoi sistemy u rabotnikov ugol'noi promyshlennosti [Frequency of cardiovascular diseases in the workers of the coal industry]. *Fundamental'nye i prikladnye issledovaniya po problemam gigieny, meditsiny truda, ekologii cheloveka: materialy 51-i nauchno-prakticheskoi konferentsii s mezhdunarodnym uchastiem.* Novokuznetsk, FGBNU «Nauchno-issledovatel'skii institut kompleksnykh problem gigieny i professional'nykh zabolevanii» Publ., 2016, pp. 108–112 (in Russian).

10. Professional'naya patologiya: natsional'noe rukovodstvo [Occupational pathology: national guide]. In: N.F. Izmerov ed. Moscow, GOETAR-Media, 2011, pp. 345–346 (in Russian).

11. Izmerov N.F., Bukhtiyarov I.V., Prokopenko L.V. [et al.]. Trud i zdorov'e [Labor and health]. Moscow, Literatura Publ., 2014, 416 p. (in Russian).

12. Mamyrbaev A.A. Toksikologiya khroma i ego soedinenii [Toxicology of chrome and its compounds]. Aktobe, 2012, 284 p. (in Russian).

13. Uzbekov A.A., Mamyrbaev E.Zh., Otarov S.A., Ibraev S.A., Perepichko N.Z. Otsenka opasnosti vozdeistviya na lyudei soedinenii khroma pri dobyche khromsoderzhashchikh rud i poluchenii ferrokhroma [Assessment of risk of exposure to human of the chromium compounds during chromium ore mining and ferrochromium gaining]. *Meditsina i ekologiya*, 2014, vol. 70, no. 1, pp. 24–27 (in Russian).

14. Mit'kovskaya N.P., Radkevich Zh.I. Novyi vzglyad na prichiny razvitiya serdechno-sosudistoi patologii u shakhterov [The new concept of cardio-vascular pathology at miners]. *Rossiiskie Meditsinskie Vesti*, 2007, vol. 12, no. 3, pp. 19–28 (in Russian).

15. Titova E.Ya., Golub' S.A. Contemporary problems of health protection for workers employed at a large industrial enterprise and working under occupational hazards. *Health Risk Analysis*, 2017, no. 4, pp. 83–90. DOI: 10.21668/health.risk/2017.4.09.eng (in Russian).

16. Lelyuk V.G., Lelyuk S.E. Ul'trazvukovaya angiologiya. Prakticheskoe posobie [Ultrasound angiology. Practical guide]. The third edition. Moscow, Real'noe vremya Publ., 2007, 398 p. (in Russian).

17. Vasyuk Yu.A., Kopeeva M.V., Korneeva O.N. Rekomendatsii po kolichestvennoi otsenke struktury i funktsii kamer serdtsa [Recommendations on quantitative assessment of heart chambers structure and functions]. *Rossiiskii kardiologicheskii zhurnal*, 2012, vol. 17, no. 3, pp. 1–28 (in Russian).

18. Feigenbaum Kh. Ekhokardiografiya [Cardiac ultrasound]. In: V.V. Mit'kova ed. Moscow, Vidar Publ., 1999, 123 p. (in Russian).

19. Glants S. Mediko-biologicheskaya statistika [Medical and biological statistics]. Moscow, Praktika Publ., 1998, 459 p. (in Russian).

20. Chetyrkin E.M. Statisticheskie metody prognozirovaniya [Statistical prediction techniques]. Moscow, Statistika Publ., 1977, 356 p. (in Russian).

21. Evseeva Ya.V., Kuril'skaya T.E., Runovich A.A. Ul'trazvukovoe issledovanie vazodilatatsionnykh reaktsii endoteliya u bol'nykh sakharnym diabetom 2 tipa, assotsiirovannym s ishemicheskoi bolezn'yu serdtsa i arterial'noi gipertoniei [Ultrasound assessment of vasodilatory endothelial reactions in patients with Type 2 diabetes mellitus, associated with coronary heart disease and arterial hypertension]. *Kardiovaskulyarnaya terapiya i profilaktika*, 2005, vol. 4, no. 6–2, pp. 87–91 (in Russian).

Ustinova O.Yu., Vlasova E.M., Nosov A.E., Kostarev V.G., Lebedeva T.M. Assessment of cardiovascular pathology risk in miners employed at deep chrome mines. Health Risk Analysis, 2018, no. 3, pp. 94–103. DOI: 10.21668/health.risk/2018.3.10.eng

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TEST-MODEL AND QUANTITATIVE R_{DDS} CRITERION INDEX WHICH ARE APPLIED TO ESTIMATE ANTIMICROBIC POTENTIAL OF NANOMATERIALS USED FOR WATER PURIFICATION AND TREATMENT: SUBSTANTIATION AND METROLOGIC ASSESSMENT

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To reduce population health risks which occur when people consume drinking water from centralized water supply systems is a vital medical-biologic and technical problem. It can be sold, among other things, via development and application of new materials for water purification and treatment. Some natural and artificial nanomaterials have antimicrobic properties as they can eliminate microorganisms of various taxonomy (bacteria, yeast-like and mold fungi) and bacterial biofilms. However, certain results which were obtained when antimicrobic potential of nanomaterials was estimated are controversial; they are frequently only qualitative or semi-quantitative due to absence of a standard test protocol and well-grounded criterial assessment apparatus. So, the goal of this paper was to give methodological grounds and to create a unified and standardized test-model; to optimize parameters of a procedure and to substantiate a system of criteria applied for quantitative assessment of antimicrobic activity which is characteristic for nanomaterials applied for water purification and treatment.

The research was performed on the following objects: samples of nanomaterials based on titanium dioxide which were applied for water purification and treatment. The authors have substantiated a test-model, suggested a criterion index R_{DDS}, made up a standard test protocol for quantitative assessment of antimicrobic potential possessed by nanomaterials.

The developed technology has been tested on samples of nanomaterials based on titanium dioxide. We have calculated and assessed metrological parameters of the procedure (repeatability standard deviation and repeatability limit) which conform to the requirements existing for similar procedures when confidence probability is assumed to be equal to 95 %; such requirements are fixed by the ISO (International Standardization Organization) and correspond to the GLP (Good Laboratory Practice) principles. The relevance of the test-model was validated; this relevance provides an objective quantitative assessment of antimicrobic potential which is possessed by materials applied for disinfection of water objects contaminated with microbiota of various taxonomy, as well as for control and prevention of bacterial infections which can be communicated with water.

Key words: *nanomaterials, test-model, antimicrobic potential, quantitative criterion index R_{DDS}, metrological assessment.*

Reduction of population health risks related to drinking water consumption from centralized water supply systems is a vital medical, biological, and technical tasks. It can be solved, among other things, by developing and implementing new materials for water treatment and purification [1–5]. Some natural and artificial nano-materials based on TiO_2 [6–8], ZnO [9], silver [10–13] and more complicated compounds [7,14–18], have antimicrobic properties and can eliminate microorganisms of various taxonomy (bacteria, yeast-like and mold fungi) as well as bacterial biofilms [19–22].

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Therefore, application of nanomaterials is of great interest for those who deal with disinfection of drinking water from centralized water supply systems [23–28].

However, experimental data on antimicrobic properties of nanomaterials are controversial and they are frequently only qualitative or semi-quantitative. Methodical procedures applied for modeling in the sphere are diverse, there are no standard test reports which could be implemented into routine practices at certified laboratories. But above all, there is no substantiated criterial apparatus for quantitative assessment of antimicrobic effects produced by nanomaterials and it prevents experts from analyzing experimental data arrays in conformity with the requirements set forth by the GLP (Good Laboratory Practice) as its standards call for strict observation of a test procedure with optimized conditions and parameters that help to obtain comparable and authentic data [19, 29–32].

Our research goal was to give procedural substantiation and to develop a unified and standardized test-model; to optimize parameters of the developed procedure and to substantiate a criterial apparatus for quantitative assessment of antimicrobic effects produced by nanomaterials applied for water treatment and purification; to test all the development on innovative nanomaterials.

Data, materials and methods. We took *Escherichia coli* ATCC 8739 and *Staphylococcus aureus* ATCC 25923 strains provided by the Russian collection of industrial microorganisms. Museum microorganisms strains had typical morphological, cultural, and physiological-biochemical features that were characteristic for corresponding taxonomic bacterial groups; they also possessed good growth properties.

To obtain standardized test-models, we cultivated them in 50-ml vials containing 10 ml of a medium at 35–37°C for 18–24 hours until a stationary growth phase was reached for an optimized medium with the following structure: 500 ml of beef-extract broth; 10.0 grams of dextrose; 1.0 gram of $CaCO_3$; 0.2 grams of $MgSO_4$; 0.02 grams of $CaCl_2$; 0.02 grams of $FeCl_3$; 0.01 ml of a 10% solution of microelements per 1,000.0 ml, pH being 7.2–7.4. Suspension of a test-culture was diluted as per McFarland standard test until we obtained operating concentration of cells Log 2 CFU/ml in saline.

To test the developed procedure, we applied samples based on nano-structured titanium dioxide TiO_2 that was deposited on various substrates via different techniques. The samples were kindly given to us by Professor V.E. Borisenko, the scientific supervisor of the Center for Nanoelectronics and Innovative Materials at the Belarus State University for Informatics and Electronics, Minsk.

Description of a modeling experiment procedure. We examined antimicrobic potential of nanomaterials based on TiO_2 making their samples enter a direct contact with a standardized suspension of test-cultures. Samples of nanomaterials sized 3.5×3.5 cm^2 were put into a sterile glass cup that contained 50 ml of a standardized test-culture. The samples were exposed to it for 30 minutes with simultaneous activation that was stimulated with a visual light lamp, its model being 01200100011(EL-PL10PW, 50 Hz, 10 wt, G23D type, pure white color. Microorganisms population after the exposure was assessed via inoculation of 0.1-1 ml of suspension on surfaces of differential-diagnostic nutrient media, Endo for *E. coli* and yolk-salt agar for *S. aureus*. Inoculations were cultivated at optimal temperature equal to 35–37°C for 18–36 hours.

Measurement results processing. To perform quantitative assessment after incubation, we calculated typical formed colonies on three parallel Petri dishes that contained not less than 250 colonies. The quantity of microorganisms, CFU/ml, was calculated as per the following formula (1):

$$X = \frac{\bar{N}}{V_1}, \qquad (1)$$

where

$\bar{N}$ – is the quantity of typical colonies on a dish;
V_1 – is the volume of an inoculated sample (0,1–1,0 ml).

An arithmetic mean of the results obtained in 5 parallel measurements was assumed to be the final measuring result.

We checked eligibility of two single measuring results obtained under repeatability conditions via calculating an absolute discrepancy between common logarithms of single measuring results; the value of this discrepancy was than compared with the value of repeatability limit *r*.

If the condition (2) was true for the value of the absolute discrepancy between common logarithms of two single measuring results

$$\left|\lg X_1 - \lg X_2\right| < r, \qquad (2)$$

than both single measuring results were considered to be eligible.

We checked homogeneity of dispersions, statistical struggling and overshoots as per Cochran's Q test.

We calculated a standards deviation in repeatability as per the following formula (3):

$$Sr = \sqrt{\sum_{i=1}^{p} \frac{(y_{i1} - y_{i2})^2}{2p}}. \quad (3)$$

The value of repeatability limit r was calculated as per the following formula (4)

$$r = 2{,}8Sr. \quad (4)$$

To quantitatively assess antimicrobic effects, we introduced a term "antimicrobic potential" and substantiated index R_{DDS} calculated as per the following formula (5):

$$R_{DDS} = \frac{Lg_0 - Lg_{30}}{Lg_0}, \quad (5)$$

where Lg_0 is a common logarithm of population level before exposure;

Lg_{30} is a common logarithm of population level after 30-minute exposure.

To perform metrological assessment of the procedure, we calculated a standard deviation in repeatability and repeatability limit according to the requirements set forth by legal metrology[1]. We excluded results with a number of colonies being greater than 250 CFU/dish from our calculations.

Results and discussion. Statistical data for assessing metrological characteristics of the procedure were obtained as per results of analysis performed on 5 measuring series that were accomplished at various time moments but under repeatability conditions (Table). Antimicrobic potential that innovative nanomaterial had was calculated as per the developed standard procedure and on the basis of RDDS criterion (Table). We developed and applied the following criterial scale for assessing antimicrobic potential of a material:

$1{,}0 \geq$ RDDS $> 0{,}7$ means antimicrobic potential is apparent;

$0{,}7 \geq$ RDDS $> 0{,}5$ means antimicrobic potential is average;

$0{,}5 \geq$ RDDS $> 0{,}1$ means antimicrobic potential is insignificant;

RDDS $\leq 0{,}1$ means a material doesn't have any antimicrobic potential.

Thus, although various specimen of water microbiota have different resistance to influence exerted by nano-structured materials as it has been mentioned in works by some authors [8, 18, 32–35], we were the first to quantitatively assess antimicrobic potential as per *RDDS* criterion [36–38].

We detected that, according to a criterial scale suggested by us, antimicrobic effects were more apparent in relation to gram-negative microflora, than in relation to gram-positive one. We also revealed that exposure to nanomaterials led to changes in phenotypic properties that were characteristic for test-cultures. There were changes in tinctorial properties of *Escherichia coli* ATCC 8739 test culture and it led to Gram staining variability, typical shapes of vegetative cells also changed and they became smaller in size.

The developed procedure for quantitative assessment of antimicrobic potential possessed by nanomaterials has its operating characteristics, and we accomplished the first metrological assessment of them. We calculated a standard deviation in repeatability Sr and repeatability limit r taking into account eligibility of single measuring results which were obtained under repeatability conditions; we also checked dispersions in terms of their homogeneity, statistical struggling and overshoots as per Cochran's Q test.

Conclusion. As we developed the procedure how to quantitatively assess antimicrobic potential of nanomaterials, we managed to substantiate the following standard conditions that are necessary to perform any research and to develop a standard test report:

1. To model real-life parameters of water treatment, testing should be made only with nanomaterials entering a direct contact with a suspension of microorganisms in saline. As opposed to application of agar-based plates, such a technique allows to provide homogenous distribution of active components in water masses and to avoid distortion of test results via eliminating effects of test-cultures shielding with organic components of nutrient media and ability of nanomaterials to diffuse into dense media.

2. An important stage in the assessment is exposure of a test-culture and a nanomaterial sample to visible light for 30 minutes under photoactivation. The suggested conditions are quite sufficient for antimicrobic properties of nanomaterials to reveal themselves even in such cases when antimicrobic potential of a nanomaterial is average or weak (insignificant). In order to assess dynamics in

[1]State Standard ISO 5725-6-2002. Accuracy (validity and precision) of measuring techniques and results. Part 6. How to apply precision values in practice: The RF State Standard. Available at: http://docs.cntd.ru/document/1200029980 (date of visit June 16, 2018).

Table

Antimicrobic potential RDDS of nanomaterials samples: test results *

Sample	*Escherichia coli ATCC 8739*					*Staphylococcus aureus ATCC 25923*				
	Lg_0	$X_{cp} \pm Sr$ r	Lg_{30}	$X_{cp} \pm Sr$ r	R_{DDS}	Lg0	$X_{cp} \pm Sr$ r	Lg_{30}	$X_{cp} \pm Sr$ r	R_{DDS}
1	2,39	2,35 ± 0,058 0,162	0	0 ± 0,00 0,00	1,00 – apparent	2,32	2,32 ± 0,029	0,30	0,18 ± 0,16 0,448	0,92 – apparent
	2,34		0			2,36		0,30		
	2,44		0			2,29		0,30		
	2,31		0			2,33		0,00		
	2,30		0			2,30		0,00		
2	2,39	2,37 ± 0,033 0,092	2,08	2,09 ± 0,067 0,188	0,12 – insignificant	2,32	2,30 ± 0,024 0,067	2,04	2,15 ± 0,098 0,274	0,07 – insignificant
	2,35		2,10			2,29		2,05		
	2,41		2,00			2,27		2,25		
	2,32		2,18			2,30		2,23		
	2,36		2,12			2,33		2,18		
3	2,38	2,36 ± 0,06 0,168	1,70	1,65 ± 0,134 0,375	0,30 – insignificant	2,35	2,35 ± 0,02 0,056	1,79	1,75 ± 0,05 0,018	0,25 – незначительный
	2,40		1,83			2,36		1,81		
	2,34		1,53			2,33		1,73		
	2,28		1,68			2,38		1,74		
	2,36		1,51			2,33		1,68		
4	2,34	2,34 ± 0,061 0,171	1	0,82 ± 0,117 0,328	0,65 – average	2,29	2,26 ± 0,049 0,138	1,18	1,01 ± 0,11 0,308	0,55 – average
	2,34		0,70			2,27		1,08		
	2,44		0,85			2,30		0,95		
	2,27		0,48			2,26		0,95		
	2,32		0,90			2,18		0,90		
5	2,38	2,38 ± 0,01 0,028	2,39	2,37 ± 0,05 0,14	0,003 – none	2,21	2,26 ± 0,11 0,308	2,22	2,27 ± 0,12 0,336	–0,002 – none
	2,38		2,34			2,23		2,24		
	2,38		2,44			2,12		2,11		
	2,37		2,31			2,37		2,37		
	2,36		2,36			2,38		2,39		

Note: the data are given as an arithmetic mean of 5 measurements; *Sr* is a standard deviation in repeatability; *r* is repeatability limit.

antimicrobic effects, other exposure schemes can be chosen.

3. Epidemically significant museum strains *Escherichia coli* ATCC 8739 and *Staphylococcus aureus* ATCC 25923 are biologic test models; *Escherichia coli* is a rod-shaped gram-negative bacteria, and *Staphylococcus aureus* is a coccal gram-positive microflora specimen. The suggested strains are widely applied in routine practices of certified microbiologic laboratories as they are standard ones used in assessing efficiency of disinfectants and antiseptics, in determining growth properties of nutrient media, including test performed in conformity with international standards.

4. It is necessary to ensure that museum test-cultures are prepared for any experiment in full conformity with standardized procedures as only such preparation can provide representative and reproducible results; it is a non-standardized test-culture that usually makes the greatest contribution into uncertainties detected in the process of testing.

5. Target concentration of test-cultures should be chosen in such a way that allows to model an actual microbe load in drinking water that is equal to 2 lg CFU/ml.

6. Working surface of samples should amount to 3.5×3.5 cm^2 that is an optimal value for revealing antimicrobic potential.

7. To quantitatively assess antimicrobic effects, we introduced a term "antimicrobic potential" and substantiated R_{DDS} index calculated as per the formula (6):

$$R_{DDS} = \frac{Lg_0 - Lg_{30}}{Lg_0},$$

where Lg_0 is a common logarithm of population level before exposure;

Lg_{30} is a common logarithm of population level after 30-minute exposure.

8. We suggested a criterial assessment scale that can be applied in every day practices:

$1 \geq R_{DDS} > 0.7$ means antimicrobic potential is apparent;

$0.7 \geq R_{DDS} > 0.5$ means antimicrobic potential is average;

$0.5 \geq R_{DDS} > 0.1$ means antimicrobic potential is insignificant;

$R_{DDS} \leq 0.1$ means a material doesn't have any antimicrobic potential.

When $R_{DDS}=1$, tested nanomaterials obviously have the maximum possible antimicrobic potential; when $R_{DDS}=0$, it means a material doesn't have any antimicrobic potential; when $R_{DDS} < -0.3$, it means that influence exerted by a nanomaterials stimulates activity of microorganisms.

The suggested approaches and criterial scale can be widely implemented into practice when it is necessary to assess antimicrobic properties of new materials applied for water purification and treatment.

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References

1. Khmel'nitskii I.K., Larin A.V., Luchinin V.V. Sovremennoe sostoyanie normativno-metodicheskogo obespecheniya bezopasnosti nanotekhnologii v Rossiiskoi Federatsii [The current state of regulatory and methodical support of nanotechnology safety in the Russian Federation]. *Biotekhnosfera*, 2015, vol. 41, no. 5, pp. 95–103 (in Russian).

2. Gmoshinskii I.V., Khotimchenko S.A. Nanotekhnologii v proizvodstve pishchevykh produktov: otsenka riskov [Nanotechnologies applied in food products manufacturing: risk assessment]. *Voprosy pitaniya*, 2014, vol. 83, no. S3, pp. 174 (in Russian).

3. Onishchenko G.G., Tutel'yan V.A., Gmoshinskii I.V., Khotimchenko S.A. Razvitie sistemy otsenki bezopasnosti i kontrolya nanomaterialov i nanotekhnologii v Rossiiskoi Federatsii [Development of the system for nanomaterials and nanotechnology safety in Russian Federation]. *Gigiena i sanitariya*, 2013, № 1, pp. 4–11 (in Russian).

4. Kazak A.A., Stepanov E.G., Gmoshinskii I.V., Khotimchenko S.A. Sravnitel'nyi analiz sovremennykh podkhodov k otsenke riskov, sozdavaemykh iskusstvennymi nanochastitsami i nanomaterialami [Comparative analysis of modern approaches to risk estimation from artificially created nanoparticles and nanomaterials]. *Voprosy pitaniya*, 2012, no. 4, pp. 11–17 (in Russian).

5. Tutel'yan V.A., Khotimchenko S.A., Gmoshinskii I.V., Shumakova A.A., Raspopov R.V. Kompleksnaya mediko-biologicheskaya otsenka bezopasnosti nanomaterialov: informatsionno-analiticheskaya i eksperimental'naya sostavlyayushchie [Comprehensive medical-biological evaluation of nanomaterials safety: communicatory-analytical and experimental constituents]. *Zdorov'e naseleniya i sreda obitaniya*, 2011, no. 5, pp. 15–18 (in Russian).

6. Saad N.A., Jwad E.R. Investigation of addition titanium dioxide on general properties of polycarbonate. *Open Access Library Journal*, 2018, vol. 5, no. 1, pp. 1–11. DOI: 10.4236/oalib.1104229

7. Akhavan O. Lasting antibacterial activities of Ag-TiO_2/Ag/a-TiO_2 nanocomposite thin film photocatalysts under solar light irradiation. *J. Colloid Interface Sci*., 2009, no. 336, pp. 117–124. DOI: 10.1016/j.jcis.2009.03.018

8. Sahin Y.M., Yetmez M., Oktar F.N., Gunduz O., Agathopoulos S., Andronescu E., Ficai D., Sonmez M., Ficai A. Nanostructured biomaterials with antimicrobial properties. *Curr. Med. Chem.*, 2014, vol. 21, no. 29, pp. 3391–3404.

9. Ng A.M., Chan C.M., Guo M.Y., Leung Y.H., Djurisic A.B., Hu X., Chan W.K., Leung F.C., Tong S.Y. Antibacterial and photocatalytic activity of TiO2 and ZnO nanomaterials in phosphate buffer

and saline solution. *Appl. Microbiol. Biotechnol*., 2013, vol. 97, no. 12, pp. 5565–5573. DOI: 10.1007/s00253-013-4889-4897

10. Huang X., Bao X., Liu Y., Wang Z., Hu Q. Catechol-functional chitosan/silver nanoparticle composite as a highly effective antibacterial agent with species-specific mechanisms. Sci. Rep., 2017, vol. 12, no. 7 (1). DOI: 10.1038/s41598-017-02008-4

11. Duran N., Duran M., de Jesus M.B., Seabra A.B., Favaro W.J., Nakazato G. Silver nanoparticles: A new view on mechanistic aspects on antimicrobial activity. *Nanomedicine*, 2016, no. 12 (3), pp. 789–99. DOI: 10.1016/j.nano.2015.11.016

12. Bukina Yu.A., Sergeeva E.A. Antibakterial'nye svoistva i mekhanizm bakteritsidnogo deistviya nanochastits i ionov serebra [Antibacterial properties and bactericidal effects exerted by silver nanoparticles and ions]. *Vestnik Kazanskogo tekhnologicheskogo universiteta*, 2012, no. 14, pp. 170–171 (in Russian).

13. Franci G., Falanga A., Galdiero S., Palomba L., Rai M., Morelli G., Galdiero M. Silver nanoparticles as potential antibacterial agents., 2015, vol. 20, no. 5, pp. 8856–8874. DOI: 10.3390/molecules20058856

14. Gajjar P., Pettee B., Britt D.W., Huang W., Johnson W.P., Anderson A.J. Antimicrobial activities of commercial nanoparticles against an environmental soil microbe Pseudomonas putida KT2440. *J. of biological Engineering*, 2009, vol. 3, no. 9, pp. 420–428. DOI: 10.1186/1754-1611-3-9

15. Raghunath A., Perumal E. Metal oxide nanoparticles as antimicrobial agents: a promise for the future. *Int. J. Antimicrob. Agents*., 2017, vol. 49, no. 2, pp. 137–152. DOI: 10.1016/j.ijantimicag.2016.11.011

16. Li J., Qiao Y., Zhu H., Meng F., Liu X. Existence, release, and antibacterial actions of silver nanoparticles on Ag-PIII TiO-films with different nanotopographies. *Intern. J. of Nanomedicine*, 2014, vol. 9, no. 1, pp. 3389–3402. DOI: 10.2147/IJN.S63807

17. Rudramurthy G.R., Swamy M.K., Sinniah U.R., Ghasemzadeh A. Nanoparticles: alternatives against drug-resistant pathogenic microbes. *Molecules*, 2016, vol. 21, no. 7, pp. 836. DOI: 10.3390/molecules21070836

18. Mamonova I.A., Babushkina I.V., Norkin I.A., Gladkova E.V., Matasov M.D., Puchin'yan D.M. Biologicheskoe deistvie nanochastits metallov i ikh oksidov na bakterial'nye kletki [Biological activity of metal nanoparticles and their oxides and their effect on bacterial cells]. *Rossiiskie nanotekhnologii*, 2015, vol. 10, no. 1–2, pp. 106–110 (in Russian).

19. Zhang L., Pornpattananangku D., Hu C.M., Huang C.M. Development of Nanoparticles for Antimicrobial Drug Delivery. *Current Medicinal Chemistry*, 2010, no. 17, pp. 585–594.

20. Grumezescu A.M., Chifiriuc C.M. Prevention of microbial biofilms - the contribution of micro and nanostructured materials. *Curr. Med. Chem*., 2014, vol. 21, no. 29, pp. 3311–3317.

21. Gladkikh P.G. Effekt nanochastits serebra v otnoshenii bioplenok mikroorganizmov (literaturnyi obzor) [Effects exerted by silver nanoparticles on biofilms made up of microorganisms (literature review)]. *Vestnik novykh meditsinskikh tekhnologii. Elektronnoe izdanie*, 2015, vol. 9, no. 1, pp. 3–4 (in Russian).

22. Wu D., Fan W., Kishen A., Gutmann J.L., Fan B. Evaluation of the antibacterial efficacy of silver nanoparticles against Enterococcus faecalis biofilm. *J. Endod*, 2014, vol. 40, no. 2, pp. 285–290. DOI: 10.1016/j.joen.2013.08.022

23. Li Q., Mahendra S., Lyon D.Y., Brunet L., Liga M.V., Li D., Alvarez P.J. Antimicrobial nanomaterials for water disinfection and microbial control: Potential applications and implications. *Water research*, 2008, vol. 42, no. 18, pp. 4591–4602. DOI: 10.1016/j.watres.2008.08.015

24. Chong M.N., Jin B., Chow C.W.K., Saint C. Recent developments in photocatalytic water treatment technology: a review. *Water Research*, 2010, vol. 44, no. 10, pp. 2997–3027. DOI: 10.1016/j.watres.2010.02.039

25. Tikhomirova E.I., Vedeneeva N.V., Nechaeva O.V., Anokhina T.V. Ochistka poverkhnostnykh vod s ispol'zovaniem innovatsionnykh fil'truyushchikh zagruzok kompleksnogo deistviya [Purification the surface waters with using the innovative complex action filters]. *Izvestiya Samarskogo nauchnogo tsentra Rossiiskoi akademii nauk*, 2016, vol. 18, no. 2 (3), pp. 812–816 (in Russian).

26. Drozdova E.V., Dudchik N.V., Buraya V.V. Razrabotka metodicheskikh podkhodov k otsenke nanostrukturirovannykh materialov na osnove dioksida titana dlya ochistki vody ot khimicheskikh i biologicheskikh zagryaznenii [Development of methodological approaches to assessment of nano-structured

materials based on titanium dioxide and applied for water purification from chemical and biological contamination]. *Rol' i mesto gigienicheskoi nauki i praktiki v formirovanii zdorov'ya natsii: sbornik tezisov mezhvuzovskoi nauchno-prakticheskoi konferentsii s mezhdunarodnym uchastiem [Role played and place occupied by hygienic science and practices in creation of a nation's health: a collection of theses issued at an interuniversity theoretical and practical conference with international participation]*. Moscow, 2014, pp. 76–78 (in Russian).

27. Vedeneeva N.V., Zamatyrina V.A., Tikhomirova E.I., Anokhina T.V., Istrashkina M.V., Bobyrev S.V. Innovatsionnye metody ochistki poverkhnostnykh i stochnykh vod s ispol'zovaniem nanostrukturirovannykh sorbentov [Innovative methods for cleaning the surface and waste water using nanostructured sorbents]. *Innovatsionnaya deyatel'nost'*, 2014, vol. 2, no. 1, pp. 26–32 (in Russian).

28. Kydralieva K.A., Terekhova V.A., Poromov A.A., Kulyabko L.S., Uchanov P.V., Fedoseeva E.V., James R.A. Antimikrobnye produkty nanotekhnologii i dezinfektsiya vodnykh sred (obzor) [Antimicrobial products of nanotechnologies and disinfection of water environments (review)]. *Voda: khimiya i ekologiya*, 2017, no. 10, pp. 45–55 (in Russian).

29. Cavassin E.D., de Figueiredo L.F., Otoch J.P., Seckler M.M., de Oliveira R.A., Franco F.F., Marangoni V.S., Zucolotto V., Levin A.S., Costa S.F. Comparison of methods to detect the in vitro activity of silver nanoparticles (AgNP) against multidrug resistant bacteria. *J. Nanobiotechnology*, 2015, vol. 13, no. 64. Available at: https://jnanobiotechnology.biomedcentral.com/articles/10.1186/s12951-015-0120-6 (16.06.2018).

30. Dudchik N.V., Sychik S.I., Drozdova E.V., Kupreeva O.V. Fotokataliticheskaya inaktivatsiya populyatsii Escherichia coli i Staphylococcus aureus pod vozdeistviem strukturirovannykh nanomaterialov na osnove dioksida titana [Photocatalytic inactivation of Escherichia coli and Staphylococcus aureus populations under exposure to structured nanomaterials based on titanium dioxide]. *Donozologiya i zdorovyi obraz zhizni*, 2015, vol. 16, no. 1, pp. 28–31. (in Russian).

31. Safavi K., Mortazaeinezahad F., Esfahanizadeh M., Asgari M.J. In Vitro antibacterial activity of nanomaterial for using in tobacco plants tissue culture. *World Academy of Science, Engineering and Technology (Conference Paper)*, 2011, no. 55, pp. 372–373. DOI: 10.13140/2.1.1236.8007

32. Deryabin D.G., Aleshina E.S., Deryabina T.D., Efremova L.V. Biologicheskaya aktivnost' ionov, nano- i mikrochastits Cu i Fe v teste ingibirovaniya bakterial'noi biolyuminestsentsii [Biological Activity of Ions, Nano- and Micro-Sized Cu and Fe Particles Determined with a Bioluminescence Inhibition Assay]. *Nanotekhnologii: razrabotka, primenenie – XXI vek*, 2012, vol. 4, no. 1, pp. 28–33 (in Russian).

33. Huang K.S., Shieh D.B., Yeh C.S., Wu P.C., Cheng F.Y. Antimicrobial applications of water-dispersible magnetic nanoparticles in biomedicine. *Curr. Med. Chem.*, 2014, vol. 21, no. 29, pp. 3312–3322.

34. Rizzello L., Cingolani R., Pompa P.P. Nanotechnology tools for antibacterial materials. *Nanomedicine (Lond)*, 2013, vol. 8, no. 5, pp. 807–821. DOI: 10.2217/nnm.13.63

35. Wang L., Hu C., Shao L. The antimicrobial activity of nanoparticles: present situation and prospects for the future. *Int. J. Nanomedicine*, 2017, vol. 14, no. 12, pp. 1227–1249. DOI: 10.2147/IJN.S121956

36. Dudchik N.V., Drozdova E.V., Sychik S.I. Al'ternativnye biologicheskie test-modeli v otsenke riska vozdeistviya faktorov sredy obitaniya [Alternative biological test models for risk assessment of environmental factors]. Minsk, Belorusskii nauchno-issledovatel'skii institut transporta «Transtekhnika» Publ., 2015, 194 p. (in Russian).

37. Dudchik N.V., Shevlyakov V.V. Prokarioticheskie test-modeli dlya otsenki biologicheskogo deistviya i gigienicheskoi reglamentatsii faktorov okruzhayushchei sredy [Prokaryotic test-models for assessing biological effects and hygienic standardization of environmental factors]. *Sovremennye metodologicheskie problemy izucheniya, otsenki i reglamentirovaniya faktorov okruzhayushchei sredy, vliyayushchikh na zdorov'e cheloveka: materialy mezhdunarodnogo Foruma nauchnogo soveta Rossiiskoi Federatsii po ekologii cheloveka i gigiene okruzhayushchei sredy [Contemporary methodological issues related to examination, assessment, and standardization of environmental factors which influence people's health: materials of the international Conference held by the RF scientific council on human ecology and environmental hygiene]*. In: Yu.A. Rakhmanin ed. Moscow, 2016, vol. 1, pp. 167–189 (in Russian).

38. Mel'nikova L.A., Dudchik N.V., Kolomiets N.D. Izuchenie effektivnosti razlichnykh metodov dezobrabotki [Research on efficiency of various disinfection techniques]. *Khranenie i pererabotka sel'khozsyr'ya*, 2003, no. 8, pp. 98–99 (in Russian).

Dudchik N.V., Drozdova E.V., Sychik S.I. Test-model and quantitative R_{DDS} criterion index which are applied to estimate antimicrobic potential of nanomaterials used for water purification and treatment: substantiation and metrologic assessment. Health Risk Analysis, 2018, no. 3, pp. 104–111. DOI: 10.21668/health.risk/2018.3.11.eng

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TOXICITY OF YESSOTOXIN IN EXPERIMENT *IN VIVO*

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Yessotoxin (YTX) is a polyether. There are more than 90 known derivatives of yessotoxin. YTX was excluded from diarrhea toxins group as it, unlike okadaic acid, doesn't cause diarrhea. YTX chemical structure is similar to that of brevetoxins and ciguatoxins that influence functioning of calcium-sodium pump and trans-membrane ion channels. So, YTX can exert influence on functioning of all the organs and systems in a body. YTX is known to promote apoptosis in the cerebral tissues. Average lethal dose LD_{50} for YTX and its analogues varied from 100 μg/kg to 500–750 μg/kg; the figures were obtained in various experiments performed on mice. Safe YTX level for acute impact (acute reference dose) amounts to 25 μM/kg of body weight.

Nowadays toxicity parameters for YTX and some of its analogues are determined; its basic action mechanisms and a role it plays in promoting apoptosis are well-known. In spite of more and more data on biological effects produced by YTX on a warm-blooded organism, experts are still unable to describe its action mechanisms precisely. Our research goal was to examine YTX toxicity in experiments in vivo in doses that were lower than the detected acute reference dose.

The experiment was performed on 72 male Wistar rats with initial body weight being equal to 100 ± 10 г. Animals were given dry balanced feedstuff produced by "Laboratortakorm" LLC (Russia) and had free access to it. We used YTX preparation produced by "National Research Council Canada" (Canada) in our experiment; the preparation was a methanol solution (YTX content was equal to 4.3 μmol). We determined mass of internal organs, biochemical and hematological blood parameters, apoptosis of brain cells, malonic dialdehyde level in the brain and reduced glutathione in the liver.

We showed that YTX doses (2, 8 and 12 μM/kg) lower than ARfD = 2 μM/kg can exert toxic impacts on a warm-blooded organism. The obtain data prove it is necessary to additionally assess risks of an increase in maximum permissible YTX contents in shellfish from 1 mg/kg to 3.75 mg/kg.

Key words: *yessotoxin, action mechanisms, in vivo, biological markers, toxicity, risk assessment, permissible level.*

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Yessotoxin (YTX) is a polyether; it consists of 11 adjacent ether rings, unsaturated side chain and two sulfate ethers. There are more than 90 derivatives of yessotoxin. It was first extracted in 1986 in Japan out of scallops *Patinopectenyessoensis*. YTX is produced by algae, namely dinoflagellates *Protoceratiumreticulatum* and *Gonyaulaxspinifera*. YTX was excluded out of diarrhea toxins group (okadaic acid and its analogues, "DSP toxins") as it, unlike okadaic acid, doesn't cause diarrhea. However YTX and its analogues are often extracted together with diarrhea toxins and give positive results in biological tests aimed at detecting diarrhea poisons in shellfish [1].

YTX chemical structure is similar to those of brevetoxins and siguatoxins that exert their impacts on functioning of calcium-sodium pump and transmembrane ion channels. Mechanism that activates phosphodiesterase with yessotoxin includes an initial increase in calcium contained in cell cytosol and available to calcium-dependent I type phoisphodiesterase; then intracellular concentration of cyclic adenosine monophosphate goes down [2, 3].

YTX makes for an increase in activity of caspase 3 and 7 in HeLa cells. It stimulates greater mitochondrial membranes penetrability in livers of rats and causes disorders in cytoskeleton of cerebellum neurons cells and their consequent apoptosis; it makes for disorders in intercellular adhesion and it, in its turn, can be a possible reason for Alzheimer disease occurrence [4–7]; it influences the immune system as it makes for higher cytokines quantity due to greater expressions of genes that code them [8]. YTX induces a mitotic disaster and genetic changes that can be interesting for studying ways of control over tumor processes development [9].

Average lethal dose LD_{50} of YTX and its analogues was determined in various experiments on mice and varied from 100 μg/kg to 500-750 μg/kg [6]. In our opinion, these different toxicity values for various yessotoxins depend on peculiarities of their chemical structure. A safe dose under acute exposure to YTX (Acute Reference Dose) amounts to 25 μM/kg of a body weight. There are practically no data on YTX toxicity for other animals [3, 6, 10]. In 2004 the Order by the European Union No. 853/2004 fixed a safe concentration of yessotoxins in shellfish; it amounted to 1 mg/kg [11]. But still, analysis of yessotoxins content in shellfish meat revealed that yessotoxins contents didn't exceed 3.75 mg of yessotoxins equivalents / kg of shellfish meat in any of examined samples [6]. Results of this analysis gave grounds for a new maximum permissible concentration of yessotoxins in shellfish, 3.75 mg/kg [12].

Therefore, nowadays there are toxicity parameters set for YTX and some of its analogues; specific molecules that are primary targets for its effects are determined as well as its role as a promoter of apoptosis; maximum permissible concentration of yessotoxin in shellfish is fixed. However, in spite of more and more data on biological effects produced by YTX on a warm-blooded organism, its exact action mechanism hasn't been determined yet.

Our research goal was to examine YTX toxicity in experiments in vivo in doses lower than the fixed acute reference dose.

Data and methods. Our experiment was performed on 72 male Wistar rats with initial body weight being equal to 100±10 g. The animals were provided by the "Russian Scientific Center for Biomedical Technologies", "Stolbovaya" subsidiary. The animals were given dry balanced feedstuff produced by "Laboratorkorm" LLC (Russia) and had free access to it. The rats were kept in cages made of polycarbonate, 2-3 animals in each, their lighting regime being 12/12 hours, and the temperature being 21±1oC. All the rats were randomly divided into 12 groups, 6 animals in each; initial body weight in groups was the same ($p>0.1$ ANOVA). All the experimental work with animals was performed in compliance with the requirements to good laboratory practice fixed in Russia[1].

We used a preparation of YTX produced by "National Research Council Canada" (Canada) in our experiment; the preparation was a methanol solution (YTX content was equal to 4.3 μmol). Directly before the experiment methanol was

[1] On approval of rules for good laboratory practice: the Order by the RF Public Healthcare Ministry No. 193 dated April 01, 2016. *Pharmakopea.rf.* Available at: http://pharmacopoeia.ru/wp-content/uploads/2016/08/Prikaz-Minzdrava-199n-ot-01.04.2016-Ob-utverzhdenii-Pravil-nadlezhashhej-Laboratornoj-praktiki.pdf (date of visit April 16, 2018)

[2] State Standard 5962-2013. Ethanol rectified out of food raw materials. technical conditions. *KODEKS: an electronic fund of legal and reference documentation*. Available at: http://docs.cntd.ru/document/1200103298 (date of visit: April 16, 2018)

removed out of the preparation via vacuum evaporation under a temperature that didn't exceed +20oC; the process was not to last longer than 4 hours. A dry residue was then dissolved again in 96% ethanol solution according to the State Standard 5962-2013[2]. To obtain working dilutions of the toxin, we diluted aliquots of YTX ethanol solution with a sterile apyrogenic solution of 0.15 M NaCl; the obtained solutions had the following concentrations: 2 μM/kg (groups 2, 6, and 10); 8 μM/kg (groups 3, 7, and 11); and 12 μM/kg (groups 4, 8, and 12): 1 mol of YTX=1187.32 g. All the experimental doses were lower than the fixed acute reference dose (ARfD) of YTX that was equal to 25 μM/kg of body weight.

YTX-containing solutions were introduced into rats from the above-mentioned test groups; there was a single intraperitoneal introduction in a dose equal to 1 ml/kg of a body weight. Animals from the reference groups (1, 5 and 9) were given saline in the same manner and quantity.

Animals were taken out of the experiment 6 hours (groups 1-4), 24 hours (groups 5-8), and 168 hours (groups 9-12) after the preparation had been introduced; they were taken out of the experiment via decapitation under ether anesthesia. Blood was collected with anticoagulant (tripotassium EDTA); samples of brains tissues were taken to determine apoptosis and malonic dialdehyde concentration; samples of liver tissues were taken to determine glutathione contents. Masses of internal organs (liver, kidneys, spleen, lungs, heart, thymus, adrenals, gonads, and brains) were determined with an electronic balance with inaccuracy being equal to ±0.01 g.

We determined biochemical parameters of blood serum with "Konelab 20i" biochemical analyzer (Finland). Malonic dialdehyde contents in the brain were detected via an optical technique with 2-thiobarbituric acid and chromogen level measuring with maximum absorption in red visible spectrum with wavelength being equal to 532 nm [13]. We determined reduced glutathione contents in rats' livers with spectrophotometry as per [14].

Hematologic parameters were determined in whole blood according to conventional techniques with a "Coulter AC TTM 5 diff OV" hematologic analyzer ("Beckman Coulter", the USA) with a regents kit ("Beckman Coulter", France). We examined brain cells apoptosis with "FC 500" flow cytofluorimeter ("Beckman Coulter International S.A.", Austria) with a painting procedure applied for brain neurons; they were painted in a suspension with the following fluorescent reagents: FITC-annexin V and 7-aminoactinomycin (7-AAD) [15].

We processed the results statistically via determining sample average, standards error, a possibility of a zero hypothesis on a coincidence of compared samplings distributions as per Student test, Mann-Whitney test, and ANOVA. Discrepancies were considered to be authentic at significance level $p<0.05$.

Results and discussion. YTX introduction in all the above-mentioned doses didn't result in any signs of diseases in all the test groups. We didn't detect any authentic changes in body masses of animals or in masses of their gonads, adrenals, or brains. However, we detected an authentic decrease ($p<0.05$) in masses of spleen, lungs, and thymus (in % of a body weight) during the whole experiment. Masses of heart, kidneys, and liver also tended to go down (Figure 1).

Determination of hematologic parameters 168 hours after YTX had been introduced revealed a decrease in lymphocytes contents ($p<0.05$) and a trend for an increase in neutrophils quantity in blood serum of the experimental animals. We revealed that when the toxin was introduced in all the experimental doses, it caused an increase in leucocytes contents during the whole experiment; it was proved by discrepancies in the values obtained in most experimental groups against the reference one ($p<0.05$) (Table 1).

Despite all changes in blood composition parameters didn't have any apparent dose-depending nature, the obtained data are an evidence that YTX can possibly exert negative impacts when it is introduced intraperitoneally in doses that, according to available data, are not supposed to be toxic for experimental animals.

Urea contents in blood serum went down non-monotonously after introduction of all the experimental doses in comparison with the reference groups during the whole experiment. We detected an increased creatinine content 6 hours after the toxin introduction; the parameter decreased 168 hours after the introduction. We revealed a trend for a decrease in crude protein contents in all the test groups and a decrease in alanine aminotransferase (ALAT) in blood plasma 6 and 24 hours after the toxin introduction. The obtained data indicate that YTX influences protein metabolism and that catabolic processes induced by the toxin prevail in bodies of warm-blooded animals (Table 2).

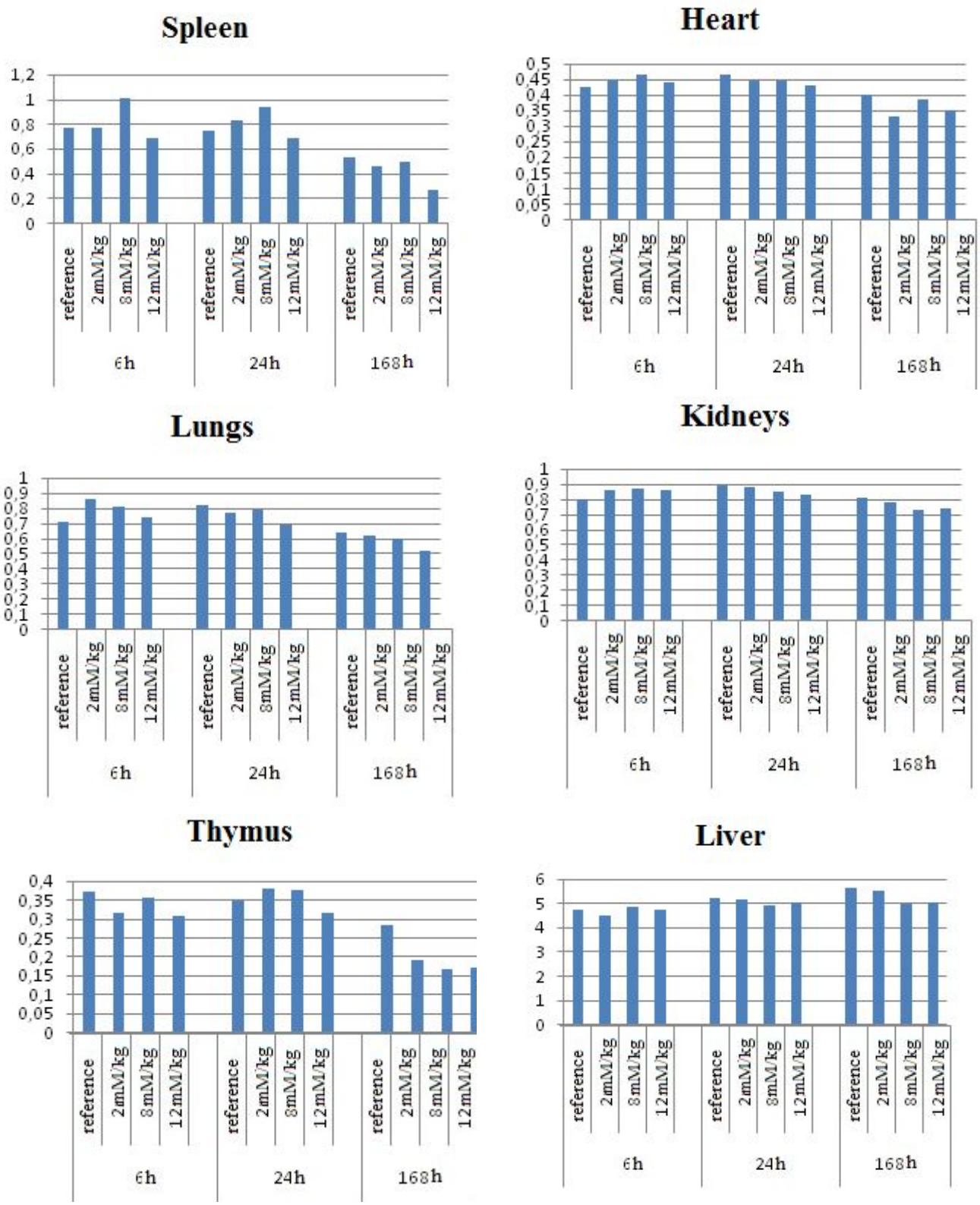


Figure 1.Dynamics of changes in masses of internal organs (in % of rats' body weight). X-axis shows doses and period of YTX introduction; Y axis shows a mass of an organ in % of a total body weight. There were 6 animals in each group.

Table 1

Hematologic parameters (erythrocytes and leukocytes), M±m of rats 6, 24 and 168 hours after YTX introduction (6 animals in each group)

Groups	YTX dose, µg/kg (mM/kg)	Period after the toxin introduction, h	Average content of Hb in erythrocyte, pg	Average Hb concentration in erythrocyte, g/l	Leucocytes, 10^9 l	Nuetrophils, %	Lymphocytes, %	Monocytes, %
1	reference	6	20,2 ± 0,4	326,5 ± 1,3	8,9 ± 1,0	24,1 ± 2,3	61,8 ± 2,8	12,6 ± 1,6
2	2		20,4 ± 1,3	326,3 ± 1,8	14,0 ± 3,2	25,8 ± 3	63,7 ± 3,0	9,2 ± 0,8
3	8		21,0 ± 0,5	322,0 ± 3,4	10,0 ± 2,6	19,9 ± 2,8	65,8 ± 3,4	11,9 ± 0,6
4	12		19,5 ± 0,4*	321,6 ± 2,8	10,7 ± 1,5*	25,2 ± 1,8	62,6 ± 2,5	10,9 ± 0,8*
5	reference	24	19,7 ± 0,3	325,3 ± 2,4	11,2 ± 1,5	23,5 ± 3,0	60,8 ± 2,6	12,6 ± 1,3
6	2		20,7 ± 0,3	324,2 ± 3,6	13,9 ± 3,6*	26,8 ± 4,6	60,4 ± 6,1	11,7 ± 1,7
7	8		20,8 ± 0,7	323,8 ± 3,1	13,3 ± 2,7*	26,3 ± 4,6	61,6 ± 4,5	11,6 ± 0,7
8	12		20,3 ± 0,3	326,0 ± 3,7	10,5 ± 1,1	23,9 ± 3,0	62,6 ± 3,2	12,0 ± 1,3
9	reference	168	19,5 ± 0,2	330,5 ± 3,6	8,4 ± 0,8	27,2 ± 2,3	57,6 ± 2,3**	13,0 ± 1,9
10	2		19,7 ± 0,3	331,8 ± 2,0	10,3 ± 1,3*	35,6 ± 2,6*	50,7 ± 2,4**	11,9 ± 1,2
11	8		20,1 ± 0,3	328,8 ± 2,7	13,7 ± 1,9*	29,3 ± 4,7	59,2 ± 4,9**	10,0 ± 1,4
12	12		19,4 ± 0,3	329,8 ± 2,2	6,4 ± 0,8	29,4 ± 2,1	54,8 ± 1,0**	13,8 ± 1,9

Note: * means authentic discrepancies from the reference group for this time period, $p<0.05$, Student T-test and/or Mann-Whitney test

** means a discrepancy between groups (6 and 168 hours after YTX introduction) is authentic for this criterion, $p<0.05$, Student T-test and/or Mann-Whitney test

Table 2

Biochemical parameters of rats' blood plasma, M±m, 6, 24 and 168 hours after YTX introduction (6 animals in each group)

Groups	YTX dose, µg/kg (mM/kg)	Period after the toxin introduction, h	Cholesterol, mmol/l	Triglycerides, mmol/l	ALT, uints/ml	AST, units/ml	Crude protein, g/l	Creatinine, µmol/l	Urea, mmol/l	Uric acid, µmol/l
1	reference	6	1,29 ± 0,20	1,01 ± 0,21	103,26 ± 11,25	184,94 ± 19,49	62,59 ± 2,93	36,15 ± 0,85	9,93 ± 0,87	213,05 ± 13,48
2	2		2,29 ± 0,07*	1,08 ± 0,10	146,42 ± 14,96*	113,64 ± 41,35	58,58 ± 0,99	44,91 ± 1,24*	6,28 ± 0,16*	222,70 ± 21,37
3	8		2,22 ± 0,08*	0,87 ± 0,10	153,35 ± 15,92*	152,75 ± 59,19	56,87 ± 1,32*	43,20 ± 3,55*	5,66 ± 0,75*	243,48 ± 24,27
4	12		1,96 ± 0,25*	0,74 ± 0,11*	140,95 ± 7,39*	160,16 ± 42,13	59,54 ± 1,48	40,25 ± 0,75*	5,95 ± 0,49*	215,21 ± 29,85
5	reference	24	1,41 + 0,16	1,01 ± 0,25	101,29 ± 9,04	182,80 ± 36,41	62,25 ± 3,78	37,66 ± 0,95	10,10 ± 1,25	195,11 ± 27,61
6	2		2,08 ± 0,15*	0,76 ± 0,08*	137,97 ± 16,01*	300,23 ± 30,72	57,53 ± 1,20*	36,36 ± 0,60	5,82 ± 0,17*	108,47 ± 11,51
7	8		1,99 ± 0,11*	0,89 ± 0,08	104,11 ± 7,05	240,16 ± 36,03	54,97 ± 1,54*	37,76 ± 0,26	7,73 ± 0,30*	171,84 ± 22,86
8	12		2,00 ± 0,17*	0,81 ± 0,07	146,54 ± 19,2*	203,70 ± 44,27	58,91 ± 1,16	40,65 ± 1,44*	7,79 ± 0,31*	191,54 ± 35,40
9	reference	168	1,94 ± 0,19	0,79 ± 0,13	106,56 ± 12,33	280,39 ± 16,19	63,72 ± 3,92	42,35 ± 1,72	9,66 ± 0,51	183,68 ± 9,71
10	2		1,83 ± 0,09	0,71 ± 0,05	91,49 ± 8,58	206,67 ± 23,28	55,38 ± 0,97*	34,40 ± 1,39*	7,69 ± 0,59*	174,08 ± 27,71
11	8		2,30 ± 0,14*	0,82 ± 0,04	116,87 ± 14,46	187,33 ± 48,06	59,25 ± 3,04	35,32 ± 2,05*	7,26 ± 0,55*	167,79 ± 53,90
12	12		1,21 ± 0,04	1,24 ± 0,04	110,77 ± 8,21	86,57 ± 29,44	59,76 ± 1,79	36,76 ± 0,71*	9,81 ± 0,62	198,33 ± 24,56

Note : * means authentic discrepancies from the reference group for this time period, $p<0.05$, Student T-test and/or Mann-Whitney test

Triglycerides contents tended to decrease and there was an authentic increase in cholesterol content in blood serum 6 and 24 hours after YTX introduction (Table 2). This dynamics is an evidence that YTX exerts its influence on lipid metabolism and that there is a possible induction of an inflammatory process caused by the toxin impacts; all the above-mentioned goes well in line with the available data on YTX action mechanism [5, 6].

We were the first to detect an authentic ($p<0.05$) dose-dependent increase in malonic dialdehyde (MDA) content in brain tissues 168 hours after YTX introduction (Figure 2) and a trend for an increase in reduced glutathione content in liver tissues (Figure 3). Besides, we revealed an authentic ($p<0.1$) dose-dependent increase in the quantity of brain neurons with early apoptosis (2.3% of cells when a dose equal to 2 mM/kg was introduced; 3.02 % of cells when a dose equal to 12 mM/kg was introduced; 1,78% of overall cells number in reference groups) and a decrease in late apoptosis activity (from 0.367% under a dose equal to 2 mM/kg to 0.180 % under a dose equal to 12 mM/kg; 0.45% of the overall cells number in reference groups) that was observed during the whole experiment (Figure 4).

The obtained data supplement those already available in literature; all the data prove that YTX induces catabolic processes. These processes become apparent via activation of free radical oxidation and brain cells apoptosis [3,6,10]. We were the first to show that YTX doses equal to 2 μM/kg, 8 μM/kg, and 12 μM/kg could produce toxic effects on a warm-blooded organism.

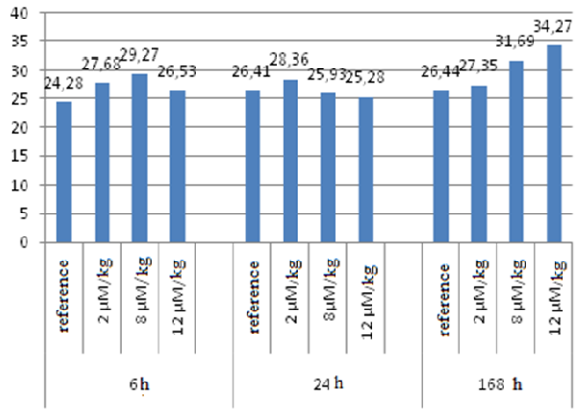


Figure 2. MDA contents in brain tissues X axis shows YTX doses; Y axis shows MDA concentration in the brain, nmol/g of tissue. There were 6 animals in each group

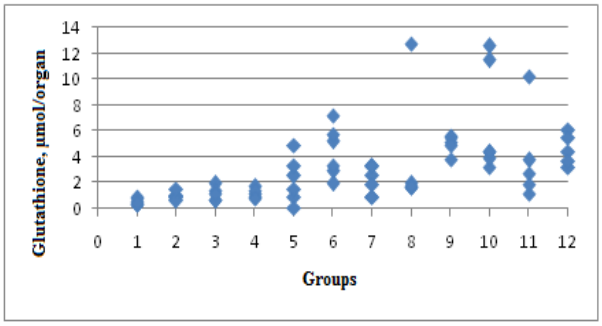
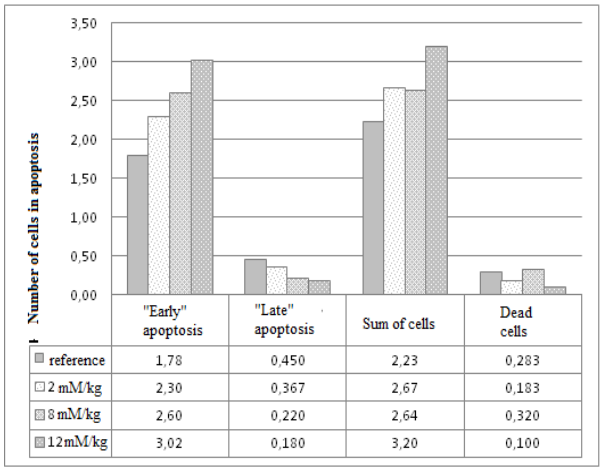


Figure 3. Reduced glutathione contents in livers of rats



	"Early" apoptosis	"Late" apoptosis	Sum of cells	Dead cells
reference	1,78	0,450	2,23	0,283
2 mM/kg	2,30	0,367	2,67	0,183
8 mM/kg	2,60	0,220	2,64	0,320
12mM/kg	3,02	0,180	3,20	0,100

Figure 4. Parameters of apoptosis in brain tissues (in % of overall number of neurons in a visual field) after YTX introduction. The obtained values of cells quantities for "early" and "late" apoptosis are authentic and dose-dependent changes in them go in opposite directions ($p<0.1$)

All the tested doses were lower than the fixed acute reference dose for YTX (ARfD = 25 μm/kg of a body weight). A dose equal to 2 μM/kg corresponds to the permissible toxin contents in shellfish, or 2.37 mg/kg. The obtained data, as well as data published in scientific works on possible toxic effects produced by YTX in doses lower than ARfD, prove that an increase in maximum permissible concentration of yessotoxins in shellfish from 1 mg/kg to 3.75 mg/kg was not well grounded.

Conclusion. Our research revealed that yessotoxin produced toxic effects when introduced intraperitoneally during the whole experiment and in all the tested doses, 2 μM/kg, 8 μM/kg, and 12 μM/kg. All the tested doses were lower than the fixed acute reference dose for YTX (ARfD), equal to 25 μM/kg of body weight. The toxic effects became apparent via:

- an authentic decrease in masses of spleen, lungs, and thymus (in % of a body weight) during

the whole experiment and trends for a decrease in masses of heart, kidneys, and liver;

- in more intense protein catabolism (a decrease in protein contends, higher creatinine, uric acid, and ALT concentration in blood plasma), and lipid catabolism (a trend for a decrease in triglycerides contents and an authentic increase in cholesterol contents in blood plasma) in all the experimental groups;

- in more intense free radical oxidation in the brain that became apparent via a dose-dependent growth in malonic dialdehyde contents 168 hours after the toxin introduction;

- in more intense processes of early apoptosis and a decrease in late apoptosis in brain tissues.

The obtained data indicate it is necessary to perform additional assessments of a risk related to an increase in maximum permissible concentration of yessotoxins in shellfish from 1 mg/kg to 3.75 mg/kg.

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Conflict of interest. The authors state there is no conflict of interests

References

1. Paz B., Daranas A.H., Norte M., Riobó P., Franco J.M., Fernández J.J. Yessotoxins, a Group of Marine Polyether Toxins: an Overview. *Mar. Drugs.*, 2008, vol. 6, pp. 73–102. DOI: 10.3390/md20080005

2. Alfonso A., de la Rosa L., Vieytes M.R., Yasumoto T., Botana L.M.Yessotoxin, a novel phycotoxin, activates phosphodiesterase activity. Effect of yessotoxin on cAMP levels in human lymphocytes. *Biochem. Pharmacol*., 2003, vol. 65, no. 2, pp. 193–208.

3. Report of the Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxins in Bivalve Molluscs. Oslo, Norway, 26–30 September 2004. Short Summary.UNESCO, 2005, 8 p. Available at: http://unesdoc.unesco.org/images/0013/001394/139421e.pdf (16.04.2018).

4. Malagoli D., Ottaviani E. Yessotoxin affects fMLP-induced cell shape changes in *Mytilusgalloprovincialis* immunocytes. *Cell. Biol. Int*., 2004, vol. 28, no.1, pp. 57–61.

5. Alfonso A., Vieytes M.R., Botana L.M. Yessotoxin, a Promising Therapeutic Tool. *Mar. Drugs*., 2016, vol. 14, pp. 30. DOI: 10.3390/md14020030

6. Marine biotoxins in shellfish – Yessotoxin group. Scientific Opinion of the Panel on Contaminants in the Food chain (Question No EFSA-Q-2006-065D). *The EFSA Journal*, 2008, vol. 907, pp. 1–62. Available at: http://www.efsa.europa.eu/sites/default/files /scientific_output/files/main_documents/907.pdf (16.04.2018).

7. Franchini A., Malagoli D., Ottaviani E. Targets and Effects of Yessotoxin, Okadaic Acid and Palytoxin: A Differential Review. *Mar. Drugs*., 2010, vol. 8, pp. 658–677. DOI: 10.3390/md8030658

8. Korsnes M.S Apoptotic events by yessotoxin in myoblast cell lines from rat and mouse. *Toxicol. in vitro*, 2006, vol. 20, pp. 1077–1087.

9. Korsnes M.S., Korsnes R. Mitotic Catastrophe in BC3H1 Cells following Yessotoxin Exposure. *Front. Cell. Dev. Biol*., 2017, vol. 5, no. 30, 18 p. DOI: 10.3389/fcell.2017.00030

10. Marine biotoxins. Food and Nutrition Paper (80). Rome: Food and agriculture organization of the united nations, 2004, 287 p.

11. Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004. *Official Journal of the European Union*, 2004. Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:139:0055:0205:EN:PDF (16.04.2018).

12. Commission Regulation (EU) No 786/2013 of 16 August 2013 amending Annex III to Regulation (EC) No 853/2004 of the European Parliament and of the Council as regards the permitted limits of yessotoxins in live bivalve mollusks. *Official Journal of the European Union*, 2013. Available at:

https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:220:0014:0014:EN:PDF (16.04.2018).

13. Ohkawa H., Ohishi N., Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal. Biochem.*, 1979, vol. 95, no. 2, pp. 351–358.

14. Razygraev A.V. Metod opredeleniya glutationperoksidaznoiaktivnosti s ispol'zovaniemperoksidavodoroda i 5,5'-ditiobis(2-nitrobenzoinoi kisloty) [A procedure for determining glutathione peroxidase activity with hydrogen peroxide and 5 5'-dithiobis(2-nitrobenzoic acid)]. *Kliniko-laboratornyikonsilium*, 2004, no. 4, pp. 19–22 (in Russian).

15. Raspopov R.V., Trushina E.N., Gmoshinsky I.V., Khotimchenko S.A. Biodostupnost' nanochastitsoksidazhelezapriispol'zovaniikhvpitanii. Rezul'taty eksperimentov na krysakh [Bioavailability of nanoparticles of ferric oxide when used in nutrition. Experimental results in rats]. *Voprosypitaniya*, 2011, vol. 80, no. 3, pp. 25–30 (in Russian).

Bagryantseva O.V., Gmoshinskii I.V., Evstratova A.D., Trushina E.N., Mustafina O.K., Soto Kh.S., Shipelin V.A., Shumakova A.A , Panova A.D., Khotimchenko S.A. Toxicity of yessotoxin in experiment in vivo. Health Risk Analysis, 2018, no. 3, pp. 112–119. DOI: 10.21668/health.risk/2018.3.12.eng

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INFLUENCE EXERTED BY *HELICOBACTER PYLORI* ON CONCENTRATIONS OF ANTI-INFLAMMATORY T-CELL CYTOKINES AND SUNPOPULATIONS THAT PRODUCE THEM

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Helicobacter pylori is a widely spread pathogenic microorganism. It penetrates the mucous tunic of the stomach and the duodenum and causes diseases in the gastrointestinal tract, including oncologic ones. This agent is able to be chronically persistent in a body and frequently there are no apparent symptoms of it; therefore, it is difficult to detect this pathogen in due time. Risk analysis related to occurrence and development of various pathologies associated with Helicobacter pylori, revealed that their clinical course was to a great extent determined by an immune response that emerged after infection. There are data that Helicobacter pylori is able to influence protective immune reactions making their balance to move to an increase in immune-suppressive components, for example, increased concentrations of T-regulatory cells and cytokines produced by them. However, some data can be found on Helicobacter pylori ability to induce anti-inflammatory responses which include those associated with T-helpers of the 1st and 17th types. Our research goal was to reveal peculiarities of effects produced by this pathogen on γ-interferon as one of basic products by 1st type T-helpers and on contents of the 17th type T-helpers determined as cells belonging to $CD4^+CD161^+$ and $CD4^+IL17^+$ phenotypes under direct contacts between bacteria and lymphocytes. Our research objects were clinical isolates of Helicobacter pylori and blood samples taken from people without helicobacter infection in their case history. We extracted lymphocytes with immunomagnetic separation out of mononuclear blood cells obtained via functioning in density gradient. Their concentrations were assessed with cytofluorometry; cytokines products, with enzyme-linked immunosorbent assay. We showed that $CD4^+CD161^+$ and $CD4^+IL17^+$ cells content didn't change when they were cultivated together for 18 hours under influence exerted by Helicobacter pylori, while products of γ-interferon increased considerably. It can probably be related to activation of the 1st type T-helpers under effects produced by direct contact with bacteria. However, we didn't detect any activation of the 17th type T-helpers. Therefore, we can assume that effects produced by Helicobacter pylori on T-helpers under direct contact cause a response in a form of the 1st type T-helpers activation.

Key words: *Helicobacter pylori, lymphocytes, T-helpers, differentiation, co-stimulation, антитела, flow cytofluorometry, cell cultures.*

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Contemporary healthcare faces variable vital tasks, and one of them is to analyze risk factors that cause occurrence and development of diseases in the gastrointestinal tract. All the age groups are susceptible to risks of damage to the digestive organs, including employable population, elderly people, children, and teenagers. High costs related to necessary treatment and rehabilitation of patients which can be rather expensive make prevention and anti- recurrent treatment of such pathologies not only medical, but also a social problem.

Helicobacter pylori (*H. pylori*) is a widely spread pathogenic microorganism associated with gastrointestinal tract diseases. *H. pylori* is well proven to selectively colonize the mucous tunic of the stomach and duodenum and is considered to be an etiological agent that causes acute and chronic gastritis, ulcer, and other diseases in the gastrointestinal tract [1, 2]. *H. pylori* has a distinctive peculiarity which is its ability to persist in a body for a long time, and this persistence quite often has no symptoms thus making the detection and eradication of the pathogen rather complicated. Such an effect is produced via impacts exerted by the pathogen on the immune system of its host that result in activation of its immune-suppressing component [3, 4]. This hypothesis is confirmed by data found in literature that in some cases helicobacter infection makes for less apparent clinical course of autoimmune and allergic diseases [5, 6].

Besides, *H. pylori* was proven to promote an authentic increase in contents of FoxP3-positive T-regulatory cells (T-reg) and cytokines produced by them; such results were obtained during laboratory tests on model animals [7, 8]. There is also a discussion in the literature on *H. pylori* ability to influence immune cells directly in the stomach thus stimulating changes both in their activity and in levels of cytokines produced by them [9–11]. *H. pylori* ability to stimulate T-reg generation under a direct contact between bacteria and human responder lymphocytes in vitro was described in our previous paper [12]. But at the same time, when attempts were made to reproduce the effect both in vivo and in vitro, there was an increase in anti-inflammatory cytokines such as gamma-interferon INF-γ (INF-γ) and interleukin-17A (IL-17A), and also, apart from T-reg, there was an induction of the 1st and 17th type T-helpers (Th1 и Th17) [13–15].

INF-γ and IL-17A play quite a variable role in development of gastroenterological pathologies. They participate in eliminating infectious agents by neutrophils and macrophages. It is a violent response by the immune system, that is considered to be the most probable cause for development of acute pathologies in the gastrointestinal tract in case of infections with *H. pylori* [16, 17]. However, apart from it, at present IL-17 and Th17 that produce them are viewed as the most probable basic mediators of *H. pylori*-associated autoimmune gastritis [18]. Data on participation of Th1 and cytokines produced by them in autoimmune gastritis development are rarely found but the role they play in development of other autoimmune pathologies has been studied and outlined quite profoundly [19, 20]. So, induction of INF-γ and IL-17A and subpopulations that produce them detected under interaction with *H. pylori* can lead to occurrence of both inflammatory pathologies in the stomach and duodenum and a wide range of extra-gastroduodenal diseases that is confirmed by data taken from literature [21].

Given all the above said, there is a vital scientific and practical task to assess anti-inflammatory effects by *H. pylori* and mechanisms that determine proneness of the agent to both regulatory and anti-inflammatory action. Besides, a preliminarily revealed ability of *H. pylori* directly, without any participating antigen-presenting cells (APC), influence at least some human T-cells subpopulations is also of great interest.

Our research goal was to assess *H. pylori* ability to stimulate occurrence of INF-γ, IL-17A and Th17 under direct contact between bacteria and T-cells, without APC participation.

Data and methods. Our research objects were samples of whole peripheral blood taken from people without *H. pylori*-infection in their case history, its absence confirmed by data obtained via objective research techniques, (n=8), and *H. pylori* isolates taken during diagnostic EGD from people suffering from chronic gastritis (n=6). Blood was only once taken in volume equal to 8-9 ml into vacuum tubes with sodium heparin (Vacuette, Germany). Samples were treated not later than 2 hours after they had been

taken. Mononuclear cells of peripheral blood (MCPB) were extracted out of blood samples via centrifuging (for 45 minutes at 1,500 turns per minute) at "Diakoll-1077" density gradient ("DiaM" Russia). After it, we extracted only $CD4^+$ cells out of obtained MCPB via immune-magnetic separation with Human naïve CD4+ T-cell enrichment Kit (Stemcell technologies, the USA). *H. pylori* was extracted out of biopsy materials taken during diagnostic EGD out of the antral section and body of the stomach; biopsy materials were taken from people with positive CLO-test. The materials were ground mechanically and then sowed on Columbian agar (Becton Dickinson, the USA) with added 10-% defibrinated donor blood as well as with antibiotics for suppressing growth of extraneous microflora and fungi (10 μg/l of Vancomycin, 5 mg/l of Trimethoprim, and 2 mg/l of Nystatin. all produced by Teva, Israel). Cultivating was performed for 7 days under microaerophilic conditions, the temperature being 37 °C. *H. pylori* was identified on the basis of cultural and morphological features.

To assess influence exerted by *H. pylori* on lymphocytes differentiation, we performed joint cultivation of lymphocytes with various concentrations of bacteria (we applied the following ratios of lymphocytes to *H. pylori* one by one: 1:10, 1:20, 1:50) for 18 hours under the following conditions 5% CO2, 37 °C, RPMI-1640 medium (Gibco, the USA) with added 10%-fetal bovine serum and 0.3 g/l of L-glutamine ("Paneko", Russia). A part of lymphocytes was cultivated with bacteria when additional stimulators were present; these stimulators were monoclonal antibodies to CD3 molecule (1 μg/ml, eBioscience, the USA) that imitated influence on T-cell receptor, or a mixture of antibodies to CD3 and CD28 (1 μg/ml, eBioscience, the USA, and 3 μg/ml, Beckman Coulter, France), that imitated influence exerted by APC on T-cells. We had the following cultures in our experiment: lymphocytes with added *H. pylori*, but without any stimulating antibodies; lymphocytes with added antibodies to CD3 and without bacteria; lymphocytes with added antibodies to CD3 and with *H. pylori*; lymphocytes with added antibodies to CD3 and CD28, and without *H. pylori*; and lymphocytes with added antibodies to CD3 and CD28 and with *H. pylori*. The last culture was included into the experiment in order to assess influence exerted by direct presence of the agent on the nature of stimulation. Experiments for all the ratios of lymphocytes and bacteria were performed separately. Lymphocytes without *H. pylori* and stimulating antibodies were negative controls for all the cultures.

After 18 hours 18 we applied cytofluorometry to estimate Th17 as cells of $CD4^+CD161^+$ и $CD4^+IL\text{-}17A^+$ phenotype in all the cultures. To paint the above mentioned markers, we applied antibodies to CD4 tagged with FITC; antibodies to CD161 tagged with PE; antibodies to IL-17A tagged with PE; all produced by eBioscience, the USA. We performed permeabilization of membranes necessary to tag IL-17A with Fix/Perm Concentrate reagents kit and Perm Buffer reagents kit (eBioscience, the USA) according to manufacturer's instructions. Analysis was conducted with FacsCalibur cytofluorimeter (Beckton Dickinson, the USA). Th1 activity was determined by measuring INF-γ concentrations in supernatants of the cultures with ELISA technique (Vector-Best, Russia). we applied Newman-Keuls test to statistically process the obtained data.

Results and discussion. An increase in INF-γ level is a significant part in immune response realization. This cytokine is a macrophages activator and it is involved into a direct response to infection attacks; besides, it enhances effects produced by α and β interferon, promotes an immune response as per Th1 type, and is able to stimulate activities of antigen-representing cells [22].

As we can see from Figure 1, when *H. pylori* was added to a suspension of extracted lymphocytes, both without additional stimulators and together with antibodies to CD3 or CD3/CD28, it led to statistically authentic increase in INF-γ production.

This production in the control culture was equal to only 10±4.08 pg/ml; when bacteria were added in a ratio 1:10, it went up to 835±351.4 pg/ml; in a ratio 1:20, 745±164.1 pg/ml; in a ratio 1:50, 135±121.8 pg/ml. INF-γ production in cultures which were additionally stimulated with antibodies had no statistical discrepancies from a variant with only bacterial stimulations; thus, INF-γ concentration in a culture consisting of T-lymphocytes with *H. pylori*

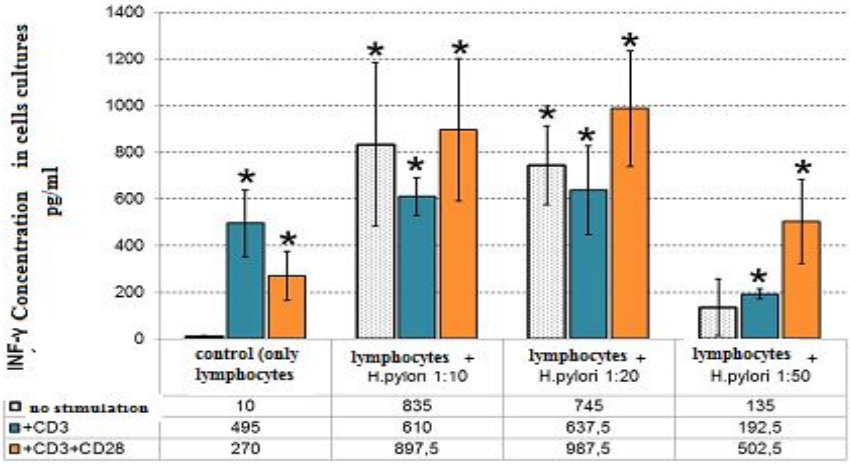

Figure 1. Influence exerted by *H. pylori* on INF-γ production. Variants of stimulation are given below the graph. Control is a culture with lymphocytes only, without added bacteria or antibodies, * means there are authentic discrepancies from the control ($p<0.05$).

and added antibodies to CD3 amounted to 610±081.3 pg/ml at a ratio being 1:10; 637.5±189.7 pg/ml at a ratio being 1:20; and 192.5±21.3 pg/ml at a ration being 1:50. INF-γ concentration in samples with T-lymphocytes with added *H. pylori* and additional stimulation with an admixture of antibodies to CD3 and CD28 amounted to 897.5±300.1 pg/ml at a ration being 1:20; 987.5±249.1 pg/ml at a ratio being 1:20; 502.5±180.01 pg/ml at a ratio being 1:50. All the obtained results coincide with data taken from literature on clinical course of *H. pylori*-associated gastritis accompanied with Th1 accumulation and increased INF-γ in the stomach mucous tunic [13].

Figures 2 and 3 show data on influence exerted by *H. pylori* on differentiation of lymphocytes towards Th17 and them acquiring $CD4^+CD161^+$ phenotype and without any dendritic cells in the cultures.

As we can see, joint cultivation of *H. pylori* and T-cells for 18 hours didn't lead to an increase in $CD4^+CD161^+$ cells number. Their average number in cultures without bacterial stimulation amounted to 20.065±0.72% from all the $CD4^+$ cells; when *H. pylori* was added to responder lymphocytes in a ratio 10:1, it amounted to 22.15±1.49 %. And concentrations of such cells in cultures with ratios 1:20 and 1:50 also had practically no differences from control concentrations of non-stimulated lymphocytes (the number amounted to 24.2±3.41% for a ratio 1:20, and to 23.15±2.73% for a ratio 1:50).

To test significance of co-stimulation, we performed additional experiments adding stimulating antibodies to CD3 and CD3+CD28 molecules; these antibodies sent a signal to T-cells which was similar to that sent by antigen-presenting cells in the process of stimulation. $CD4^+CD161^+$ cells concentration amounted to 23.745±7.3% in a culture of T-lymphocytes without *H. pylori* but with added antibodies to CD3. But at the same time, when both *H. pylori* and antibodies to CD3 were added to a culture, $CD4^+CD161^+$ cells concentration amounted to 23.83±3.30% for a ratio 1:10; 25.4±2.42% for a ratio 1:20; and 25.4±1.75% for a ratio 1:50.

CD161 molecule under its co-expression with CD4 molecule is widely used in world scientific practice as a Th17 population marker. However, occurrence of membrane phenotypic markers doesn't guarantee that responder cells are functionally able to produce IL-17A or, in other words, to fulfill basic Th17 function. Also, some authors state, that it is more reliable to assess Th17 concentration as per occurrence of intracellular IL-17A or its products than to apply CD161 in the process. Given all the above stated, we assessed concentrations of intracellular IL-17A in cultures of lymphocytes that responded to *H. pylori*. To do that, we performed permeabilization of responder cells membranes and

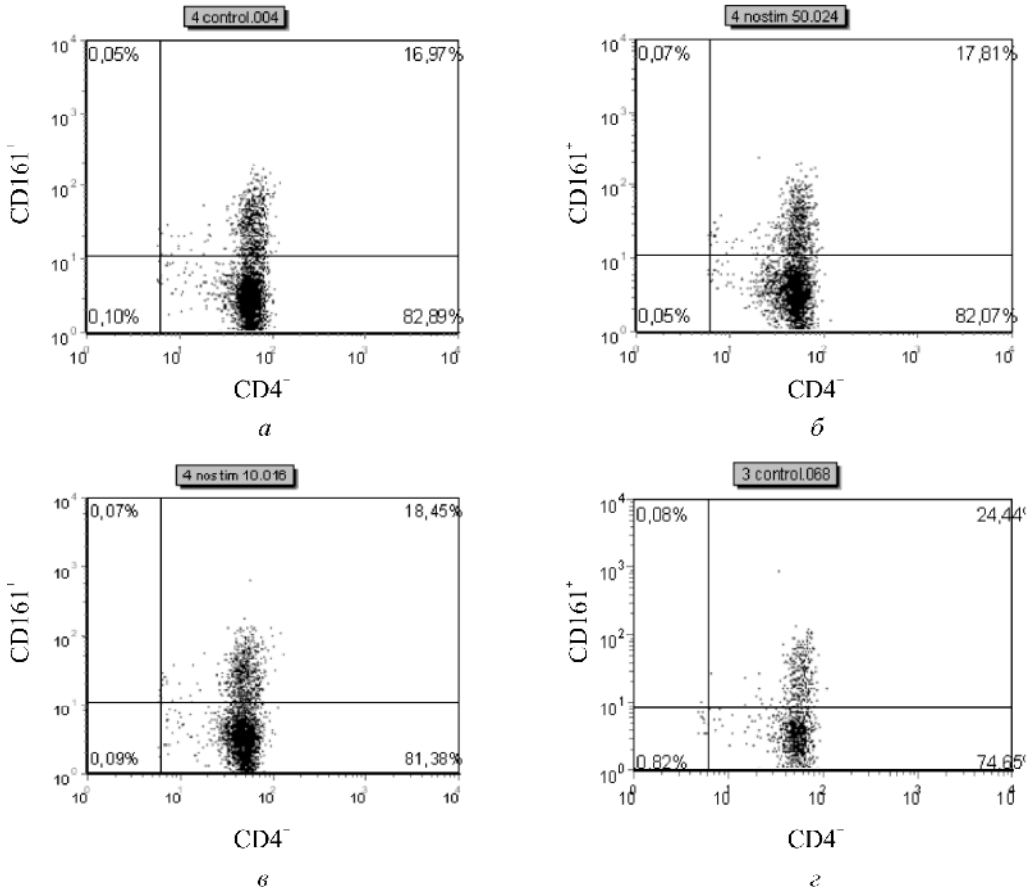

Figure 2. $CD4^+CD161^+$ cells concentrations in T-lymphocytes cultures under joint cultivation with *H. pylori* without additional stimulation, in % of the overall CD4+ cells number (data obtained via a representative experiment): A is a control suspension of lymphocytes without *H. pylori*; B is joint cultivation with *H. pylori* in a ratio 1:10, C and D is joint cultivation with *H. pylori* in ratios 1:20 and 1:50 respectively. A per cent content of cells is given in the angles of the quadrants.

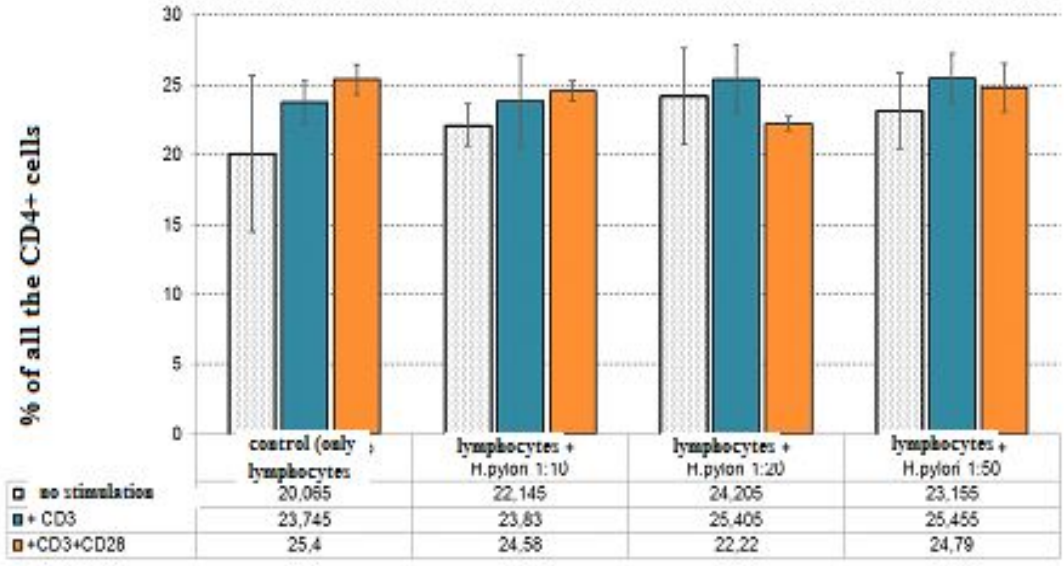

Figure 3. Influence exerted by *H. pylori* on $CD4^+CD161^+$ cells concentration. variants of stimulation are given below the graph. Control is a culture with lymphocytes only, without added bacteria or antibodies

Table

IL-17A$^+$CD4$^+$ cells concentrations under joint cultivation with *H. pylori* and/or additional stimulation with antibodies to CD3 and CD28

IL-17A$^+$ cells concentration (% from all CD4$^+$ cells)	Lymphocytes without *H. pylori* (control)	Lymphocytes without *H. pylori*, CD3	Lymphocytes without *H. pylori*, CD3 and CD28	Lymphocytes + *H. pylori* (1:10)	Lymphocytes + *H. pylori* (1:10), CD3	Lymphocytes + *H. pylori* (1:10), CD3 and CD28
	0,27 ± 0,08	0,21 ± 0,02	0,23 ± 0,033	0,43 ± 0,07	0,26 ± 0,03	0,14 ± 0,04

painted them with monoclonal antibodies to IL-17A. We detected that most cells don't stimulate greater IL-17A expression under cultivation conditions applied in our experiments (Table).

Thus, IL-17A$^+$ cells concentration didn't exceed 0.5% of all the CD4$^+$ cells in any of the applied variants of stimulation and ratios of responder cells and bacteria; such concentration doesn't have any discrepancies from standard IL-17$^+$ cells concentration in human blood [23–25].

Conclusions.

Direct joint cultivation of extracted T-lymphocytes with *H. pylori* promotes a drastic increase in INF-γ production, and it, under these experimental conditions, can most probably mean that Th1 activation occurs. However, Th17 concentrations in % (determined both as CD4$^+$CD161$^+$, and as CD4$^+$IL17A$^+$) changed only slightly under such conditions. We can assume that a response from T-helpers to a direct contact with *H. pylori*, given its anti-inflammatory effects, develops as per Th1 type, without Th17 being significantly involved in the process. A mechanism that determines *H. pylori* ability to stimulate activity of both Th1 and T-reg (which was shown by us earlier) requires further investigation. Overall, the authors think that mechanisms and acting agents that help a pathogen to exert direct influence on a prevailing type of an immune response are of great fundamental and practical interest; they potentially can be applied in development of medications that guide an immune response to a right direction. They are also important for assessing risks of hyper-stimulated immune response development in patients infected with *H. pylori.*

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References

1. Van der Sloot K.W.J., Amini M., Peters V., Dijkstra G., Alizadeh B.Z. Inflammatory bowel diseases: review of known environmental protective and risk factors involved. *Inflamm Bowel Dis.*, 2017, vol. 9, pp. 1499–1509.

2. Pachathundikandi S.K., Müller A., Backert S. Inflammasome activation by *Helicobacter pylori* and its Implications for persistence and immunity. *Curr. Top. Microbiol. Immunol*., 2016, vol. 397, pp. 117–131.

3. Rosenplänter C., Sommer F., Kleemann P., Belkovets A., Schmidt A., Lohoff M. *Helicobacter pylori* polyclonally activates murine CD4$^+$ T-cells in the absence of antigen-presenting cells. *Eur. J. Immunol*., 2007, vol. 37, no. 7, pp. 1905–1915.

4. Lerner A., Arleevskaya M., Schmiedl A., Matthias T. Microbes and viruses are bugging the gut in celiac disease. Are they friends or foes? *Front Microbiol.*, 2017, vol. 8, pp. 1392.

5. Chen Y., Blaser M.J. *Helicobacter pylori* colonization is inversely associated with childhood asthma. *J. Infect. Dis*., 2008, vol. 198, pp. 553–560.

6. Bartels L.E., Jepsen P., Christensen L.A., Gerdes L.U., Vilstrup H., Dahlerup J.F. Diagnosis of *Helicobacter Pylori* infection is associated with lower prevalence and subsequent incidence of Crohn's disease. *Journal of Crohn's and Colitis*, 2016, vol. 10, no. 4, pp. 443–448.

7. Arnold I.C., Dehzad N., Reuter S., Martin H., Becher B., Taube C., Müller A. *Helicobacter pylori* infection prevents allergic asthma in mouse models through the induction of regulatory T cells. *Journal Clin.*

Invest., 2011, vol. 121, no. 8, pp. 3088–3093.

8. Amedei A., Codolo G., Del Prete G., de Bernard M., D'Elios M.M. The effect of *Helicobacter pylori* on asthma and allergy. *Journal Asthma. Allergy*, 2010, vol. 3, pp. 139–147.

9. Bamford K.B., Fan X., Crowe Sh.E., Leary J.F., Gourley W.K., Luthra G.K., Brooks E.G., Graham D.Y., Reyes V.E., Ernst P.B. Lymphocytes in the human gastric mucosa during *Helicobacter pylori* have a T-helper cell 1 phenotype. *Gastroenterology*,1998, vol. 114, no. 3, pp. 482–492.

10. Tarkkanen J., Kosunen T.U, Saksela E. Contact of lymphocytes with *Helicobacter pylori* augments natural killer cell activity and Induces Production of Gamma Interferon. *Infection and immunity*, 1993, vol. 61, no. 7, pp. 3012–3016.

11. Tsai H.-F., Hsu P.-N. Interplay between *Helicobacter pylori* and immune cells in immune pathogenesis of gastric inflammation and mucosal pathology. *Cellular & Molecular Immunology*, 2010, vol. 7, pp. 255–259.

12. Matveichev A.V., Talaeva M.V., Talaev V.Yu., Neumoina N.V., Perfilova K.M., Lapaev D.G., Mokhonova E.V., Tsyganova M.I., Koptelova V.N., Nikitina Z.I., Lapin V.A., Melent'ev D.A. Influence exerted by *Helicobacter pylori* on regulatory t-cells differentiation. *Health Risk Analysis*, 2017, no. 1, pp. 21–28. DOI: 10.21668/health.risk/2017.1.03.eng

13. Windle H.J., Ang Y.S., Athie-Morales V., McManus R., Kelleher D. Human peripheral and gastric lymphocyte responses to *Helicobacter pylori* NapA and AphC differ in infected and uninfected individuals. *Gut.*, 2005, vol. 54, no. 1, pp. 25–32.

14. Käbisch R., MejíasLuque R., Gerhard M., Prinz C. Involvement of Toll-like receptors on Helicobacter pylori-induced immunity. *PLoS One*, 2014, vol. 9, no. 8, pp. e104804.

15. Shiu J., Blanchard T.G. Dendritic cell function in the host response to *Helicobacter pylori* infection of the gastric mucosa. *Pathog. Dis.*, 2013, vol. 67, no. 1, pp. 46–53.

16. Tanaka S., Nagashima H., Cruz M., Uchida T., Uotani T., Jiménez Abreu J.A., Mahachai V., Vilaichone R., Ratanachu-ek T., Tshering L., Graham D.Y., Yamaoka Y. Interleukin-17C in human *Helicobacter pylori* gastritis. *Infect Immun.*, 2017, vol. 85, no. 10, pp. e00389–e00417.

17. Permin H., Andersen L.P. Inflammation, immunity, and vaccines for Helicobacter infection. *Helicobacter*, 2005, vol. 10, no. 1, pp. 21–25.

18. Huter E.N., Stummvoll G.H., DiPaolo R.J., Glass. D.D., Shevach E.M. Pre-differentiated Th1 and Th17 effector T cells in autoimmune gastritis: ag-specific regulatory T cells are more potent suppressors than polyclonal regulatory T cells. *Int. Immunopharmacol.*, 2009, vol. 9, no 5, pp. 540–545.

19. Pravada N.S., Budritskii A.M. Kompleksnaya terapiya s primeneniem immunotropnykh preparatov pri tuberkuleze i sistema interferona-gamma [Complex therapy with the use of immune preparations in tuberculosis and interferon-gamma system]. *Vestnik Vitebskogo gosu-darstvennogo meditsinskogo universiteta*, 2015, vol. 14, no. 4, pp. 5–14 (in Russian).

20. Bazzazi H., Aghaei M., Memarian A., Asgarian-Omran H., Behnampour N., Yasdani Y. Th1-Th17 ratio as a new insight in rheumatoid arthritis disease. *Iran J. Allergy Asthma Immunol.*, 2018, vol. 17, no. 1, pp. 68–77.

21. Bar-dakhch'yan E.A., Lomov S.Yu., Kharlanova N.G., Kamneva N.V. Rol' *Helicobacter Pylori* pri razvitii ekstragastroduodenal'nykh zabolevanii [Role of *helicobacter pylori* in different gastroduodenal diseases]. *Eksperimental'naya i klinicheskaya gastroenterologiya*, 2005, no. 3, pp. 20–27 (in Russian).

22. Lutskii A.A., Zhirkov A.A., Lobzin D.Yu., Rao M., Alekseeva L.A., Meirer M., Lobzin Yu.V. Interferon-γ: biologicheskaya funktsiya i znachenie dlya diagnostiki kletochnogo immunno-go otveta [Interferon-γ: biological function and applicationfor study of cellular immune response]. *Zhurnal infektologii*, 2015, vol. 7, no. 4, pp. 10–22 (in Russian).

23. Miao J., Zhang K., Qiu F., Li T., Lv M., Guo N., Han Q., Zhu P. Percentages of $CD4^{+}CD161^{+}$ and $CD4^{-}CD8^{-}CD161^{+}$ T cells in the synovial fluid are correlated with disease activity in rheumatoid arthritis. *Mediators Inflamm*, 2015, vol. 2015, P ID 563713.

24. Church L.D., Filer A.D., E Hidalgo., Howlett K.A., Thomas A.M.C., Rapecki S., Scheel-Toellner D., Buckley C.D., Raza K. Rheumatoid synovial fluid interleukin-17-producing CD4 T cells have abundant tumor necrosis factor-alpha co-expression, but little interleukin-22 and interleukin-23R expression. *Arthritis Res. Ther.*, 2010, vol. 12, no. 5, pp. R184.

25. Shen H., Goodall J.C, Hill Gaston H.J.S. Frequency and phenotype of peripheral blood Th17 cells in ankylosing spondylitis and rheumatoid arthritis. *Arthritis & Rheumatism.*, 2009, vol. 60, no. 6, pp. 1647–1656.

Tsyganova M.I., Talaeva M.V., Talaev V.Yu., Neumoina N.V., Perfilova K.M., Mokhonova E.V., Lapin V.A., Melent'ev D.A. Influence exerted by helicobacter pylori on concentrations of anti-inflammatory т-cell cytokines and sunpopulations that produce them. Health Risk Analysis, 2018, no. 3, pp. 120–127. DOI: 10.21668/health.risk/2018.3.13.eng

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HYGIENIC ASSESSMENT OF MEASURES AIMED AT RISKS REDUCTION AND HEALTH PRESERVATION FOR CHILDREN IN SECONDARY SCHOOLS

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We questioned 1,064 school students from 5–11 grades and 720 parents of schoolchildren from 1–4 grades and assessed health of 2,512 children and teenagers via comparative examination performed in two secondary schools with similar sanitary-epidemiologic situation in them but different preventive activities accomplished and different medical care provided. The results we obtained via questioning and examination revealed that school children's health is preserved and improved due to targeted development of preventive activities and medical care, better nutrition in school, an increase in physical activities, and a growth in number of children who wish to pursue health-preserving behavior patterns. When a prevention and rehabilitation unit was established in a school it allowed to improve medical care and achieve a substantial decrease in morbidity among school children, first of all, with respiratory organs diseases which were a basic reason for absence from classes. Most children (77.5 %) who were made healthier or recovered in school had suffered from respiratory organs diseases.

Improvement of preventive activities aimed at creating health culture and attitudes towards healthy life style had positive influence on children's motivation and formation of such behavior stereotypes that helped to preserve their health. It was confirmed by questioning results as well as by lower levels of common and primary morbidity and better physical development. Share of practically healthy school students without any risk factors (the 1st health group) increased from 5.61 % in 2009 to 8.54 % in 2017; share of school students who were in the 2nd health group (had functional deviations or ran risks of chronic pathology development) decreased from 86.28 to 83.98 % ($p < 0.05$).

Key words: *preventive activities, medical care, school, school children, health, questioning.*

Educational organizations are a priority part of schoolchildren environment and they can frequently cause health risks for them. The primary reasons here are them being not compliant with sanitary and epidemiologic requirements and standards in terms of their territory and buildings, organization of educational process [1–3] and nutrition [4, 5], physical activities [6, 7], and medical support [8–12]. Educational process is becoming more intense and it causes risk-associated health disorders among schoolchildren [13]. Social and economic factors also exert negative influence on children's health as they determine their lifestyle and form health-preserving culture, healthy life-

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styles, and children's leisure activities [14].

The necessity to manage schoolchildren's health risks led to development of recommendations on updating preventive activities and medical support for children and teenagers within scientific systems of knowledge [15, 16]. Issues of healthy lifestyle formation and unified preventive space in educational organizations have been revised [17, 18]. But still, there is not enough research that focuses on analyzing implementation practices related to preventive and health-improving activities and it predetermined the performance of the present research.

Our research goal was to assess results of long-term activities aimed at improvement of prevention work and medical support in educational organizations.

Data and methods. We performed our research in Penza and chose two comprehensive secondary schools as our research objects; the school No. 74 was a test one, and the school No. 68 was a reference one. We examined sanitary-hygienic parameters of intra-school environment and analyzed nutrition that schoolchildren received. We assessed activities accomplished by a prevention and rehabilitation unit in the test school; examined educational process conditions and health of children who attended 1-11 forms. our samplings included 1,136 and 1,376 school students correspondingly.

Both schools were located close to each other (420 meters from one to another) in the same city district (a dormitory area) with the same ecological conditions; both schools were built according to a typical building project. Nutrition units in both school were modernized in 2008 within the frameworks of a federal experimental project. Comparative hygienic assessment of the schools was performed taking into account all the specifications fixed in sanitary-epidemiologic requirements.

Prevention work aimed at improvement of schoolchildren's health has been accomplished since 2006 in the school No. 74, as opposed to the school No. 68. We questioned parents of elementary school pupils and parents of schoolchildren who attended 5-11 forms. We analyzed 366 questionnaires filled in by parents and 430 questionnaires filled in by school students who attended the school No. 74 (70% of the total schoolchildren number). We also analyzed 354 questionnaires filled in by parents and 634 questionnaires filled in by schoolchildren who attended the school No. 68 (71.8% of the total schoolchildren number). Actual nutrition received by schoolchildren was analyzed via examining two-week autumn (2017) and spring (2018) menus that included breakfast and lunch.

We assessed schoolchildren's health. The results were statistically processed with conventional techniques.

Results and discussion. Parameters of microclimate, electric and magnetic fields strength inside classrooms were measured in 2018; the results revealed there were only insignificant differences between the schools and all the parameters corresponded to standards in both of them.

Daylight factor in classrooms amounted to 6.99±0.82 in the school No. 74; 2.55±0.76, in the school No. 68 ($p < 0.05$).

Noise level in the corridors, gymnasium, canteen, and technology classes of the school No. 74 was within 51.4–80.5 decibels, and in IT classrooms, within 43.1–45.7 decibels; in the school No. 68, within 58.9–82.1 and 47.8–48.2 decibels correspondingly.

We didn't reveal any significant discrepancies in adverse substances concentrations in classrooms between the compared schools. Microbe contamination of the air also didn't differ significantly as the total microbe quantity ranged from 174 to 1,100 per 1 m^3 (497.5 on average) in the school No.74; from 300 to 1,200 per 1 m^3 (650 on average) in the school No. 68. School furniture didn't conform to height and age standards in 27.8% cases in the school No. 74; and in 53%, in the school No. 68 (p We detected that nutrition rations provided for elementary school pupils (1-4 forms) corresponded to this age group and deviated from recommended ones only slightly. Actual food value was 4.5% higher than the standard in the test school. Proteins, fats, and carbohydrates contents were 3.7, 5.6 and 2.7% higher, their ratio was 1:1.1:4.3. Actual food value of nutrition ration provided in the reference school was 6.4% lower than the standard, proteins, fats, and hydrocarbons contents being 6.6, 3.8, and 4.1% lower correspondingly; macronutrient ratio was 1:1.1:4.8.

Most children (73.8 and 81.2 %; $p < 0.05$) received such nutrition in their families that couldn't be called healthy. Ratio of basic food components (proteins, fats, and carbohydrates) in daily rations amounted to 1:1.3:5.5 and 1:1.4:5.9 in the compared groups correspondingly. Unbalanced daily rations as per ratios of basic food components were accompanied with excessive fats and carbohydrates consumption and overall prevalence of fats and carbohydrates in rations.

Preventive work accomplished in the school No. 74 had two basic lines, namely organi-

zation of medical support for schoolchildren directly in school; targeted formation of knowledge and skills related to pursuing a healthy lifestyle.

In 2006 in the school No. 74 conventional medical support for schoolchildren was supplemented with an innovative prevention and rehabilitation unit (PRU). The PRU target was to implement preventive and health-improving activities among schoolchildren, and to improve health of everybody who needed it without any breaks in their educational process. An expected outcome would be a decrease in morbidity among children. Schoolchildren can receive physiotherapy and other health-improving procedures in the PRU when they are prescribed by a physician; there are no breaks in the educational process. Schoolchildren can also visit a pediatrician and a dentist in the PRU. The unit functions all the year round, even during school vacations when health-improving camps are open for children.

The PRU is a structural unit of a medical organization that provides medical personnel for it and equips medical rooms with all the necessary medical devices. The PRU includes a pediatrician room, therapeutic physical training room, massage room, physiotherapy room, and a dentist room. The school was to provide rooms prepared for the PRU organization. The PRU as per its functions is a unit that provides medical support for schoolchildren. Its activities are harmonized with European approaches to school healthcare [7].

The PRU functioning in the school No. 74 fully corresponds to the requirements stated in the Order by the RF Public Healthcare Ministry issued on November 5, 2013, No. 822 n "On approval of order for providing medical support to under-aged citizens, including the period of education in educational organizations"[1]. 10,119 schoolchildren attending the school No. 74 improved their health and received rehabilitation procedures over 2007 – 2017 (from 893 to 1,197 annually).

Children with musculoskeletal pathologies (38.8%) and with respiratory organs diseases (19.9%) prevailed among those who applied for medical aid to the PRU, improved their health, and received rehabilitation procedures. A number of children who needed to improve their health due to eye and its accessory apparatus diseases was significantly lower and amounted to 12.3%. A share of children with nervous system diseases amounted to 11.9%; with injuries, 9.1%; digestive organs diseases, 4.1%; other diseases, 3.9%. Physiotherapeutic procedures accounted for more than a half of all the rehabilitation activities (54.3%). Therapeutic physical training accounted for 29.6%; health-improving massage and massotherapy, for 16.1%.

Types and structure of rehabilitation activities are determined by a diagnosis. Physiotherapeutic treatment is mostly applied to improve health of children with respiratory organs diseases and injuries (91.4%). Ear and mastoid diseases and digestive organs diseases require only therapeutic procedures. Therapeutic physical training is applied in almost half of cases when musculoskeletal system diseases, as well as eye and its accessory apparatus diseases are diagnosed. Massage is the most labor-consuming medical procedure and it is applied much more rarely. It is most frequently applied in case of nervous system diseases.

Health-improving activities for children performed by the PRU in the school No. 74 in 2007-2017 gave the following results in terms of all the diseases. 27.6% out of 10,119 children treated by the PRU recovered; 71.5% improved their health; there were no changes in health of 0.9% children; there were no cases in which children's health deteriorated. The most recovered children were detected among children with respiratory organs diseases (77.5%) and ear and mastoid diseases (62.4%).

An increase in number of children who were included into the 1st health group to attend physical training (without any limitation) and a decrease in number of children with the 2nd and the 3rd health groups (children who run risks of chronic pathologies or who already suffer from them or have physical development disorders) also prove that the PRU activities are quite efficient. Thus, a number of children with the 1st health group in the school No. 74 increased from 86.1% in 2009-2010 school year to 93.7% in 2017-2018 school year ($p < 0.05$); accordingly, there was a decrease in number of children with the 2nd and the 3rd health groups from 13.9 to 6.3% ($p > 0.05$).

A decrease in acute morbidity among chil-

[1] On approval of order for providing medical support to under-aged citizens, including the period of education in educational organizations: The Order by the RF Public Healthcare Ministry dated November 5, 2013 No. 822n. *Garant.RU: information and legal portal*. Available at: https://www.garant.ru/products/ipo/prime/doc/70471454/ (date of visit March 25, 2018).

dren (measured as a number of absence cases per 1 child) is another proof that the PRU activities are efficient. Absence due to acute morbidity decreased by 3.5% ($p > 0.05$). As for the reference school, a number of children with the 1st health group changed only slightly over the examined period, from 89.3% in 2009-2010 to 90.2% in 2017-2018; absence increased by 1.9% ($p > 0.05$).

Issues of health lifestyle formation have been solved in the school No. 74 through intersectoral partnership since 2008; as for the reference school, only conventional ways have been applied there.

Healthy lifestyle formation among children attending 1-11 forms is implemented with educational technologies created with the help of Ropotrabnazor experts and HEE teaching staff, as well as social, medical, and information technologies. First of all, application of multi-subject technologies allows to achieve better awareness about risk factors among children, patens, and school personnel; secondly, it provides motivation and creates conditions for healthy lifestyle formation; thirdly, it can help to develop and secure health-preserving behavioral skills in children and teenagers.

In order to increase physical activity of students, in 2008-2009 two gymnasiums, a swimming pool and a training ground near the school No. 74 were re-equipped.

We performed sociologic questioning among parents whose children attended 1-4 forms; the questioning revealed that almost all pupils ate cooked meals at school, 96.9% in the school No. 74 and 96.7% in the school No. 68. 89.3% of children attending the school No. 74 had a snack (fruit) between breakfast, lunch, and dinner; only 71.2% of those attending school No. 68 ($p < 0.001$) did it. This difference is not caused by material well-being of a family as 78.4% of parents whose children attended the test school and 88.9% of parents whose children attended the reference school ($p < 0.05$) considered their material well-being quite satisfactory. A share of children who consumed sweets and French fries between breakfast and lunch was higher in the reference school than in the test one, 70.5% against 58.7% correspondingly ($p < 0.01$). Children who attend the school No. 74 much more rarely consume fast-food outside the school than children from the school No. 68, 27% against 42.6% correspondingly ($p < 0.01$). Therefore, four out of ten children attending the school No. 68 consume food that can hardly be called healthy and their eating habits are not health-preserving ones.

The results of questioning performed among students attending 5-11 forms prove that children and teenagers from the test school are much more motivated to pursue a healthy lifestyle than their counterparts from the reference school (Table). Thus, a share of children with correct eating habits is authentically higher in the school No. 74 than in the school No. 68. But at the same time, only 32.2% of schoolchildren from the school No. 74 considered school meals to be good; 27.7% gave the same estimation in the school No. 68 ($p > 0.05$). 44% and 38% correspondingly considered school meals to be satisfactory ($p > 0.05$); 23,8% and 34,3 % correspondingly thought them to be unsatisfactory ($p < 0.05$). These rather low scores given to school meals by schoolchildren can be caused by incomplete provision of cooked meals that are not enough for every schoolchild; such a situation, in its turn, can exert negative influence on schoolchildren's health.

Table

Results of questioning performed among students attending 5–11 forms in the compared schools

Students' answers	School No. 74, %	School No. 68, %	*p*
Have breakfast at home	88,3	83,7	0,040
Have second breakfast at school	57,9	35,1	0,000
Have cooked meal for lunch	83,9	82,1	0,457
Have dairy products every day	72,1	61,5	0,022
Have meat products every day	80,0	71,6	0,002
Have fruit every day	80,0	63,1	0,000
Eat fast-food	55,3	59,8	0,130
Go to school on foot	87,2	76,4	0,000
Do morning exercises	33,5	25,4	0,005
Do sports	67,8	62,9	0,117
Walk on foot a day: more than 2 km	72,4	65,3	0,015
Spend from 1 to 3 hours a day working on a PC	74,2	64,5	0,026
Watch TV from 1 to 3 hours a day	86,9	87,1	1,00
Night sleep lasts 8 hours or more	54,6	51,4	0,53

More than a half of children do sports at sport clubs, 63.9 and 64.9% correspondingly; but only each fourth or fifth student does morning exercises, 21.8 and 24.3% correspondingly. And parents tend to overestimate physical activities of their children as 88.2 and 92.6% of them correspondingly consider them to be sufficient. Parents of children who attend the school No. 74 more frequently give a good example to their children showing them physical exercises and activity is useful for health than their counterparts whose children attend the school No. 68. But still, this obvious good example isn't in line with a share of children who do morning exercises.

Almost all schoolchildren attending both schools have a walk outdoors every day. But at the same time, it is rather alarming that children from the reference school break a daily regime as 19.8% of children sleep less than 8 hours at night. A share of such children in the test school is authentically lower. Uncontrolled TV watching and time spent at a PC is a reason for shorter sleep on weekdays. Thus, 8.1% and 5.9% of children from the school No. 74 watch TV or work on a PC for more than 3 hours correspondingly; these figures amount to 10.8 and 7.2% of children from the school No. 68 correspondingly.

Schoolchildren from the test school are more active physically than their counterparts from the reference school where respondents obviously tend to overestimate their daily physical activity. Meanwhile, 93.7% of respondents from the school No. 74 have the 1st health group (without any risk-factors), and only 90.2% of children from the school No. 68 have the same health group. Besides, a share of children who go to school on foot or walk more 2 km a day is significantly higher in the test school.

Most children from the test school, and considerably fewer children from the reference school, believe their parents give them a good example how to pursue a healthy lifestyle. 95.1% of respondents from the school No. 74 think that a school should take active part in building skills of healthy behavior and healthy lifestyle in schoolchildren; only 80.4% of schoolchildren who attended the school No. 68 gave the same answer ($p < 0.001$). Unsurprisingly, 93.7% of respondents from the test school think that creation of a healthy lifestyle is being accomplished quite actively in their school; only 67.3% of schoolchildren from the school No. 68 are of the same opinion ($p < 0.001$).

There was a question "How do you assess medical support provided for children in the school?"; parents gave the following answers to it: "good" was given by 64.2 % in the school No. 74 and by 52.5 % in the school No. 68 ($p < 0.01$); "satisfactory", by 28.7 and 39.4 % ($p<0.01$) correspondingly; "unsatisfactory", by 7.1 and 8.1 % correspondingly. Students attending 5-11 forms gave other evaluation of medical support in their schools: "good" was given by 56.1 and 45.6 % ($p = 0.001$); "satisfactory", by 32.7 and 33.9 %; "unsatisfactory", by 11.2 and 20.5 % ($p = 0.005$) correspondingly.

As for core values of life, family took the first place in the lists of respondents from both schools, 89.3% in the test school, and 85.9% in the reference one; students from the test school gave the second place to health (77.2%) while their counterparts from the reference school to friends (61.3%); the third place was given to friends (66.2%) and health (59.7%) correspondingly; the fourth place was given to education (62.4 and 49.8 %).

We analyzed the results of questioning performed among parents whose children attended 1-4 forms and 5-8 forms and can state that updating of prevention work aimed at creating health culture and a healthy lifestyle in schoolstudents had positive effects on their motivation and building of behavioral stereotypes that helped to preserve and improve their health. But still we should note that a great number of children don't have enough sleep, spend too much time at a PC, are not physically active, and don't have cooked meals at school. Although a share of such children is much lower in the test school than in the reference one, all these parameters of a lifestyle are in this case a field where prevention activities should be performed in future.

Morbidity among children was taken as a performance criterion for activities aimed at healthy lifestyle formation. In 2017 prevalence of diseases among children in the school No. 74 amounted to 1,353.2 ‰, that was lower than the same parameter among children in the school No. 68, 1,524.6 ‰ ($p < 0.001$). This discrepancy between overall morbidity levels was mostly due to different prevalence of respiratory organs diseases, 587.1 ‰ against 808.7 ‰ correspondingly ($p < 0.001$). We also detected a significant discrepancy in primary morbidity levels among children from the schools under comparison, 640.8 and 854.3 ‰ ($p < 0.001$); this discrepancy was mostly due to higher morbidity with respiratory organs diseases,

555.2 against 760.1 ‰ ($p < 0.001$). Schoolchildren who attend the school No. 74 suffer from respiratory organs diseases 1.36 times less frequently. We didn't detect any other significant discrepancies between the two schools as per other nosologies ($p > 0.05$).

Assessment of schoolchildren's physical development performed in 1-4 forms revealed that a share of children with average height and body weight parameters (4-5 centile ranges) was practically the same, 34.9% in the test school, and 32.2% in the reference one. A share of children with physical development parameters being higher than average values (6-8 centile ranges) amounted to 41.4% and 40.3% correspondingly; lower than average values (1-3 centile ranges), 23.7% and 27.5% correspondingly. Distribution of children as per body mass index revealed that there were more children with optimal nutrition status in the school No. 74 than in the school No. 68, 55.5% against 43.6% ($p<0.05$). Insufficient nutrition status was detected in 13.4% of children from the test school and in 15.0% of children from the reference one; the excessive nutrition status was detected in 31.1% and 41.4% of children correspondingly.

Compression force of a hand was higher in children from the test school than in children from the reference one. The examined parameter of a right hand amounted to 13.03 kg in the test school, and to 10.17 kg, in the reference one ($p<0.05$). Compression force of a left hand amounted to 7.83 and 11.2 kg correspondingly ($p<0.05$). We also revealed that there was an authentic discrepancy in vital capacity of lungs in children from the compared schools, 1.43 l in the school No. 74 against 1.29 l in the school No. 68 ($p<0.05$).

Our assessment of adaptation capacities revealed that they were higher in children from the test school than in those from the reference one; satisfactory adaptation was detected in 15.3% and 12.8% correspondingly; strain in adaptation mechanisms, in 46.7 and 41.7%; unsatisfactory adaptation, in 19.4 and 24.7%; adaptation mechanisms failure, in 18.6 and 20.8% of children correspondingly.

A share of practically healthy children (the 1st health group) attending school No. 74 increased from 5.61% in 2009 to 8.54% in 2017. A share of children with the 2nd health group (children with functional deviations who run risks of chronic pathology development) decreased from 86.28% in 2009 to 83.98% in 2017 ($p < 0.05$). But at the same time there were only slight changes in a share of children who suffered from chronic pathologies at compensation stage and had the 3rd health group and a share of children who had the 4th health group and suffered from chronic diseases at subcompensation stage, from 7.28% to 6.25% and from 0.83% to 1.23% correspondingly.

We detected quite different trends in the school No. 68. Thus, a share of children with the 1st and 2nd health group practically didn't change, 7.41% and 8.03%; 81.84% and 81.75%. A share of children with the 3rd health group increased from 7.06 to 8.82% ($p < 0.05$), and a share of children with the 4th health group increased from 0.72% to 4%.

Conclusions. We performed comparative examination of two schools with the same sanitary-epidemiologic well-being but different preventive activities implemented and medical support provided in them; the examination included sociologic questioning and assessment of health of children who attended these two schools. The examination results revealed that targeted modernization of preventive activities and medical support, improvement of school meals, greater physical activity, and an increase in number of children with health-preserving behavioral attitudes had positive effects on formation of schoolchildren's health. Positive changes have occurred in that school where preventive activities have been implemented for many years; first of all, they were changes in motivation and children's drive for health-preserving behavior.

Modernization of medical support via organization of a prevention and rehabilitation unit (PRU) in the school allowed to achieve a significant decrease in morbidity among schoolchildren, first of all, with respiratory organs diseases that were a basic reason for absence from classes. The greatest share of children who recovered after visiting the PRU had previously suffered from respiratory organs diseases (77.5 %).

Our questioning revealed the most significant risk factors that required development and implementation of preventive activities; the factors included nutrition behavior defects, incomplete provision of all the children with cooked meals, disorders in daily regime, and more than 3 hours spent at a PC. These and some other problems are more apparent in the reference school and require immediate attention.

Results of the research that generalized long-term experience in creating a unified prevention environment in a secondary school substantiated creating and implementing scientifically grounded recommendations in the region.

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References

1. Mylnikova I.V. Gigienicheskaya otsenka vnutrishkol'noi sredy gorodskikh i sel'skikh obrazovatel'nykh uchrezhdenii [Hygienic assessment of intraschool environment in rural and urban secondary school institute ons]. *Gigiena i sanitariya*, 2016, vol. 95, no. 12, pp. 1193–1197 (in Russian).

2. Haverinen-Shaughnessy U., Shaughnessy R. J., Cole E. C., Toyinbo O., Moschandreas D.J. An assessment of indoor environmental quality in schools and its association with health and performance. *Building and Environment*, 2015, vol. 93 (part 1), pp. 35–40. DOI: 10.1016/j.buildenv.2015.03.006

3. Valina S.L., Ustinova O.Yu., Maklakova O.A., Ivashova Yu.A. Sravnitel'naya otsenka funktsional'nogo sostoyaniya serdechno-sosudistoi i vegetativnoi nervnoi sistemy u detei doshkol'nykh obrazovatel'nykh organizatsii obshcherazvivayushchei napravlennosti s razlichnoi napolnya-emost'yu grupp [Comparative evaluation of the functional state of the cardiovascular and the vegetative nervous system in children of general preschool educational establishments with various representation of groups]. *Fundamental'nye issledovaniya*, 2015, no. 1–7, pp. 1334–1338 (in Russian).

3. Hrebtova A.Yu., Goreva E.A., Petrenko A.V. Stereotipy pitaniya detei v shkol'nykh kollektivakh [Stereotypes of the children nutrition at school associations]. *Uchenye zapiski universiteta im. P.F. Lesgafta*, 2015, no. 4, pp. 190–196 (in Russian).

4. Esaulenko I.E., Nastausheva T.L., Zhdanova O.A., Minakova O.V., Logvinova I.I., Ippolitova L.I. Regulyarnoe pitanie v shkole kak faktor fizicheskogo razvitiya detei i podrostkov: rezul'taty kogortnogo issledovaniya [Regular meals at school as a factor of physical development of children and adolescents: results of a cohort study]. *Voprosy sovremennoi pediatrii*, 2016, vol. 15, no. 4, pp. 364–370 (in Russian).

5. Gvozdareva O.V. Rezul'taty issledovaniya vliyaniya dvigatel'noi aktivnosti na zdorov'e shkol'nikov Gorno-Altaiska [Results of investigation of influence of motor performance on the health of schoolchildren of Gorno-Altaisk]. *Zdorov'e naseleniya i sreda obitaniya*, 2017, vol. 288, no. 3, pp. 47–50 (in Russian).

6. Van Kann D.H.H., De Vries S.I., Schipperijn J., De Vries N.K., Jansen J.M.W., Kremers S.P., Choolyard J. Characteristics, Physical Activity, and Sedentary Behavior: Combining GPS and Accelerometry. *Journal of School Health*, 2016, vol. 86, no. 12, pp. 913–921.

7. Sokolova S.B., Kuchma V.R. Kontseptsiya otsenki kachestva meditsinskoi pomoshchi obuchayushchimsya v obrazovatel'nykh organizatsiyakh [Framework for quality of the health care in educational organization]. *Zdorov'e naseleniya i sreda obitaniya*, 2016, vol. 281, no. 8, pp. 8–12 (in Russian).

8. Kuchma V. R., Makarova A. Yu., Rapoport I. K. Sostoyanie meditsinskogo obespecheniya detei v obrazovatel'nykh organizatsiyakh [Status health care for children in educational institutions]. *Voprosy shkol'noi i universitetskoi meditsiny i zdorov'ya*, 2017, no. 2, pp. 37–45 (in Russian).

9. Baranov A.A., Kuchma V.R., Anufrieva E.V., Sokolova S.V., Skoblina N.A., Virabova A.N., Makarova A.Yu., Trofimenko E.V., Kvilinskii P.N., Sapunova N.O. Otsenka kachestva okazaniya meditsinskoi pomoshchi obuchayushchimsya v obrazovatel'nykh organizatsiyakh [Quality Evaluation of Healthcare Services in Schools]. *Vestnik Rossiiskoi akademii meditsinskikh nauk*, 2017, vol. 72, no. 3, pp. 180–194 (in Russian). DOI: 10.15690/vramn830

10. Michael S.L, Merlo C.L., Basch C.E., Wentzel K.R, Wechler H. Health and Academics Critical Connections: Health and Academics. *Journal of School Health*, 2015, vol. 85, no. 11, pp. 740–758. DOI: 10.1111/josh.12309

11. Hunt P., Barrison L., Telljohann S.K, Mazyck D.A. Whole School Approach Collaborative Development of School Health Policies, Processes, and Practices. *Journal of School Health*, 2015, vol. 85, no. 11, pp. 802–809. DOI: 10.1111/josh.12305

12. Ustinova O.Yu., Valina S.L., Kobyakova O.A., Nikiforova N.V., Alekseeva A.V. Obosnovanie optimal'noi napolnyaemosti grupp doshkol'nykh obrazovatel'nykh organizatsii obshcherazvivayushchei napravlennosti [Rationale for the optimal group occupancy in preschool educational institutions of general enrichment orientation]. *Gigiena i sanitariya*, 2016, vol. 95, no 1, pp. 57–63 (in Russian).

13. Elgar F.J., Pförtner T.-K., Moor I., De Clercq B., Stevens G.W., Currie C. Socioeconomic inequalities in adolescent health 2002–2010: A time-series analysis of 34 countries participating in the Health Behaviour in School-Aged Children study. *Lancet*, 2015, vol. 385 (9982), pp. 2088–2095. DOI: 10.1016/S0140-6736 (14) 61460-4

14. Sukharev A.G., Stan V.V., Ignatova L.F. Rol' obrazovatel'noi organizatsii v formirovanii u uchashchikhsya motivatsii k zdorov'yu i zdorovomu obrazu zhizni [The role of educational organizations in the development of students" motivation to health and healthy lifestyle]. *Voprosy shkol'noi i universitetskoi meditsiny i zdorov'ya*, 2016, no. 2, pp. 32–35 (in Russian).

15. Kovtun O.P., Anufrieva E.V., Nozhkina N.V., Malyamova L.N. Shkol'naya meditsina: analiz dostignutykh rezul'tatov i poisk novykh reshenii [School medicine: analysis of achieved results and search for new solutions]. *Vestnik ural'skoi meditsinskoi akademicheskoi nauki*, 2018, vol. 15, no. 1, pp. 136–145 (in Russian). DOI: 10.22138/2500-0918-2018-15-1-136-145

16. Kuchma V.R. Formirovanie zdorovogo obraza zhizni detei i edinogo profilakticheskogo prostranstva v obrazovatel'nykh organizatsiyakh: problemy i puti resheniya [Hygiene of children and teenagers in the formation of health of the nation]. *Gigiena i sanitariya*, 2015, vol. 94, no. 6, pp. 20–25 (in Russian).

17. Stiefel L., Prescott M.P., Schwartz A.E. School Wellness Programs: Magnitude and Distribution in New York City Public Schools. *Journal of School Health*, 2017, vol. 87, no. 1, pp. 3–11. DOI: 10.1111/josh.12463

18. Zahnd W.E, Smith T., Ryherd S.J., Cleer M., Rogers V., Steward D.E. Implementing a Nutrition and Physical Activity Curriculum in Head Start Through an Academic-Community Partnership. *Journal of School Health*, 2017, vol. 87, no. 6, pp. 465–473. DOI: 10.1111/josh.12515.

Vasilyev V.V., Perekusikhin M.V. Hygienic assessment of measures aimed at risks reduction and health preservation for children in secondary schools. Health Risk Analysis, 2018, no. 3, pp. 128–135. DOI: 10.21668/health.risk/2018.3.14.eng

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PROPORTIONS OF ARSENIC AND ANTIMONY IN BIOGEOCHEMICAL PROVINCES AS HEALTH RISK FACTORS

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To perform efficient activities aimed at managing population health risks, it is necessary to examine regularities related to distribution of chemical elements in the biosphere; especially in so called biogeochemical provinces of natural or technogenic origin. We used semimetals of arsenic and antimony as an example to show that similarity of their physical and chemical properties is accompanied with similar effects they produce on living organisms. However, amphoteric character of arsenic and antimony determines wide range of possible interactions between these elements and biological molecules in a body. As a result, combined influence exerted by these substances on living organisms leads to both antagonistic relations and competition between them and to synergy as well. Basing on reviewed literature data, we showed that animals selectively limited accumulation of arsenic in their bodies and consumed less toxic antimony in greater quantities in case of biochemical anomalies while plants were much less selective and accumulated toxic arsenic easily. Accordingly, any activities aimed at population health risk reduction that are to be performed on territories of biogeochemical provinces should take into account peculiarities related to accumulation of these elements in bodies of warm-blooded animals and people. These peculiarities should also be taken into account when hygienic research programs and hygienic inspections are drawn up. When such research is performed experts should do the following: to analyze ways and chemical forms of elements migration in the environment; to determine molecular mechanisms of elements penetration into a cell and conditions of various scenarios of their metabolism and biological efficiency.

Key words: *arsenic and antimony compounds, biogeochemical provinces, biogeocenosis, population health, medical and prevention activities.*

Live organisms existing within a specific biogeochemical province have to rearrange their life processes. It leads to a specific elements imbalance in a body that is to be eliminated with special medical and preventive technologies [1–4].

Absorption of chemical elements from the environment by warm-blooded organisms depends on chemical properties and aggregate state of an element, its quantity, accompanying elements, and properties of body tissues that contact it as well [5]. The conditions are multiple and it makes absorption of chemical elements by a body a truly situational process. Therefore, given specific conditions existing in this or that biogeochemical province, it is necessary to determine regularities of introduction, accumulation, and excretion out of a body for elements that are specific for it. Given this multiple dependency of toxic effects produced by chemicals, I.M. Trakhtenberg noted [6] that it was necessary to perform an obligatory examination of overall quantitative contamination of the environment in biogeochemical provinces in order to work out efficient preventive measures.

Biogeochemical anomalies, both natural and technogenic ones, have been studied for more than 50 years and it allowed to determine what

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substances occurred in them, as well as reasons and conditions for formation of biogeochemical provinces; to understand and formulate regularities related to their formation; to work out strategy and tactics of activities aimed at providing prevention of population health disorders [7]. Growth in industrial outputs requires new resource provision based on new technological solutions both in production and in exploration of new mineral deposits and in recultivation of previously used ones [8].

Arsenic is a widely spread element which is contained in a lot of minerals, especially metals-containing ones. Arsenic is a metalloid, that is, it is a substance that is between metals and non-metals; so, if we want to get a better insight into regularities of its dispersion, it is interesting to analyze biogeochemical properties of other metalloids. We can take antimony as an example as it is another element that has been used by people from the earliest times and, what is also important, also accompanies a lot of other metals [9]. Antimony (Sb) and its compounds were enlisted among toxic or hazardous substances that require immediate attention on the 43th session of the World Health Assembly held in Geneva in 1990 [10, 11].

Metals and metalloids have a common capability to interact with sulfhydryl groups of biological molecules that participate in nervous impulses conduction, tissue respiration, muscle contraction, cellular membranes penetrability etc. A reaction between ions of metals and metalloids with SH-groups results in occurrence of insoluble compounds, so called mercaptides, that leads to disorders in certain biochemical processes underlying development of intoxication [12].

Our research goal was to perform a comparative analysis of toxicometry and toxicokinetics parameters of arsenic and antimony under conditions of their biogeochemical anomaly.

Arsenic is unique due to its occurrence everywhere, in minerals, rocks, soils, and water, in plants and animals. Average arsenic concentration in rivers is equal to 3 μg/l; in surface waters, about 10 μg/l; in seas and oceans, just about 1 μg/l[1]. Arsenic concentration in soils usually varies from 0.1 to 40 mg/kg. Much greater quantities of arsenic, up to 8 g/kg, can be found in areas where arsenic ores occur, as well as in volcanic regions [13].

Increased arsenic concentrations in soils can exert negative influence on agricultural crops due to arsenic becoming a food chain component [14]. Geochemical background of arsenic (As) which is detected in landscape components around tailings dams of mining enterprises is characterized with high arsenic pollution, namely 57-300 mg/kg [15]. Arsenic concentration in plants that grow on a territory of natural-technogenic landscapes varies considerably, from such low values as 0.001 to 847.29 mg/kg. Average arsenic contents in plants growing in this landscape are 2.7 times higher than in plants growing in quarry-dump landscapes and almost 28 times higher than in plants growing in natural landscapes [15]. Arsenic also migrates in the environment in a form of volatile arsenic-organic compounds [13].

Arsenic concentration in a living organism usually amounts to about 6 μg/kg. Daily introduction of arsenic into a human body is insignificant and varies from 50 to 100 μg, and its semi-excretion period amounts to 30-60 hours[2]. When arsenic enters a body, it then concentrates in the thyroid gland, liver, kidneys, spleen, lungs, bones, hair, brain tissues, and the muscles. There are some data on arsenic accumulation in the thyroid gland making for endemic goiter development [16].

Chronic negative effects produced by arsenic are damage to skin, neurotoxicity, cardiovascular diseases, diabetes, and cancer. The International Agency for Research on Cancer (IARC) rank arsenic and its non-organic compounds as "Carcinogenic to Humans" (group I) (IARC, 1980[17]). EFSA Food Contamination Panel detected that provisional tolerable weekly intake of arsenic shouldn't exceed 15 μg/kg*day (EFSA contam PANEL, 2009)[3] [18].

Geometric average arsenic concentrations in

[1] Turbinskiy V.V. Hygienic grounds for sanitary protection of cross-border and border sources of drinking water supply for the RF population: dissertation …for Doctor Of Medical Sciences. Novosibirsk, 2012. 376 p. Available at: http://www.dissercat.com/content/gigienicheskie-osnovy-sanitarnoi-okhrany-transgranichnykh-i-pogranichnykh-istochnikov-pitevo (date of visit February 13, 2018).

[2] Chemical structure of Russian food products: reference book. In: I.M. Skurikhin ed. Moscow, Deli print Publ., 2002, 236 p.

[3] P 2.1.10.1920-04. Guidelines on assessment of population health risk under exposure to chemicals that pollute environment. Moscow, Federal center for Sanitary and Epidemiologic Surveillance of The RF Public healthcare Ministry Publ., 2004,143 p.

umbilical blood of parturient women are equal to 0.92 ± 1.01 ng/ml, at 0.43 ± 0.88 ng/ml (n = 296) in healthy newborns [19]. An inhibition of arsenic elimination out of a body was detected under single oral exposure to arsenous anhydride in a dose equal to 30 mg/kg which coincided with a threshold of acute action produced by arsenous anhydride on changes in SH-group contents in blood[4].

Arsenic concentration in chicken that consumed it with forage in a dose equal to 0.5-5.0 mg/kg amounted to 0.11-0.2 mg/kg in muscle tissues; 0.09-0.12 mg/kg in liver; 0.09-0.34 mg/kg in kidneys; and 0.12-0.21 mg/kg in eggs[5].

Oral introduction of arsenic oxide (As_2O_3) into sheep bodies in a dose equal to 0.5 mg/kg of an animal body weight didn't cause any clinical intoxication symptoms during 3 months after exposure. But arsenic accumulated in a dose equal to 0.2-0.3 mg-kg in the kidneys, skin, liver, and spleen; about 0.12 mg/kg, in muscle tissues and lungs; about 0.25-0.3 mg/kg, in the abomasum, duodenum, jejunum, and ileum [20].

High arsenic concentrations in drinking water, 200-500 μg/l, are toxic for the human endocrine system [21]. Cumulative exposures to arsenic with food and drinking water are higher in people suffering from the II type diabetes than in healthy people [22, 23] and it proves it is necessary to conduct further research on a role played by moderate and low arsenic concentrations (500-200 μg/l) in water [24].

Experts used models of animal cells cultures to show that arsenic acted as endocrine destroyer. They detected disorders in gene expression of steroid receptor (SR) in cells exposed to non-organic arsenic (arsenite, iAs (+3)). Low iAs (+3) concentrations (0.1–0.7 μM) stimulate hormone-induced transcription, but higher non-cytotoxic arsenic concentrations (1-3 μM) inhibit transcription [25].

Antimony is a considerably rare element in the earth's crust, $4*10^{-5}$ %, although it, like arsenic, can occur in high concentrations in some regions [26]. In nature antimony usually has valence +3, more rarely +5 [27]. Compounds of tervalent positive antimony (sulfides, thiosalts, antimonites, trioxide) are most widely spread; the next place belongs to compounds of tervalent negative antimony (antimonides). Compounds of pentavalent antimony are rarely met in nature. Antimonial glitter Sb_2S_3 (stibuite, antimonite) is the most widely spread antimony-containing mineral; it occurs in hydrothermal deposits as antimonial ores seams and tabular deposits [28].

Background antimony concentrations in upper soils layers amount to 0.76 mg/kg in sod-podzol soils; 0.99 mg/kg, in black earth; 0.28 mg/kg, in peaty soils. Antimony concentrations in Siberian rivers (Irtysh, Ob', Tom' and Amur) amounts to 0.0007–0.002 mg/dm^3 [5].

Antimony concentrations in tissues of trees and bushes that grow in areas with ores mineralization reach 7-50 mg/kg of dry solid matter; its average concentrations in plants parts above ground level amounts to 0.06 mg/kg of dry solid matter. Antimony concentrations in edible plants vary within 0.02-4.3 μg/kg of raw matter. Antimony concentration in corn grains and potato tubers doesn't exceed 2 μg/kg of dry solid matter; it reaches 29 μg/kg in grass. Antimony concentration in barley and flax rootage amounts to 122 and 167 μg/kg of solid dry matter respectively, and it is considerably higher than in leaves where it amounts to 10 and 27 μg/kg of solid dry matter [28]. As concentrations of heavy metals in soils become very high, their concentrations in various parts of plants also increase. But a ratio between heavy metals concentrations in rots, culms, leaves, and reproductive organs is preserved.

Complex research performed on Dyukov Log waste storage where sulfide-containing wastes from Salairskiy ore mining and processing enterprise were kept helped to outline migration routes for drainage flows that contained increased antimony concentrations (96 MPC) and arsenic concentrations (6 MPC). It was detected that polluted drainage water penetrated water-bearing horizons that, among other things, were used as water supply sources for communal needs and drinking [29]. Plants growing on pasture lands and land-

[4]Zhuruli M.O. Studies on toxicokinetics of arsenous anhydride under various exposure in order to fix hygienic standards: dissertation….Candidate of Medical Sciences. Moscow, 1984, 179 p. Available at: http://www.dissercat.com/content/izuchenie-toksikokinetiki-myshyakovistogo-angidrida-pri-razlichnykh-rezhimakh-ego-vozdeistvi#ixzz5CNZZqPjy (date of visit January 19, 2018).

[5]Chupakhina O.K. Toxicity of arsenic for chicken and its distribution in poultry organs and tissues: thesis of dissertation…Candidate of Veterinary Sciences. Moscow, 1983, 21 p.

scape plants in Kadamjaiskaya biogeochemical antimony province accumulate substantial antimony concentrations, 1.2 – 16 MPC.

As per data obtained in some research, antimony can be found in a human body: in blood, 0.0033 mg/l; bone tissue, (0.01–0.6)*10–4 %; muscle tissues, (0.42–19.1)*10–6 %; a toxic dose amounts to 100 mg. Average daily introduction of antimony into a human body with food and water amounts to approximately 50 μm. Antimony is rather slowly excreted from a body [30, 31].

Antimony in concentrations equal to 0.41-0.55 mg/kg and arsenic in concentrations equal to 0.79-0.82 mg/kg were detected in bone fragments belonging to a gray rat Rattus Norvegicus found in pellets of a long-eared owl that usually spends a winter in Tashkent and adjacent territories [32].

Elimination of antimony is equally related to its valence in a specific compound. Thus, when antimony trioxide was added to rats forage, 80-100 μm of this metal were daily excreted with urine, and up to 100 mg, with stool. Pentavalent antimony is primarily excreted with urine even when it is introduced intragastrically [33].

Antimony (Sb) is similar to arsenic as per its properties; it was detected that antimony exerted inhibiting influence on enzymes that participate in carbohydrates, fats, and lipids metabolism. Just as arsenic, antimony reacts with sulfhydryl groups, has toxic properties, can probably cause immune deficiency [34], and causes functional disorders in various organs (heart, kidneys, CNS, liver, lungs, intestines, lymphatic system and others) [35, 36].

Inhalation exposure to antimony aerosols that occur in working area air causes its higher concentrations in workers' bodies; they increase from 0.5 mg% to 2.1 mg% in blood; from 0.86 mg% to 1.86 mg% in urine; from 1.6 mg% to 7,8 mg% in hair [37].

Fivefold intraperitoneal introduction of metal antimony suspension in peach oil into white rats in a dose equal to 50 mg/kg of a body weight caused increased antimony concentrations in blood (10.46+1.22; 6.58+0.74 mg%). Antimony accumulated in internal organs in the following concentrations: muscles, 1.49 ± 0.35 mg%; lungs, 1.38+ ±0.2 mg%; skin, 1.14+0.3 mg% [38].

Antimony concentrations in sheep bodies on a territory of antimony biogeochemical province amount to 3.66–12.7 mg/kg in the heart; 4.00–12.16 mg/kg, lungs; 2.6–10.2 mg/kg, kidneys; 3.6–10.0 mg/kg, muscles; concentration gradient is 2–2.4 [39]. Daily antimony introduction into a human body detected in Kadamdjayskaya antimony province, Republic of Kirgizstan, amounts to 8.54 mg while it is equal to only 1.22 mg per day on a reference territory [40], and a reference dose of antimony for chronic oral introduction into a body amounts to 0.0004 mg/kg. This increased antimony introduction exerts its negative influence primarily on dextrose and cholesterol contents in blood[3].

Table

Arsenic/antimony ratio in geological and biological environment in biogeochemical provinces

Environmental object	Arsenic, mg/kg min-max average	Antimony, mg/kg min-max average	Average As/Sb ratio
Soil	0,1–40,0 10,0	0,28– 0,99 0,76	13,1
Water	0,0007–0,005 0,0029	0,00005– 0,0007 0,00037	7,8
Plants (antimony and arsenic biogeochemical province) Background (reference territory)	57–300 100 0–6,01 1,4	7–50 20 0,02–4,3 0,7	5,0 2,0
Animals: - wild rats (bones)	0,79–0,82 0,80	0,41–0,55 0,47	– 1,7
- sheep (lungs, kidneys, muscles)	0,41–1,54 0,98	6,41–8,08 7,25	0,14
- people (blood)	0,43–0,92 0,68	3,3 3,3	0,21
Threshold toxic does, mg/day	20,0	100,0	0,2
Lethal dose for a man, mg	50–340 180	500–1000 750	0,24

Research conducted in antimony biogeochemical provinces located in Fergana Valley revealed that adult population living there daily consumed approximately 0.1-0.15 mg of antimony with food and water and it was 10-15 times higher than a usual introduction on a reference territory [41].

Each pathology has its specific element structure and concentrations, including maximum ones, as well as changes in an aggregate parameter of their accumulation [42–44]. Antimony and arsenic are endocrine destroyers [45].

As/Sb ratios are obtained on the basis of collected data on arsenic and antimony concentrations in geological and biological objects. The results are shown in the Table.

The obtained ratios show that arsenic concentrations are 2-13 times higher than antimony ones in geological environmental objects, and, on the contrary, antimony concentrations are 5-20 times higher in biological media of living organisms. Arsenic contents in bones is 1.7 times higher than antimony contents, just like in geological objects.

Higher antimony concentrations than arsenic ones in a body are determined by antimony being less toxic than arsenic.

Therefore, plants are less selective and tend to accumulate toxic arsenic easily when growing in biogeochemical anomalies while animals selectively limit its introduction into their bodies and try to consume less toxic antimony instead. Accordingly, all medical and prevention activities performed in biogeochemical provinces with increased arsenic and antimony occurrence are to take into account peculiarities of these elements accumulation in bodies of warm-blooded animals and people. Programs for in-depth research within hygienic examinations, inspections, or investigations should also take these peculiarities into account. Research should include analysis of directions and chemical forms in which elements migrate in the environment, establishment of molecular mechanisms with which elements penetrate into a cell, and conditions for various scenarios of their metabolism and biological activity.

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References

1. Efimova N.V., Myl'nikova I.V., Katul'skaya O.Yu., D'yakovich M.P. Problemyadaptatsiidetei i podrostkov v usloviyakh Vostochnoi Sibiri: monografiya [Issues related to adaptation of children and teenagers in eastern Siberia: Monograph]. Irkutsk, RIO GBOU DPO IGMAPO Publ., 2012, 140 p. (in Russian).

2. D'yakovich M.P., Rukavishnikov V.S., Kazakova P.V., Finogenko I.A., Bokmel'der E.P., Solov'eva I.Yu. Kachestvozhizni, svyazannoesozdorov'em: otsenka i upravlenie [Health-related life quality: assessment and management]. In: V.S. Rukavishnikoved. Irkutsk, NTsRVKh SO RAMN Publ., 2012, 168 p. (in Russian).

3. Gurvich V.B., Plotko E.G., Kuzmin S.V., Selyankina K.P., Ryzhov V.V., Makarenko N.P., Nadeenko V.G. Aktual'nyeproblemyprofilakticheskoimeditsiny v Ural'skomregione [Vital issues of preventive medicine in the Urals]. *Sbornik nauchnykh trudov i nauchno-prakticheskikh rabot, posvyashchennyi 80-letiyu gossanepidsluzhby Rossii*. Ekaterinburg, 2002, p. 76–81 (in Russian).

4. Kovalevskii A.L. Biogeokhimicheskiepoiskirudnykhmestorozhdenii [Biogeochemical searching for ore deposits]. The2rded. Moscow, Nedra Publ., 1984, 172 p. (in Russian).

5. AvtsynA.P. Mikroelementozycheloveka: etiologiya, klassifikatsiya, organopatologiya [Human microelementosis: etiology, classification, and organopathology]. Moscow, Meditsina Publ., 1991, 496 p. (inRussian).

6. Trakhtenberg I.M. Narusheniekhimicheskogoravnovesiyakakprichinaboleznei [Chemical balance disorder as a cause of diseases]. *Zdorov'yaUkraini: meditsinskii portal*. Availableat: http:\\www.health-ua.com (04.02.2018) (inRussian).

7. Osipov V.I., Aksyutin O.E., Ishkov A.G., Grachev V.A. Vzaimodeistvie cheloveka s prirodnoi sredoi – vazhneishii factor sushchestvovaniya tsivilizatsii itogam goda ekologii v rossiiposvyashchaetsya [Interaction between a man and the environment as a vital factor of civilization existence: dedication to

the results of the Environmental Year in Russia]. *Vestnik Rossiiskoi akademii nauk*, 2018, vol. 88, no. 2, pp. 99–106. DOI: 10.7868/S0869587318020019 (in Russian).

8. Ivanter V.V. Perspektivy vosstanovleniya ekonomicheskogo rosta v Rossii [Prospects for recovery of economic growth in Russia]. *Vestnik Rossiiskoi akademii nauk*, 2017, vol. 87, no. 1, pp. 15–28 (in Russian).

9. Mel'nikov S.M., Rozlovskii A.A., Shuklin A.M. [et al.]. Sur'ma [Antimony].In: S.M. Mel'nikov ed. Moscow, Metallurgiya Puibl., 1977, 535 p. (in Russian).

10. Solodukhina M.A., Yurgenson G.A. Sur'ma v stepnykhpochvakh, tekhnozemakhiartemisiagmelinii weber ex stechmsherlovogorskogo rudnogo raiona (vostochnoe zabaikal'e) [Antimony in the steppe soils, technoself and artemisiagmelinii weber ex stechmsherlovogorskoe ore district (eastern Transbaikalia)]. *Uspekhi sovremennogo estestvoznaniya*, 2017, no. 4, pp. 114–119 (in Russian).

11. Hoet P., Lauwerys R. Metally I metalloorganicheskie soedineniya [Metals and metal-organic compounds]. Available at: http://base.safework.ru/iloenc?navigator&spack=110LogLength%3D0%26LogNumDoc%3D8574000 33%26listid%3D0 10000000100%26listpos%3D2%26lsz%3D6%26nd%3D857400033%26nh%3D1%26 (29.01.2018) (in Russian).

12. Tiolovyeyady, mekhanizmdeistviya [Thiol poisons, action mechanisms]. Available at: https://studopedia.org/5-77519.html (11.02.2018) (in Russian).

13. Mysh'yak v prirode [Arsenic in nature]. *Vuzlit.ru*. Available at: https://vuzlit.ru/740028/myshyak_prirode (18.02.2018) (in Russian).

14. Schwarzkopfova K., Farago T., Jurkovič L. Mobilization of arsenic from technosols in a short-term dynamic column experiment. *Toxicological & Environmental Chemistry*. Available at: https://doi.org/10.1080/02772248.2018.1443339 (22.03.2018).

15. Mikhailova L.A., Solodukhina M.A. Prirodnye i antropogennye geokhimicheskie anomalii Zabaikal'skogo kraya [Geochemical environment and public health in the Zabaykalye region]. *Sovremennye problemy nauki i obrazovaniya*, 2016, no. 5, p. 310 (in Russian).

16. Toksikologo-gigienicheskaya kharakteristika mysh'yaka [Toxicological and hygienic characteristics of arsenic]. *Maga Lektsii*. Available at: https://megalektsii.ru/s43057t1.html (21.03.2018) (in Russian).

17. IARC on the evaluation of the carcinogenic risk of chemicals to humans: Sorne Antineoplastic and Irnmunosuppressive Agent. *World Health Organization; International Agency for Research on Cance*. Lyon, 1981, vol. 26, 396 p.

18. Scientific Opinion on Arsenic in Food. *EFSA Journal*, 2009, vol. 7, no. 10, pp.1351. DOI: 10.2903/j.efsa.2009.1351

19. Lin Z., Chen X., Xi Z., Lin S., Sun X., Jiang X., Tian H. Individual heavy metal exposure and birth outcomes in Shenqiu county along the Huai River Basin in China. *Toxicology Research*, 2018, no. 3. Available at: http://pubs.rsc.org/en/Content/ArticleLanding/2018/TX/C8TX00009C#!divAbstract (21.04.2018).

20. Zhulenko V.N., Golubitskaya A.V. Ekspress-metody opredeleniya metallosoderzhashchikh soedineniii mysh'yaka v biomateriale, kormakh [Express-tests for determining metal-containing compounds and arsenic in biological materials and feedstuffs]. Obninsk, 1992, 15 p. (in Russian).

21. Del Razo L.M., Garcia-Vargas G.G., Valenzuela O.L., Castellanos E.H., Sánchez-Peña L.C., Currier J.M., Drobná Z., Loomis D., Stýblo M.Exposuretoarsenic in drinking water is associated with increased prevalence of diabetes: a cross-sectional study in the Zimapán and Lagunera regions in Mexico. *Environmental Health*, 2011, no. 10, pp. 73–80. DOI: 10.1186/1476-069X-10-73

22. Makris K.C., Christophi C.A., Paisi M., Ettinger A.S. Apreliminaryassessmen to flow levelarsenicexposureanddiabetesmellitus in Cyprus. *BMC Public Health*, 2012, no. 12, pp. 334.

23. Steinmaus C., Yuan Y., Liaw J., Smith A.H. Low-level population exposure to inorganic arsenic in the United States and diabetes mellitus: a reanalysis. *Epidemiology*, 2009, vol. 20, no. 6, pp. 807–815.

24. Gosse J.A., Taylor V.F., Jackson B.P., Hamilton J.W., Bodwell J.E. Monomethylated trivalent arsenic species disrupt steroid receptor interactions with their DNA response elements at non-cytotoxic cellular concentrations. *J. Appl Toxicol*., 2014, vol. 34, no. 5, pp. 498–505. DOI: 10.1002/jat.2898

25. O vliyanie sur'my na organizm cheloveka (kratkii obzor literatury) [On influence exerted by antimony on a human body (short literature review)]. *DocPlayer.ru*. Available at:

https://docplayer.ru/82958586-O-vliyanie-surmy-na-organizm-cheloveka-kratkiy-obzor-literatury.html (15.02.2018) (in Russian).

26. Raspredeleniesur'my v sistemepochva-rastenie [Distribution of antimony in plant-soil system]. *Geolike.ru*. Available at: http://geolike.ru/page/gl_1357.htm (22.01.2018) (in Russian).

27. Biokhimiya I toksikologiya soedinenii mysh'yaka, sur'myivismuta - [Biochemistry and toxicology of arsenic, antimony and bismuth compounds]. *AllBest*. Available at: https://otherreferats.allbest.ru/chemistry/00131620_0.html (22.04.2018) (in Russian).

28. Kubatbekov T.S., Aitmatov M.B., Ibraimakunov M. Sur'ma v prirodno-tekhnogennykh usloviyakh biosfery: voda, pochva, rasteniya [Antimony in natural-technogenic conditions of the biosphere: water, soil, plants].*Vestnik Rossiiskogo universiteta druzhby narodov. Seriya: Agronomiya i zhivotnovodstvo*, 2012, no. 4, pp. 56–60 (in Russian).

29. Epov M.I., Yurkevich N.V., Bortnikova S.B., Karin Yu.G., Saeva O.A. Opredelenie sostava gorno-rudnykh otkhodov geokhimicheskimi I geofizicheskimi metodami (na primere khvostokhranilishcha Salairskogo gorno-obogatitel'nogo kombinata) [Analysis of mine waste by geochemical and geophysical methods (a case study of the mine tailing dump of the Salair ore-processing plant)]. *Geologiya i geofizika*, 2017, no. 12, pp. 1944–1954 (in Russian).

30. Ershov Yu.A., Pleteneva T.V. Mekhanizm y toksicheskogo deistviya neorganicheskikh soedinenii [Toxic action mechanisms of non-organic compounds]. Mocow, Meditsina Publ., 1989, 271 p. (in Russian).

31. Gashev S.N., Bykova E.A. Osobennosti nakopleniya mikroelementov v organizme melkikh mlekopitayushchikh v usloviyakh urbanizatsii [Peculiarities of microelements accumulation in the organism of small mammals in the urbanization conditions]. *Izvestiya Samarskogo nauchnogo tsentra Rossiiskoi akademii nauk*, 2014, vol. 16, no. 1–4, pp. 1144–1148 (in Russian).

32. Levin E.N. Obshchaya toksikologiya metallov [Common toxicology of metals]. Leningrad, Meditsina Publ., 1972, 183 p. (in Russian).

33. Makdermott M. Sekrety endokrinologii [Secrets of endocrinology]. Moscow–St. Petersburg, Binom, Nevskiidialekt, 2000, 464 p. (in Russian).

34. Sur'ma «Rvotnyikamen'» ["Emetic stone" antimony]. Available at: http://pharmacognosy.com.ua/index.php/makro-i-mikro-chudesa/surma-rvotniy-kamen (21.12.2017) (in Russian).

35. Klinicheskaya mikroelementologiya. Sur'ma [Clinical microelemntology. Antimony]. Available at: www.microelement.ru/uslovno-toksichnye/99-surma.html (21.03.2018) (in Russian).

36. Chonbasheva Ch.K., Sulaimanova Ch.T. Khronicheskaya sur'myanaya intoksikatsiya u rabotnikov sovremennogo proizvodstva Kyrgyzstana [Chronic intoxication with antimony in workers employed at contemporary productions in Kyrgyzstan]. *Vestnik Kyrgyzsko-Rossiiskogo slavyanskogo universiteta*, 2014, vol. 14, no. 5, pp.188–190 (in Russian).

37. K voprosu nakopleniya sur'my v krovi i nekotorykh organakh krys s privitoiopukhol'yu sarkoma-45 (material imetodika) [On accumulation of antimony in blood and some organs of rats with indyced sarcoma-45 (data and methods)]. *Medchitalka: meditsinskaya biblioteka*. Available at: http://www.medchitalka.ru/voprosy_klinicheskoy_i_eksperimentalnoy_onkologii/voprosy_eksperimentalnoy_onkologii/3147.html (15.03.2018) (in Russian).

38. Kubatbekov T.S., Aitmatov M.B., Ibraimakunov M. Kumulyatsiyasur'my v biosredakhovets, soderzhashchikhsyavblizisur'makombinata [Accumulation of antimony in bioenvironment of sheeps contained in the vicinity of antimony combine]. *Vestnik Rossiiskogo universiteta druzhby narodov. Seriya: Agronomiya i zhivotnovodstvo*, 2013, no. 2, pp. 45–50 (in Russian).

39. Posypanov G.S., Dolgodvorov V.E., Zherukov B.Kh. [et al.]. Rastenievodstvo [Crop production]. In: G.S. Posypanov ed. Moscow, Kolos Publ., 2006, 612 p. (in Russian).

40. Endemii i endemicheskie zabolevaniya. Endemiyasur'my [Endemias and endemic diseases. Antimony endemia]. Availableat: http://belki.com.ua/minerali-endemia.html (27.02.2018) (in Russian).

41. L Rikhvanov. P., Baranovskaya N.V., Ignatova T.N., Sudyko A.F., Sandimirova G.P., Pakhomova N.N. Elementny I sostav organov I tkanei cheloveka [Elemental structure of human organs and tissues]. *Problemy biogeokhimii I geokhimicheskoi ekologii*, 2009, vol. 9, no. 1, pp. 67–77(in Russian).

42. Rikhvanov L.P., Baranovskaya N.V., Ignatova T.N., Sudyko A.F., Sandimirova G.P., Pakhomova N.N. Khimicheskii elementny I sostav organov I tkanei cheloveka i ego ekologicheskoe

znachenie [Trace elements in human organs and tissues and their significance for environmental monitoring]. *Geokhimiya*, 2011, no. 7, pp. 779–784 (in Russian).

43. Fernando Barbosa Jr. Toxicology of metals and metalloids: Promising issues for future studies in environmental health and toxicology. *Journal of Toxicology and Environmental Health, Part A*, 2017, vol. 80, no. 3, pp. 137–144. DOI: 10.1080/15287394.2016.1259475

44. Khaidulina Kh.Kh., Dorofeeva E.V. Endokrinnye razrushiteli (Endocrine Disrupters). Sovremennoe sostoyanie problem [Endocrine disruptors. Present status of the problem]. *Toksikologicheskii vestnik*, 2013, no. 2, pp. 51–54.

Turbinsky V.V., Bortnikova S.B. Proportions of arsenic and antimony in biogeochemical provinces as health risk factors. Health Risk Analysis, 2018, no. 3, pp. 136–143. DOI: 10.21668/health.risk/2018.3.15.eng

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CREATION OF HEALTH-ORIENTED CITY SPACE AS A WAY TO MANAGE POPULATION HEALTH RISK

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Nowadays intense urbanization is taking place, cities with a number of dwellers over a million and urban agglomerations appear, and it calls for new ways how to preserve and improve health of urban population who are exposed to various risk factors, primarily environmental and behavioral ones. One of such ways could be development of a city as health-oriented physical, social, and semantic space; that is, it should be an environment that has natural, material, socio-cultural and other resources and they are used to create possibilities for individuals and social groups to preserve and improve their health. Parameters of a physical component in health-oriented space and their possible indicators can be found in foreign concepts and international projects ("healthy city", "active city", "age-friendly city"), as well as in Russian management practices ("Creation of comfortable urban environment" project, a concept of urban space quality). This article focuses on a detailed system of indicators that can be applied to assess whether a health-oriented urban environment is well-developed; the system is based on risk-oriented approach and includes two groups of indicators. The first one comprises indicators that describe a health-preserving component in urban space that allows to control health risk factors better; the second one includes indicators that are related to a health-improving component that helps to improve health and to promote stability. As morbidity and mortality among urban population vary greatly in their structure depending on countries and regions, health-oriented urban space should be created taking into account health peculiarities of population living on a specific territory.
In other words, detected leading causes for mortality and morbidity among urban population in Russia as well as manageable risk factors that cause them should serve as grounds for a creation of such a body-space urban environment that will be oriented at reduction in negative impacts exerted by chemical contamination of the environment on population health (planting, alternative transport infrastructure, compliance of drinking water sources with sanitary-epidemiologic requirements, quality of water supplies and distribution systems); such system will also provide conditions for sufficient physical activity and health nutrition.

Key words: *urban space, health-oriented space, healthy city, health risk, risk management.*

High urbanization rates in the second half of the 20th – beginning of the 21st century, typical for most countries of the world, resulted in a fact that today more than half of the population lives in cities (54.7%, according to the World Bank). In developed countries, this indicator in 2017 was at the level of 70–80% (in Germany, urban population share made 76%, in France: 80%, Canada: 82%, Great Britain: 83%, Japan: 94%). According to Federal State Statistics Service (Rosstat), in Russia the urban population exceeds significantly the rural (74.3% vs. 25.7%, respectively), and since 1959 the urban population share in our country has increased by more than 20%.

An intensive development of cities, emerging “million-plus cities” and formation of urban agglomerations, often counting of tens of millions dwellers (for example, the number of Japanese agglomeration of Tokyo-Yokohama is over 37 million people), made it relevant to find new ways for preserving and improving health

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of urban residents exposed daily to various risk factors. The latter include environmental (air pollution from toxic emissions of motor vehicles, noise pollution of urban environment, pollution of drinking water with industrial wastewaters) and social factors (atomization of urban community, a dominant of "depersonalized" interaction of citizens, high social inequality, mostly sedentary lifestyle). Modern cities architecture has a negative impact on urban population health: typical buildings, plurality of identical repetitive elements (for example, windows of multi-storey buildings), poor greening of new areas.

Numerous scientific studies show that citizens health has its own distinct features – in cities there is a higher risk of developing chronic diseases [1], a higher chance of being injured in a car accident [2], urban lifestyle characterized by irregular meals, eating fast food and low physical activity increases risk of overweight [3] and diseases of cardiovascular system [4]: in cities with a sizeable population number, communication of infectious diseases is probably higher than in rural areas [5].

Growth of urban population and multiplicity of factors that affect citizen health mainstreamed the task of urban development so that physical and social environment would contribute as high as possible to preservation and improvement of residents' health. This task was most shown up in the initiatives of the global movement "Healthy Cities" under the auspices of the World Health Organization (WHO), whose principles, among other things, are human-centered urban planning, increasing population resilience to adverse external effects of environment, fighting inequality regarding health [6].

In addition to the "healthy city" concept, WHO advocates the need to develop cities as spaces that are friendly to older people ("age-friendly city"), children ("child-friendly city") and people with disabilities ("disabled-accessiblecity"). The common ground between all of these concepts is that they are aimed primarily at prioritizing health in urban policies and combining the efforts of administrations at various levels, specialized institutions and local community to create in cities the conditions for living and personal development, ranging from its active and healthy evolvement (in case of children), and ending with productive and healthy aging (in case of the elderly). The integral principles here are equal access and fairness that defines an approach to a city as a physical and social space in which equal opportunities for saving and improving one's health by all categories of citizens must be ensured.

The idea of health-oriented city space ("health-friendly city"), like the concept of healthy cities, is the result of two interdirectional movements in the field of healthcare and public health, and in the field of urban planning and urban design. The first movement is related to social factors influence on population health. The first attempts of this movement were observed in the work of Health Councils in Italy of the Renaissance, the works and activities in the field of social hygiene by Frank I.P., the creation of public health system of Great Britain by the initiative of E. Chadwick [7], as well as the medical, anthropological and political activities of R. Virchow in the field of social medicine. These scientists and public figures work led to the formation and evolvement of socio-medical health paradigm, in which medicine is a social science destined to interfere in social and political life to solve health problems. Such an insight that improving social conditions in some cases makes it possible to extend human life faster and more efficiently than medical progress has also been associated with studying the effects of not only biological, but also social roots on epidemics, as well as analysis of link between low health indicators of slum dwellers and their living conditions.

The *second* trend, which promoted healthy urban space idea, is associated with a working (social, to a wider extend) issue, creation of public organizations in a number of countries (the Social Science Association in the UK, the American Social Science Association in the USA, the Union for Social Policy in Germany, etc.), having united the academic community and politicians for expert guidance in the field of social reform. This resulted, firstly, in the emergence of a number of urban studies in the field of living conditions and lifestyle of working and lower classes [8, 9]; secondly, led to urban planning movements (B.W. Richardson's "City of Health" [10], the concept and movement of a

‘Garden City’ by G. Ebenezer [11], the City Beautiful movement [12], the movement for middle class "settlements" in poor urban areas for educational and charitable purposes [13], etc.). The central idea was to achieve the highest possible life quality through certain principles in the field of urban planning. However, the practice of implementing a number of urban projects such as “Garden City”, as well as projects for demolition of slums and construction of high-rise buildings as a solution to the problems of poverty, led to the insights that physical urban environment significance in maintaining and improving health were supplemented by such socio-cultural factors as an importance of social ties, preservation of local community, etc. Thus, the problem of health turns out to be equally related to the issues of urban planning, self-organization of urban communities, as well as to medical services.

In various fields of expertise and social practice, approaches to healthy city will focus on various aspects. Therefore, public health experts L. Dahl and T. Hancock, the creators of "Healthy Cities" project, suggested using a holistic approach to the healthy city concept, which in addition to public health included the ideas from sociology, urban geography, urban planning, ecology, politics, economics, philosophy and many other disciplines [14]. The need for a systematic approach to analyzing citizens’ health in the context of urban space is promoted by Sharp Roux A.V., emphasizing the “system essence” of both the ‘city’ and ‘public health’ [15].

City is an artificial habitat [16], a complex, self-regulating system, on the one hand, producing hazards to human life and health, and on the other, capable of providing effective ways to counter these hazards. Hence, the creation of a “safe urban environment” (for example, within the framework of “Safe City” program, operating in many cities of Russia and designed to contribute to improving security “on streets and roads”, to resist “criminal and terrorist threats").

A safe urban environment presupposes safety of dwellers in terms of all sorts of threats, primarily of external nature. It is not only about citizen life and health, but also about their rights and freedoms, material interests, personal information, etc. Urban space safety implies the conditions created to minimize various risk factors effects on public health, i.e. the environment allows inhabitants to ***preserve*** health. The concept of health-oriented city space integrates, along with the health-preserving aspect, the ***health-improving*** one, which is explained by differentiating health factors into resistance factors (anti-risk) that have a positive effect on health, increase body's resistance to external threats, and risk factors that increase probability of developing diseases. With regard to public health, it is expected that the effectiveness of anti-risk factors will be higher than the elimination of regular risk factors. Also the key point here is that in medicine the paradigm of pathogenesis is being substituted for the paradigm of salutogenesis [17]. For the former, the origin and source of diseases, as well as their prevention, is relevant, while for the latter it is a search for sources of physical and mental health and ways to improve it. Thus, within the framework of health-oriented city space, health-preserving components allow for better control over health risk factors, and health-strengthening components – for improving health, i.e. promoting factors of resistance.

Health-oriented city space is understood to mean physical, social, and semantic environment of a city, which, with its resources (natural, material, socio-cultural, etc.) creates opportunities for individuals and social groups to maintain and strengthen their health.

The physical component of health-oriented city space is a body-space environment, “city design” [18], “first order reality” [19], including, for example, health care system infrastructure, parks and public gardens, pedestrian zones and squares, outdoor recreation and sports equipment (street sports mini-centers), etc. In social aspect, health-oriented city space is a world of social relations in which people interact with each other, create social facts and at the same time conform their behavior with coercive influence of these facts, in a word, construct social reality and objectify it. We are talking about social institutions, norms, values and behavioral practices aimed at preserving health, urban communities and institutions that contribute to the development of healthy lifestyles and self-preserving behavior through their activities. The semantic aspect of city space reflects it as a “field of values”, as a construct, as a value-semantic structure, and its analysis should be

based on phenomenological method, and precede the construction of socio-urban theories. City residents "themselves create an environment for their life" [20] endowing both physical and social objects of this environment with these or other values. Hence, it seems important not only to hold the existing infrastructure in a city (both physical and social) that is designed to preserve health, but also whether this infrastructure is perceived by citizens as suitable, affordable, and attractive to implement health preservation and promotion practices.

This study is focused on healthy-oriented city space as the world of physical objects, the physical (real) environment, the body-space environment of city residents, and analyzing its completeness in modern cities requires a clear system of criteria to evaluate the development of certain environmental components and set the direction for its further improvement.

One of the most comprehensive approaches to assessing the formation degree of a health-oriented city space was developed by the ideologists of “Healthy Cities” movement T. Hancock and L. Dahl, who proposed 11 city parameters for assessing its “health” degree [14]. These parameters describe not only the physical, but also the social space (for example, “community strength” or “participation and control”, reflecting the degree of local communities involvement in making meaningful decisions for a city and an ability to support citizens).

The physical component of health-oriented space within the framework of the healthy city concept is proposed to be characterized, first, through cleanliness, safety and quality of physical environment, including the provision of housing. Indicators of this parameter may be, for example, air pollution level, green spaces share in a city’s territory, share of housing that meets national or international standards. Moreover, physical environment influence is taken into account not only at the somatic, but also at the mental health and psychological comfort level, which is reflected, for example, in the concept of therapeutic landscapes [21]). Secondly, through possibilities for citizens to satisfy their demand for medical care, which is measured using a number of indicators: physical accessibility of outpatient and high-tech care, specialized rehabilitation institutions, etc. Third, through development of infrastructure aimed at meeting basic needs, whose indicators may be availability of grocery stores focused on different nutritional needs, or availability of drinking water.

A number of indicators for health-oriented city space development are proposed in another project of the World Health Organization “Active City”, aimed at stimulating active lifestyle of citizens, including physical education and sports [22]. As indicators for measuring the development level of an artificially created body-space environment (“built environment”), it is proposed here to use an accessibility of sports infrastructure (number of gyms, fitness clubs, swimming pools, street gym sites, etc.), as well as the development level of cycling and pedestrian infrastructure (toll and free bike paths, number of bike parking lots, and length and illumination of footpaths, including in forest-park areas, flexibility of pedestrian areas to the needs of limited mobility populations groups).

The basic definition of a city friendly to older people (age-friendly city) as having an “inclusive and accessible environment (both physical and social) that optimizes opportunities for maintaining health ... and ensuring rightful life quality for people as they’re aging” [23] makes the indicators proposed under this concept noteworthy. This is, firstly, the accessibility of green spaces and public places adapted to the needs of the elderly (for example, enough “seating areas”), secondly, the availability of sidewalks that are safe for health of the elderly (wide, free from high curbs or other obstacles and road crossings), thirdly, the development of urban hygienic infrastructure (for example, access to public toilets), fourthly, the provision of elderly people with medical care [24].

Indicators related to city environment health-focus are used by the British Economist Intelligence Unit (EIU), which makes annual rating of cities in the world by Habitat Safety Index (“safe cities index”) [25]. For example, when calculating the index, safe and quality food available for citizens is taken into account. Moreover, the 2017 report points out serious problems of small North American cities, called “food deserts”, where locals have to eat fast food or low-quality stuff from small stores [26]. Also, when calculating the index, accessibility criteria of health facilities, atmospheric air and drinking

water quality, proportion of population living in slums, road and transport infrastructure quality, and development of pedestrian-friendly urban environment are used. The latter implies not just a hypothetical opportunity for a pedestrian to go through a certain route, but such a quality and level of comfort of pedestrian network that the preferred way to get around the city is not a personal or public transport, but a walk. This is facilitated by a high level of safety (separation from auto-road), road surface quality, greening of a territory in the direction of walking, etc. [27].

Another EIU compiled rating – the global cities "liveability" rating contains indicators related to health of permanent residents of a city and its guests, such as humidity and temperature rating, climate discomfort for travelers, accessibility of sports facilities, road network and public transport quality, availability of good quality housing [28].

The concept of "global cities" [29], even more focused on economic aspects of city life, in some methodologies takes into account urban environment quality, since it is a factor in attracting labor resources to a region. Thus, the Global Power City Index, developed by the Institute for Strategic Urban Development with the support of Mori Memorial Fund (Japan), includes such indicators as: viability of a city (average rent rate for housing, variety of retail stores and catering and others), environment (CO_2 emissions, density of sulfur dioxide and nitrogen dioxide, percentage of renewable energy, percentage of waste disposal, level of greening, comfortable temperature, etc.) and availability (punctuality and scope of public transport, deaths due to road traffic accidents) [30, 31]. Unlike most other approaches, the Global Power City Index takes into account also the subjective assessments – particular perceptions of urban space quality by residents [32].

Health oriented city space is taken into account in the concepts of sustainable cities ("sustainable city", "eco-city"), slow cities ("cittaslow"), cities with low carbon emissions ("zero-carbon city", "low carbon city") [33], cities without cars ("car-free city") [34] and garbage [35]. International Environmental City Standards developed by the experts of the British Columbia Institute of Technology and the American non-profit organization Ecocity Builders imply the achievement of certain levels in terms of indicators [36]:

- medial distance between housing, work and places for everyday goods and services purchases;
- functional qualities of construction materials in both residential and commercial buildings;
- environment friendly transport system (percentage of pedestrians, cyclists, public transport passengers and drivers of personal vehicles);
- air quality inside and outside premises;
- greenhouse gas emissions;
- quantity and quality of water supplies available;
- availability of healthy food (percentage of plant-based diet).

The approaches being developed in the Western Europe and North America aimed at minimizing anthropogenic pollution of urban environment and reducing its impact on health of residents cannot be directly transferred to the Russian practice of urban management due to significant differences in socio-economic, socio-cultural and climatic parameters of the countries

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[1]Passport of the priority project "Creation of comfortable urban environment" / Approved by Presidium of the Council on Strategic Development and Priority Projects under the President of the Russian Federation (Minutes No. 10 of November 21, 2016). Available at: http://static.government.ru/media/files/WoyaBZP00CYeyfDQ2Ai2tJ18zZHt7HnS.pdf (access date: 20.08.2018) Passport of the priority project "Creation of comfortable urban environment" / Approved by Presidium of the Council on Strategic Development and Priority Projects under the President of Russian Federation (Minutes No. 5 of April, 18, 2017). Available at: http://static.government.ru/media/files/JEnYAAfDkMAyyIAjsAxDzkxXGPuaEJSu.pdf (access date: 20.08.2018)

[2]On approval of the Method for determining Quality Index of urban environment for municipalities of the Russian Federation: Order of the Ministry of Construction of Russia No. 1494/pr of October 31, 2017. Available at: http://www.minstroyrf.ru/upload/iblock/ddc/prikaz-1494pr.pdf (access date: 20.08.2018)

[37]. As a result, certain developments in assessing the focus of urban space on preservation and strengthening health of citizens are proposed within the framework of national science and management practice.

So, in 2016, Russia adopted a priority project "Creation of comfortable urban environment"[1], aimed, inter alia, at reducing the incidence rate of the population in urban areas. The Russian Federation subjects are rated annually by the quality of urban environment assessed using the "quality index of urban environment for municipalities"[2]. The calculating method of this index involves characterization of six types of space (housing and adjacent areas, greenery and water spaces, street infrastructure, social leisure infrastructure and public business infrastructure and adjacent areas, citywide space) by 5 criteria (safety, comfort, environmental friendliness, identity and diversity, modernity of environment), each one represented by a certain indicator in accordance with the named types of space. The health of a city can be described, for example, through such indicators as share of public green areas (parks, gardens, etc.) in the area of all green spaces in general, pedestrian accessibility index, safety of movements near institutions of social services for citizens, accessibility of sports grounds for citizens, etc.

As part of "urban space quality" concept [38, 39] Ilyina I.N. identifies a number of parameters that can be attributed to the physical aspect of a health-oriented city space: health, safety, affordability of quality housing and services, accessibility to urban public recreation and open spaces, a variety of transport accessibility options, waste management, minimization of environmental pollution and this process management, adaptation to climate changes and natural disasters mitigation [40]. The urban environment quality is proposed to be assessed according to three classification blocks: quality of "framing" (basic) infrastructure of a city, quality of urban space, and safety and comfort of living, and availability of services for all socio-demographic categories of population.

A number of approaches emphasize the quality assessment of town-planning objects viability from the point of their socio-psychological successfulness. For example, criteria for analyzing planning decisions, divided into characteristics of socio-psychological safety and socio-psychological comfort, and satisfaction with living environment, can include the presence of identifiable boundaries of public and private space, residential areas planning following the "closed spaces" principle, possibility for visual viewing of a territory, yard areas arrangements, landscaping, sports grounds, level of provision with elements of social and engineering infrastructure, extending functions of structural components in residential environment, and others [41].

The considered approaches are complex, focused on ensuring the high quality of citizens' life and stable urban development. Preserving and strengthening urban population health is a more local task, the specific tools and developed systems of indicators are required to ensure effective management of citizen health. One of the solutions to this problem may be a system for assessing the degree of formation of a health-oriented city environment, following a risk-based approach.

The health of urban environment in the context of managing public health risks means that the physical space of a city is, firstly, focused on minimizing the impact of environmental and behavioral factors on citizens health, and secondly, increasing human body resilience, preventing "the root causes of poor health" [42], "the disease origins" [43]. For example, anti-noise screens on roads within the city limits or public places that are free from smoking allow you to ***keep*** residents ***healthy***, reducing the risks caused by acoustic and chemical pollution of environment. Outdoor exercise complexes or bicycle lanes are more aimed at ***improving*** citizens' health.

Since the structure of urban population morbidity and mortality has the signified country and regional peculiarities, the creation of a city's health-oriented space should be carried out taking into account the specific health aspects of a particular territory' inhabitants. Thus, the leading cause of urban population mortality in Russia are diseases of circulatory system (the share of this category causes in total citizens mortality in 2017, according to Rosstat, was 48%, including of ischemic heart disease which made up 26% of cases, of cerebrovascular disease: 15%). The contribution of this cause to mortality in the

largest cities of Russia is almost the same [44]. The controlled risk factors for circulatory diseases include unhealthy lifestyles (smoking, low levels of physical activity, malnutrition [45]), chemical pollution of natural environment (air and drinking water [46]), as well as socio-psychological factors (for instance, depression, various anxiety symptoms and disorders [47]). Malignant tumors are the second most common cause of death among urban population in Russia (16.9%), including malignant neoplasm of digestive organs: 6.4%, respiratory organs: 3%, female genital organs and mammary gland: 2 6%.

According to the US National Cancer Institute [48], the leading modifiable risk factors for cancer are anthropogenic pollution of environment with carcinogenic substances and low level of self-preserving behavior (alcohol abuse, smoking, improper diet, untimely access to a doctor). The main cause of morbidity among urban population in Russia is respiratory disease. So, in 2016, the prevalence of acute upper respiratory tract infections, per 100 thousand city dwellers, was 25251.6[3] cases [49]. The leading risk factors for development of respiratory diseases in modern cities are chemical pollution of atmospheric air [50], living conditions quality, and also smoking [51].

Hence, developing a modern Russian city as a health-oriented one implies a targeted activity of municipal authorities and local communities towards creating such a body-space environment, which will, first of all, reduce the level of effects on citizen health from environment chemical pollution, and provide conditions for an adequate level of physical activity and healthy diet.

To assess the degree of health-oriented city space formation in practice it is proposed to use a system of indicators (Table). This assessment can be done within the framework of monitoring the quality of urban living environment, socio-hygienic monitoring and the system for monitoring risk factors for non-communicable diseases provided for in the draft Strategy for Formation of a Healthy Lifestyle of Population, Prevention and Control of Non-Communicable Diseases for the period up to 2025 developed by the Russian Federation Ministry of Health [52].

Developing a city as a health-oriented one involves not only the definition of indicators for physical space formation degree that contributes to health preservation and strengthening, but also to establishment of their target values, which should be a guideline for implementation of effective territorial management tasks. One of the approaches may be to choose target parameters in the "healthiest" cities in the world. For example, according to the World Cities Culture Report prepared by BOP Consulting Editorial Team in 2015, the share of public green areas in Sydney (Australia) and Vienna (Austria) made 46%, in Shenzhen (China): 45% [53].

In Russia, today, the system of regulations has partially developed in the formation of health-oriented space of a city (see Table). For example, Code 42.13330.2016 "Urban planning. Planning and Development of Urban and Rural Settlements. The updated version of SNiP 2.07.01-89"[4] defines green area of a microdistrict (a quarter) for residential area multidwelling development at the level of at least 25% of a quarter's area. In addition, it indicates the need for landscaping at least 50% of yard areas with trees and shrubs. In March 2018, the Ministry of Sports of Russia approved the criteria for the minimum allowable provision level with sports facilities based on the indicator "one-time capacity of a sports facility" of 122 persons per 1,000 of population. This indicator was calculated on the basis of the set strategic goal for physical culture and sports development in Russia – attracting the entire working-age population (under 79 years old) and children (aged from 3 years) to regular (3 hours per week) physical culture and sports activities by 2030.

In some regions and cities of Russia (Ulyanovsk Region, Tver, Omsk), the concepts and development programs for cycling, bike transport and bike-cycling infrastructures, including separate target indicators, have been

[3] Health care in Russia. 2017 / Stat. Sat Rosstat. Moscow, 2017, 170 p.

[4] Code 42.13330.2016 Urban planning. Planning and Development of Urban and Rural Settlements. Updated version of SNiP 2.07.01-89. *Code: electronic fund of legal and regulatory and technical documentation.* Available at: http://docs.cntd.ru/document/456054209 (access date: 20.08.2018)

Table

Indicators for the formation degree of health-oriented city space

No	Risk factors for urban population health	Characteristics of urban space	Indicator
1	Atmospheric air chemical pollution	Green spaces areas	– Green spaces area of public use, per inhabitant (m^2) – Level of green spaces in housing development areas (%) – Environmental stability factor
		Formation degree of alternative transport infrastructure	– Share of roads equipped with dedicated lanes for public transport in the total length of local roads (%) – Ratio of the length of roads equipped with lanes for cyclists to the total length of local roads – Number of public bicycle parking places, per 1 inhabitant – Number of parking spaces in the adjacent bicycle parking, per 1 resident
2	Drinking water chemical contamination	Compliance of drinking water supply sources with sanitary and epidemiological requirements	Share of surface sources for centralized drinking water supply having no sanitary protection zone (%)
		Quality of water supply and distribution network	– Share of water pipes provided with water purification and disinfection treatment (%) – Share of sewer networks requiring replacement (%) – Share of treatment facilities requiring capital repairs (%) – Share of sewage treatment facilities equipped with wastewater sludge treatment (%)
3	Sedentary lifestyle	Formation degree of infrastructure for physical culture and sports	– Number of sports facilities of various types, per 100 thousand people – One-time capacity of sports facilities of various types, per 10 thousand people
4	Improper diet	Formation degree of healthy nutrition infrastructure	– Provision of spaces for retail and catering, per 1,000 people – Number of public catering enterprises providing social catering services

approved. However, the values and indicators proposed in the context of national regulatory documents cannot be considered as targets in the long term, since they are aimed at ensuring a minimum level of health-oriented city.

In general, the urgent task is to strengthen the development focus of Russian cities on preserving and strengthening the citizen health, on integrating the decisions on green areas arrangement into the system of priority actions, creating a healthy nutrition infrastructure and physical activity for all categories of citizens, and ensuring a safe environment. A considerable problem here is the lack of criteria worked out for the formation of a health-oriented city environment, and their low integration into performance indicators of municipal programs. The synthesis and discussion of the best practices for

organizing various components of health-oriented city environment both in Russia and abroad is of relevance.

The health-focus of a modern city space is not just a way to improve people's living conditions quality, but a key to a successful socio-economic development of a city, a way to accumulate its human potential. Solving the problem of developing a health-oriented city environment requires the consolidated actions of municipal authorities, expert community, business entities, public organizations and population. In addition, the ability of urban space to provide opportunities for preserving and strengthening citizens' health means, it's formed not only at the physical, but also at the social and symbolic levels, i.e. integrated development.

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References

1. Eckert S., Kohler S. Urbanization and health in developing countries: a systematic review. *World Health & Population*, 2014, vol. 15, no. 1, pp. 7–20. DOI: 10.12927/whp.2014.23722

2. Welle B., Li W., Adriazola C., King R., Obelheiro M., Sarmiento C., Liu Q. Cities Safer by Design. Urban Design Recommendations for Healthier Cities, Fewer Traffic Fatalities. *World Resources Institute*, 2015. Available at: http: //www.wri.org/publication/cities-safer-design (20.08.2018).

3. Christiani Y., Byles J.E., Tavener M., Dugdale P. Do women in major cities experience better health? A comparison of chronic conditions and their risk factors between women living in major cities and other cities in Indonesia. *Global Health Action*, 2015, vol. 8, no. 1, pp. 1–9. DOI: 10.3402/gha.v8.28540

4. Mozaffarian D., Hao T., Rimm E.B., Willett W.C., Hu F.B. Changes in diet and lifestyle and long-term weight gain in women and men. *The New England Journal of Medicine*, 2011, vol. 364, pp. 2392–2404. DOI: 10.1056/NEJMoa1014296

5. Rocha L.E., Thorson A.E., Lambiotte R. The Non-linear Health Consequences of Living in Larger Cities. *Journal of Urban Health*, 2015, vol. 92, no. 5, pp. 785–799. DOI: 10.1007/s11524-015-9976-x

6. Healthy Cities Vision. *World Health Organization*. Available at: http: //www.euro.who.int/en/health-topics/envionment-and-health/urban-health/who-european-healthy-cities-network/healthy-cities-vision (20.08.2018).

7. Sklyarova E.K. Edvin Chedvik: preventivnaya ideya i obshchestvennoe zdravookhranenie [Edwin Chadwick: preventive idea and public health]. *Gumanitarnye i sotsial'nye nauki*, 2010, no. 2, pp. 50–57 (in Russian).

8. Booth C. Life and labour of the people in London. Available at: https://archive.org/details/lifeandlabourpe02bootgoog (20.08.2018).

9. Balch E.G. Review: Hull House Maps and Papers: A Presentation of Nationalities and Wages in a Congested District of Chicago, Together with Comments and Essays on Problems Growing Out of the Social Conditions. *Publications of the American Statistical Association*, 1895, vol. 4, no. 30, pp. 201–203. DOI: 10.2307/2276290

10. Richardson B.W. Modern sanitary science – a city of health. *Van Nostrand's Eclectic Engineering Magazine*, 1876, no. 14, pp. 31–42. Reprinted from *Nature*, 1875, no. 12, pp. 523–525. Available at: http: //urbanplanning.library.cornell.edu/DOCS/rich'son.htm (20.08.2018)

11. The Garden City: Past, present and future. Ed. by S.V. Ward. London, 2005, 240 p.

12. Wilson W.H. The City Beautiful Movement. Baltimore, The Johns Hopkins University Press, 1989, 365 p.

13. Wade L.C. Settlement Houses. *Encyclopedia of Chicago. Chicago Historical Society*, 2004. Available at: http: //www.encyclopedia.chicagohistory.org/pages/1135.html (20.08.2018).

14. Hancock T., Duhl L. Promoting Health in the Urban Context. WHO Healthy Cities Papers No. 1. Copenhagen, Denmark, FADL Publishers, 1988, 54 p.

15. Diez Roux A.V. Health in cities: is a systems approach needed? *Cadernos de SaúdePública*, 2015, vol. 31, no. 1. Available at: http: //www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2015001300009 (20.08.2018).

16. Zaborova E.N., Islamova A.F. Gorod kak sotsial'noe prostranstvo [The city as a social space]. *Sotsiologicheskie issledovaniya*, 2013, no. 2, pp. 97–100 (in Russian).

17. Lindström B., Eriksson M. Salutogenesis. *Journal of Epidemiology & Community Health*, 2005, vol. 59, no. 5, pp. 440–442. DOI: 10.1136/jech.2005.034777

18. Mikhailov S.M., Mikhailova A.S., Nadyrshin N.M. Dizain goroda: osnovnye etapy istoricheskogo razvitiya [City design: milestones of historical development]. *Vestnik Orenburgskogo gosudarstvennogo universiteta*, 2014, vol. 166, no. 5, pp. 4–9 (in Russian).

19. Bourdieu P. Sotsiologiya politiki [Sociology of Politics]. Moscow, Sotsio-logos, 1993, 336 p. (in Russian).

20. Frolov A.V., Sukhodol'skaya N.P. K fenomenologii gorodskogo prostranstva [Towards a phenomenology of city space]. *Vestnik MGSU*, 2010, vol. 3, pp. 394–399 (in Russian).

21. Bell S.L., Foley R., Houghton F., Maddrell A., Williams A.M. From therapeutic landscapes to healthy spaces, places and practices: A scoping review. *Social Science and Medicine*, 2018, vol. 196, pp. 123–130. DOI: 10.1016/j.socscimed.2017.11.035

22. Edwards P., Tsouros A.D. A healthy city is an active city: a physical activity planning guide. WHO Regional Office for Europe, 2008. Available at: http: //www.euro.who.int/document/E91883.pdf (20.08.2018)

23. Kano M., Rosenberg P.E., Dalton S.D. A Global Pilot Study of Age-Friendly City Indicators. *Social Indicators Research*, 2018, vol. 138, no. 3, pp. 1205–1227. DOI: doi.org/10.1007/s11205-017-1680-7

24. Global Age-friendly Cities: a Guide Global Age-Friendly Cities: a guide. France, WHO, 2007. Available at: http: //www.who.int/ageing/publications/Global_age_friendly_cities_Guide_English.pdf (20.08.2018)

25. Safe Cities Index Interactive Tool. 2017. Available at: http: //safecities.economist.com/safe-cities-index-2017-interactive-tool (20.08.2018).

26. Safe cities index 2017: security in a rapidly urbanizing world. A report from The Economist Intelligence Unit. 2017. Available at: https: //dkf1ato8y5dsg.cloudfront.net/uploads/5/82/safe-cities-index-eng-web.pdf (20.08.2018).

27. Shamsuddin S., Abu Hassan N.R., Bilyamin S.F.I. Walkable Environment in Increasing the Liveability of a City. *Procedia - Social and Behavioral Sciences*, 2012, vol. 50, pp. 167–178. DOI: 10.1016/j.sbspro.2012.08.025

28. The Global Liveability Index 2018. A free overview. A report by The Economist Intelligence Unit. 2018. Available at: http: //www.eiu.com/public/thankyou_download.aspx?activity=download&campaignid=Liveability2018 (20.08.2018).

29. Sassen S. The Global City: New York, London, Tokyo. Princeton: Princeton University Press, 1st ed., 1991, 416 p.

30. Global Power City Index 2017. Summary. Institute for Urban Strategies, The Mori Memorial Foundation. 2017. Available at: http: //mori-m-foundation.or.jp/pdf/GPCI2017_en.pdf (20.08.2018).

31. Ichikawa H., Yamato N., Dustan P. Competitiveness of global cities from the perspective the Global Power City Index. *Procedia Engineering*, 2017, vol. 198, pp. 736–742. DOI: 10.1016/j.proeng.2017.07.125

32. Aleksandrova A.Yu. Reitingi global'nykh gorodov mira kak turistskikh destinatsii i mesto v nikh Moskvy [Ranking of world global cities as tourist destinations and Moscow particular position]. *Regional'nye issledovaniya*, 2014, no. 3, pp. 122–130 (in Russian).

33. Theme Cities: Solutions for Urban Problems. Ed. by W.K.D. Davies. London, Springer (GeoJournal Library No. 112), 2015, 615 p.

34. Crawford J.H. Carfree Design Manual. International Books, 2009, 600 p.

35. Global Principles For Zero Waste Communities. *Zero Waste International Alliance:* the official website. Available at: http: //zwia.org/standards/zw-community-principles/#ref3 (20.08.2018).

36. Ecocity Focus Lab: Final Report Bcit Downtown Campus, 2016. Available at: http: //www.ecocitystandards.org/ecocity-standards-headline-indicators/ (20.08.2018).

37. Voloshinskaya A.A., Komarov V.M. Kontseptsii ekogoroda: rekomendatsii dlya Rossii [Ecocity concepts: recommendations for Russia]. *Terra economicus*, 2017, vol. 15, no. 4, pp. 92–108 (in Russian).

38. Kyvelou S., Filho W.L., Sustainable management and urban space quality in the Mediterranean: Challenges and perspectives. *Management of Environmental Quality: An International Journal*, 2006, vol. 17, no. 5, pp. 611–624. DOI: 10.1108/14777830610684576

39. Adams M. Quality of Urban Spaces and Wellbeing. Eds by R. Cooper, E. Burton, C.L. Cooper. Wellbeing, A Complete Reference Guide, vol. II, Wellbeing and the Environment. Wiley-Blackwell, 2014, 736 p. Available at: https: //onlinelibrary.wiley.com/doi/pdf/10.1002/9781118539415.wbwell064 (20.08.2018).

40. Ilina I.N. Kachestvo gorodskoi sredy kak faktor ustoichivogo razvitiya munitsipal'nykh obrazovanii [Quality of the urban environment as a factor of sustainable development of municipalities].*Imushchestvennye otnosheniya v Rossiiskoi Federatsii*, 2015, no. 5, pp. 69–82 (in Russian).

41. Pulyaevskaya O.V. Metody sotsial'no-psikhologicheskoi otsenki zhilykh kvartalov istoricheskoi zastroiki [Methods of socio-psychological evaluation of historical residential quarters]. *Vestnik IrGTU*, 2014, vol. 95, no. 12, pp. 128–134 (in Russian).

42. What is health promotion? *World Health Organization*. Available at: http: //www.who.int/features/qa/health-promotion/en/ (20.08.2018).

43. Link B.G., Phelan J. Social conditions as fundamental causes of disease. *Journal of Health and Social Behavior*, 1995, Extra Issue, pp. 80–94.

44. Shartova N.V., Vatlina T.V. Smertnost' gorodskogo naseleniya v Rossii: sovremennoe sostoyanie i regional'nye razlichiya [Mortality of urban population in Russia: current state and regional differences]. *Vestnik Moskovskogo gosudarstvennogo oblastnogo universiteta. Seriya: Estestvennye nauk*, 2018, no 1, pp. 66–76 (in Russian).

45. Maksimova T.M., Belov V.B., Lushkina N.P. Rasprostranennost' povedencheskikh faktorov riska i boleznei sistemy krovoobrashcheniya [The prevalence of behavioral risk factors and diseases of the circulatory system]. *Problemy sotsial'noi gigieny, zdravookhraneniya i istorii meditsiny*, 2014, no. 1, pp. 3–7 (in Russian).

46. Artamonova G.V., Shapovalova E.B., Maksimov S.A., Skripchenko A.E., Ogarkov M.Yu. Okruzhayushchaya sreda kak faktor riska razvitiya ishemicheskoi bolezni serdtsa v urbanizirovannom regione s razvitoi khimicheskoi promyshlennost'yu [Environment as a risk factor for the development of coronary heart disease in an urbanized region with a developed chemical industry]. *Kardiologiya*, 2012, vol. 52, no. 10, pp. 86–90 (in Russian).

47. Pogosova G.V. Depressiya – faktor riska razvitiya ishemicheskoi bolezni serdtsa i prediktor koronarnoi smerti: 10 let nauchnogo poiska [Depression as a risk factor for the development of coronary heart disease and a predictor of coronary death: 10 years of scientific research]. *Kardiologiya*, 2012, vol. 52, no. 12, pp. 4–11 (in Russian).

48. Risk Factors for Cancer. *National Cancer Institute (USA)*. Available at: https: //www.cancer.gov/about-cancer/causes-prevention/risk (20.08.2018)

49. Zaytseva N.V., Ustinova O.Yu., Zemlyanova M.A., Maklakova O.A. Nauchno-metodicheskie podkhody k obosnovaniyu i organizatsii profilakticheskoi pomoshchi detyam s zabolevaniyami organov dykhaniya, assotsiirovannymi s vozdeistviem khimicheskikh faktorov sredy obitaniya [Scientific and methodical approaches to the justification and organization of preventive care for children with respiratory diseases associated with exposure to chemical environmental factors]. *Gigiena i sanitariya*, 2014, vol. 93, no. 6, pp. 104–107 (in Russian).

50. Bilichenko T.N., Bystritskaya E.V., Chuchalin A.G., Belevskii A.S., Batyn S.Z. Smertnost' ot boleznei organov dykhaniya v 2014-2015 godakh i puti ee snizheniya [Death rate from respiratory diseases in 2014-2015 and ways to reduce it]. *Pul'monologiya*, 2016, vol. 26, no. 4, pp. 389–397 (in Russian).

51. Proekt Strategii formirovaniya zdorovogo obraza zhizni naseleniya, profilaktiki i kontrolya neinfektsionnykh zabolevanii na period do 2025 goda [Draft Strategy for Healthy Living, Prevention and Control of Noncommunicable Diseases for the period up to 2025]. *Federal State Institution "National Medical Research*

Center for Preventive Medicine" of the Ministry of Healthcare of the Russian Federation: *The official website*. Available at: https: //www.gnicpm.ru/UserFiles/stragedy_project_fin_2512.pdf (20.08.2018) (in Russian).

52. World Cities Culture Report 2015. *World Cities Culture Forum.* Available at: http: //www.worldcitiesscultureforum.com/publications/world-cities-culture-report-2015 (20.08.2018).

Prokofyeva A.V., Lebedeva-Nesevrya N.A. Creation of health-oriented city space as a way to manage population health risk. Health Risk Analysis, 2018, no. 3, pp. 144–155. DOI: 10.21668/health.risk/2018.3.16.eng

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SOCIAL CAPITAL AS A FACTOR THAT CONTRIBUTES INTO POPULATION HEALTH: ANALYTICAL REVIEW

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The paper contains a review of both domestic and foreign scientific works that focus on influence exerted by social capital on population health. The authors describe different approaches to interpretations of social capital as an attribute of an individual or a social group. At an individual level, different types of social capital are shown to influence a person's health via his or her involvement into a social group; this social group minimizes adverse effects produced by stress factors (a case in which we can speak about a social capital that "unites") and provides resources necessary to solve health-related problems (here we speak about a social capital that "brings us together"). The authors highlight that social capital and a social status which an individual or a social group has are interdependent.

At a group level, social capital is a mechanism that influences an individual's behavior as regards his or her health. A group can set certain models for health-preserving behavior and apply informal sanctions in case an individual's behavior is deviant thus reducing health risks. The authors also showed that health-related information tended to spread faster among those groups in which social capital was quite high. At a country level, social capital makes citizens to actively solve health-related problems and, consequently, determines activities performed by the state and aimed at providing citizens' safety and well-being. The authors also give special attention to a negative effect produced by group social capital, namely spread of risky behavioral practices within "poorly developed" social groups.

The paper gives two viewpoints on contributions made by individual and group social capital into formation of health. The first one states that direct contacts are more important for an individual than his or her civic stand as the latter depends on a personal psychological type. The second viewpoint is that individual social capital can be a significant health factor only when it is included into a group with high social capital. The authors think it is very important to understand how significant social capital is for determining health as such understanding will help to develop new approaches to creation of conditions that are favorable for preservation of citizens' health.

Key words: *social capital, social risk factors, social determinants, social networks, health.*

In 2015 the UN member states adopted Sustainable Development goals that were to be achieved by 2030; these goals are in many ways related to population health and most of them are aimed at resisting social factors that cause health risks. If they are achieved, it will lead to a decrease in a number of people who have low social status that means unfavorable living conditions, limited access to healthy nutrition and drinking water; it will help to raise adherence to a healthy lifestyle and rational consumption and to develop infrastructure for physical training and recreation etc. [1]. The WHO experts spoke about the significance of social factors for human health on the World Conference on Social Determinants of Health held in 2011. They highlighted the necessity to improve conditions of people's everyday life and to provide equal access to health-preserving resources for everybody [2].

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Experts have been discussing a leading role that belongs to socioeconomic (low income and poor education) and behavioral (smoking, alcohol abuse, poor physical activity, improper nutrition, and unsafe sexual behavior) factors in determination of an individual's health since 70ties last century; these discussions can be found in scientific works that have been published starting from that period of time [3–8]. Besides, they have repeatedly mentioned a role played by macrosocial contexts (technological development of a country, its political regime, migration intensity etc.) in formation of socially determined etiologies [9, 10]. A new concept, "social capital", appeared and was integrated in the discourse on social determination of health in late 1990s. On one hand, it can be explained by popularization of social capital theory in works by J.S. Coleman [11] and R.D. Putnam [12] published at that time. On the other hand, there was a necessity for public healthcare systems in the developed countries to search for new solutions to challenges associated with inequality in the healthcare.

In spite of almost 30 years devoted to research on a correlation between social capital and health, the issue is still being discussed due to the fact that there is no unified view on the essence and structural components of social capital. It is primarily related to its interpretation either as an individual's attribute (this approach was first formulated in works by P. Bourdieu [13]) or as an attribute of a social group (interpretation by R.D. Putnam [14]).

Individual social capital is an ability of a person to benefit from his or her affiliation with various social networks [15]. Individuals are assumed to "invest" into social networks in order to gain "a return in a form of instrumental acts" [16]. Relations between those who participate in social relations are converted into various resources (money, reputation, power, information etc.), and in case of necessity individuals, via their strong or weak connections in various social networks, are able to either mobilize these resources available to them in social networks [17], or use their own resources more efficiently with the help of their social connections [18]. A size of individual social capital is determined by an individual's social status, his or her position in a social network and a purpose of an interaction (instrumental or expressive one) [19]; and possibilities to accumulate this capital depend on interiorized standards, strong social unity, or its orientation at reciprocity [15].

Social capital as an attribute of a group or a society as a whole means that if a society (existing on a specific territory, in region or a country) has high collective social capital, then even individuals with low individual social capital can somehow benefit from it (they are also "beneficiaries") [20]. Social capital at a group level has two dimensions, a structural one (social networks that are formalized to a various extent), and a cultural one (common standards that are shared by all members of a social network and that secure trust existing between interaction participants) [21]. Standards created within a group (including reciprocity) are generalized and then applied to a society as a whole thus making it more united and raising its solidarity [14]. Trust is a significant measure of social capital at a society level; here we mean generalized interpersonal trust ("people in general") and institutional one [22]. Results of trust measuring gave grounds for a significant number of empirical research on social capital [23–26].

And how is social capital related to individual and public health? We can offer several explanations at an individual level. First of all, if a person is involved into social networks (family, friends, occupational and confessional ones, etc.), it provides him or her with various social support (emotional, instrumental, evaluative, and informative one) [27]. This support can be a "buffer" that minimizes adverse effects produced by stress factors [28]. An action mechanism of such a "buffer" is "reevaluation" of stress, a decrease in a stress factor significance, wider range of possible ways to solve a problem, stronger coping strategies, changes in individual's moods, etc. [29, 30]. A classic "Roseto effect" can be found exactly in high intra-group support; this effect explained significantly lower mortality caused by cardiovascular diseases in Roseto, an American-Italian town (Pennsylvania, the USA), in comparison with its neighbor town Bangor in 1935-1965 [31]. Secondly, involvement into social networks gives an individual a possibility to use material and organizational resources available in this or that network [32]. We can illustrate it with an example of individuals resorting to

"social relations chains" in case of health problems [33] when they try to find better medical experts; it often happened in the USSR and still happens now. The third explanation is related to interdependence between social capital and an individual's social status where having the former leads to an increase in the latter which, in its turn, means an access to qualitative nutrition, sport and recreational infrastructure, safe housing, and qualified medical services [34]. Besides, high social status creates a "positive feeling of being a select one" and leads to a decrease in stress [35].

High individual social capital is often combined with high socioeconomic status and health [36] and it is explained with such mediator categories as "healthy lifestyle" and "self-preserving behavior". Thus, research conducted in the UK and Sweden revealed that individuals with high socioeconomic status and "strong" social capital tended to consume healthy nutrition that included a lot of fruit and vegetables [37, 38]. There are some works that dwell on the analysis of correlation between neighborhood socioeconomic status, social capital, and health: their authors conclude that people who live in wealthy neighborhood and who obviously already have a certain social status also enjoy a better opportunity to invest into social networks development [39]. "Wealthy" districts are safer and, consequently, people who live there (especially children and elderly people) can meet each other more frequently and do things together; therefore, they have better opportunity to accumulate social capital and to use it to improve their health [40]. At the same time, research that focused on poor districts revealed that people who lived there could also be involved into social networks with great trust between participants, unity, and readiness to provide mutual support, that is, they could also have certain social capital in spite of their low socioeconomic status [41].

Various types of individual social capital are not equally involved into producing effects on health. As social capital at an individual level reflects a person's involvement into social networks, it is usually divided into "bonding" capital that describes relations between close relatives and friends, "bridging" capital that describes networks with weaker relations (colleagues or neighbors) [42], and "linking" capital [43] that describes vertical connections between people from various social strata. If a person has bonding social capital, it helps to get social support, while "bridging" or "linking" capital provide access to information or organizational resources.

If we consider social capital as a collective attribute, we can spot out two ways in which it can influence health. The first one is related to impacts exerted by social groups on individual health-related behavior. Such groups possess clear and shared standards for reciprocity (mutual support) and high level of trust; they set (or even dictate) certain behavioral standards and models to their members, including those related to health. A lot of empirical research performed by I. Kawachi, a professor at Harvard University, revealed that people who lived in local "neighborhoods" with strong social integration were more inclined to adhere to standards of self-preserving behavior declared by society leaders and approved by society members; in particular, they tended to more willingly attend their doctors bearing prevention in mind, and they more frequently went to parks and public gardens to relax [44]. Besides, strong group unity allows to apply informal sanctions efficiently in cases when group members pursue deviant behavioral patterns [45], thus lowering both individual and social health risks. Finally, if a group has high social capital, health-related information spreads faster within it, for example, information about environmental contamination hazards, new opportunities and innovations in the sphere of health preservation and improvement etc.

It is important to note that social capital has its negative effects; for example, they become apparent in groups with strong unity and adverse group standards (that contradict conventional ones). Risky behavioral practices (smoking, alcohol abuse, and unsafe sex) can be spread in such communities with the help of pressure exerted by a group and a certain lifestyle can be imposed upon its members [46].

The second way in which group social capital can influence health is related to civil involvement that is often called a social capital indicator [47, 48]. Groups with higher social capital are more likely to be socially active and

ready to get themselves involved into decision-making processes in the health sphere. They are also more likely to show initiative, to participate in local projects aimed at preservation and improvement of health in a community [49]. At a country level, this correlation becomes apparent via a developed system of social control and public management [50]: the higher interpersonal trust and social solidarity in a society is, the more efficient institutions of social control are, and, consequently, the more socially-oriented is a state that provides better safety and welfare for its citizens.

Social capital at a community level is usually divided into a structural one that reflects a variety of social connections and interactions, and a cognitive one that describes a quality of these connections with a level of trust and "social harmony" [51] that means being ready to provide support and share resources [52]. There was a research based on data provided by the European Social Survey performed in 2008-2009; the research focused on health of people living in 28 European countries and levels of their structural and cognitive social capital. The research revealed that in postmodern countries trust exerted great influence on public health while in less developed ones systematic contacts with close friends and relatives had greater significance. It is explained by the fact that in postmodern countries active social policy is combined with developed public structures; therefore, people don't tend to seek support only among their closest friend and relatives, and, on the contrary, given high level of trust in a society, try to enter various associations and groups that consequently helps them improve their health [53].

A matter of principle here is a type of social capital that exerts the greatest influence on health. In 2013 experts from the National Scientific Research Institute for Public Health of the Russian Academy of Medical Sciences described a correlation between health and social capital as per data obtained in the course of research on global aging and health of the population in the RF over 2007-2010 (the sampling included 4,335 people) [54]. Health was self-estimated as per a 5-score scale which then was grouped into three categories: "very good and good", "satisfactory", and "bad and very bad". Social capital was measured via interpersonal trust and social activity. Parameters obtained for different social-demographic groups were compared. Validity of discrepancies was estimated with Student's t-test. It was detected that a level of generalized trust influenced a sense of security an individual had and self-estimation of his or her health; the same is true for interpersonal trust, and if an individual doesn't have anyone whom he or she trusts unreservedly among his or her family or close friends, there is a greater probability that he or she will estimate his or her health as being bad. Finally the authors came to a conclusion that direct contacts had greater significance for an individual's health than the overall atmosphere in the society and participation in public organizations since the latter to a great extent depends on a personal psychotype.

In 2015 experts performed comparative research on influence exerted by cognitive social capital on self-estimation of a person's health and probability of depression in men and women in Sweden and Ukraine. The research revealed that there was a more apparent correlation between cognitive social capital and self-estimation of one's health in Sweden, moreover, a level of capital was also higher in that country [55]. Experts detected a statistically significant relationship between self-estimation of one's health and a level of institutional trust, as well as between probability of depression and not feeling sufficiently safe; the relationship was detected both for men and women in Sweden while in Ukraine it was true only for women.

British experts showed in their research that when both types of social capital, individual and collective ones, were simultaneously included into an analysis, it didn't exert any significant influence on health [37], while data obtained by Norwegian experts revealed that social capital was equally significant both at individual and collective level [56]. The Report issued by the WHO European Regional Agency and based on the analysis of data obtained in the course of the European Social Survey conducted in 2002 and 2004 in 21 country contains a conclusion that individual social capital can be a significant factor that influences an individual's health only when this individual is involved into social groups with high collective social capital [57].

Conclusion. Application of social capital category to analyze ways of preserving and improving population health in the contemporary world can yield good results. There are certain ways to improve health of people living on this or that territory via accumulation of social capital; they include development of local communities, an increase in their social activity and involvement into finding solutions to local problems, assistance to non-commercial organizations and involvement of representatives from different social groups into their activities.

Risk-communications in health sphere can be made more efficient and important information can be spread faster due to implementation of activities aimed at enhancing social connections between neighbors or employees of the same organization.

A better insight into a contribution made by collective social capital into determination of health calls for new approaches to development of modern cities where unavoidable processes of individuals' atomization should be slowed down by creating conditions for "strong communities" able to build up an environment that is the most favorable for preservation of citizens' health.

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References

1. Tseli v oblasti ustoichivogo razvitiya [Goals in the field of sustainable development]. *Official website of the United Nations*. Available at: https://www.un.org/sustainabledevelopment/ru/sustainable-development-goals/ (06.09.2018) (in Russian).

2. Sotsial'nye determinanty zdorov'ya: itogi Vsemirnoi konferentsii po sotsial'nym determinantam zdorov'ya (Rio-de-Zhaneiro, Braziliya, 2011 g.): doklad sekretariata [The social determinants of health: the outcome of the World Conference on Social Determinants of Health]. *World Health Organization*, 2011, 20 p. Available at: http://apps.who.int/gb/ebwha/pdf_files/EB130/B130_15-ru.pdf?ua=1 (09.09.2018) (in Russian).

3. Marmot M.G., Rose G., Shipley M., Hamilton P.J. Employment grade and coronary heart disease in British civil servants. *Journal of epidemiology and community health*, 1978, vol. 32, no. 4, pp. 244–249.

4. Whitehead M. Inequalities in health: the black report and the health divide. London, Penguin Books, 1992, 464 p.

5. Adler N.E., Stewart J. Preface to the biology of disadvantage: socioeconomic status and health. *Annals of New York academy of sciences*, 2010, vol. 1186, pp. 5–23. DOI: 10.1111/j.1749-6632.2009.05337.x

6. Allen J., Balfour R., Bell R., Marmot M. Social determinants of mental health. *International review of psychiatry*, 2014, vol. 26, no. 4, pp. 392–407. DOI: 10.3109/09540261.2014.928270

7. Braveman P., Gottlieb L. The social determinants of health: it's time to consider the causes of the causes. *Public health reports*, 2014, vol. 129, no. 2, pp. 19–31. DOI: 10.1177/00333549141291S206

8. Lisitsyn Yu.P., Zhuravleva T.V., Khmel' A.A. Iz istorii izucheniya vliyaniya obraza zhizni na zdorov'e [From the history of studying the impact of style of life on health]. *Problemy sotsial'noi gigieny, zdravookhraneniya i istorii meditsiny*, 2014, vol. 22, no. 2, pp. 39–42 (in Russian).

9. Galea S. Macrosocial determinants of population health. New York, Springer Publishing Company, 2007, 502 p. DOI: 10.1007/978-0-387-70812-6

10. Stuckler D. Population causes and consequences of leading chronic diseases: a comparative analysis of prevailing explanations. *The Milbank quarterly*, 2008, vol. 86, no. 2, pp. 273–326. DOI: 10.1111/j.1468-0009.2008.00522.x

11. Coleman J.S. Social capital in the creation of human capital. *American journal of sociology. Supplement: Organizations and institutions: sociological and economic approaches to the analysis of social structure*, 1988, vol. 94, pp. S95–S120.

12. Putnam R.D. Bowling alone: America's declining social capital. *Journal of democracy*, 1995, vol. 6, no. 1, pp. 65–78. DOI: 10.1353/jod.1995.0002/

13. Bourdieu P. The forms of capital. Handbook of theory and research for the sociology of education. In: J.G. Richardson ed. New York, Greenwood Publ., 1986, pp. 241–258.

14. Putnam R.D., Leonardi R., Nanetti R. Making democracy work: civic traditions in modern Italy. Princeton, Princeton University Press Publ., 1993, 280 p.

15. Portes A. Social capital: its origins and applications in modern sociology. *Annual review of sociology*, 1998, no. 24, pp. 1–24. DOI: 10.1146/annurev.soc.24.1.1

16. Lin N. Building a network theory of social capital. *Connections INSNA*, 1999, vol. 22, no. 1, pp. 28–51.

17. Gudkova T.V. Sotsial'nyi kapital kak faktor sotsiokul'turnogo i ekonomicheskogo razvitiya obshchestva [Social capital as a factor of socio-cultural and economic development of society]. *Filosofiya khozyaistva*, 2015, no. 2, pp. 197–204 (in Russian).

18. Tikhonova N.E. Sotsial'nyi kapital kak faktor neravenstva [Social capital as a factor of inequality]. *Obshchestvennye nauki i sovremennost'*, 2004, no. 4, pp. 24–35 (in Russian).

19. Lin N. Social capital: a theory of structure and action. New York: Cambridge University Press, 2001, 294 p. DOI: 10.1017/CBO9780511815447

20. Putnam R.D. Bowling alone: the collapse and revival of American community. New York: Simon and Schuster, 2000, 541 p.

21. Block M., Golovin N.A. Sotsial'nyy kapital: k obobshcheniyu ponyatiya [Social capital: the generalization of the concept]. *Vestnik Sankt-Peterburgskogo universiteta. Seriya 12: Psikhologiya. Sotsiologiya. Pedagogika*, 2015, no. 4, pp. 99–111 (in Russian).

22. Fukuyama F. Velikii razryv [Great Gap]. In: A.V. Aleksandrova ed. Moscow, Izd-vo ACT Publ., 2004, 474 p. (in Russian).

23. Bykov I.A. Sotsial'nyy kapital i politika v Rossii: portret na fone Yevropy [Social capital and politics in Russia: a portrait against the backdrop of Europe]. *Politicheskaya ekspertiza*, 2011, no. 1, pp. 102–116 (in Russian).

24. Kozyreva P.M. Mezhlichnostnoye doveriye v kontekste formirovaniya sotsial'nogo kapitala [Interpersonal trust in the context of the formation of social capital]. *Sotsiologicheskiye issledovaniya*, 2009, vol. 297, no. 1, pp. 43–54 (in Russian).

25. Latov Yu. Kakov sotsial'nyy kapital sovremennoy Rossii? (sravnitel'nyy analiz mezhlichnostnogo i institutsional'nogo doveriya) [What is the social capital of modern Russia? (comparative analysis of interpersonal and institutional trust)]. *Leont'yevskiye chteniya: Elektronnyy zhurnal*, 2010, no. 7, pp. 216–230. Available at: http://uisrussia.msu.ru/docs/ nov/leontief /2010/Latov.pdf (09.09.2018) (in Russian).

26. Stebakov A.A. Metody izmereniya urovnya sotsial'nogo kapitala v Rossii i za rubezhom [Methods for measuring the level of social capital in Russia and abroad]. *Izvestiya Saratovskogo universiteta. Novaya seriya. Seriya: Ekonomika. Upravleniye. Pravo*, 2014, vol. 14, no. 2-2, pp. 430–436 (in Russian).

27. House J.S. Work stress and social support. Addison-Wesley Reading, Mass, 1981, 156 p.

28. Cohen S., Wills T.A. Stress, social support, and the buffering hypothesis. *Psychological Bulletin*, 1985, vol. 98, no. 2, pp. 310–357.

29. Uchino B.N., Carlisle M., Birmingham W., Vaughn A.A. Social support and the reactivity hypothesis: conceptual issues in examining the efficacy of received support during acute psychological stress. *Biological psychology*, 2011, vol. 86, no. 2, pp. 137–142. DOI: 10.1016/j. biopsycho.2010.04.003

30. Lifintseva A.A. Sotsial'naya podderzhka kak faktor preodoleniya negativnykh posledstviy stressa [Social support as a factor in overcoming the negative consequences of stress]. *Vestnik Baltiyskogo federal'nogo universiteta im. I. Kanta. Seriya: Filologiya, pedagogika, psikhologiya*, 2012, no. 5, pp. 56–61 (in Russian).

31. Egolf B., Lasker J., Wolf S., Potvin L. The Roseto Effect: a 50-year comparison of mortality rates. *American journal of public health*, 1992, vol. 82, no. 8, pp. 1089–1092.

32. Berkman L.F., Glass T. Social integration, social networks, social support, and health: Social epidemiology. In: L.F. Berkman, I. Kawachi eds. New York, Oxford University Press Publ., 2000, pp. 137–173.

33. Byusse S. Sotsial'nyy kapital i neformal'naya ekonomika v Rossii [Social Capital and the Informal Economy in Russia]. *Mir Rossii*, 2002, no. 2, pp. 93–104 (in Russian).

34. Marmot M. Status syndrome. How your social standing directly affects your health and life expectancy. London, Bloomsbury Publ., 2004, 311 p.

35. Eriksson M. Social capital and health: implications for health promotion. *Global health action*, 2011, vol. 4, no. 1, pp. 1–11. DOI: 10.3402/gha.v4i0.5611

36. Uphoff E.P., Pickett K.E., Cabieses B., Small N., Wright J. A systematic review of the relationships between social capital and socioeconomic inequalities in health: a contribution to understanding the psychosocial pathway of health inequalities. *International journal for equity in health*, 2013, vol. 12, no. 1, pp. 1–12. Available at: https://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-12-54 (09.09.18).

37. Poortinga W. Do health behaviors mediate the association between social capital and health? *Preventive medicine*, 2006, vol. 43, no. 6, pp. 488–493. DOI: 10.1016/j.ypmed.2006.06.004

38. Lindström M., Hanson B.S., Ostergren P.O. Socioeconomic differences in leisure-time physical activity: the role of social participation and social capital in shaping health related behavior. *Social science and medicine*, 2001, vol. 52, no. 3, pp. 441–451.

39. Veenstra G. Social capital, SES and health: an individual-level analysis. *Social science and medicine*, 2000, vol. 50, no. 5, pp. 619–629.

40. Lucumi D., Gomez L.F., Brownson R.C. and Parra D. Social capital, socioeconomic status, and health-related quality of life among older adults in Bogotá (Colombia). *Journal of aging and health*, 2015, vol. 27, no. 4, pp. 730–750. DOI: 10.1177/0898264314556616

41. Altschuler A., Somkin C.P., Adler N.E. Local services and amenities, neighborhood social capital, and health. *Social science and medicine*, 2004, vol. 59, no. 6, pp. 1219–1229.

42. Gittell R., Vidal A. Community organizing. Building social capital as a development strategy. California, SAGE Publications Publ., 1998, 206 p.

43. Szreter S., Woolcock M. Health by association? Social capital, social theory, and the political economy of public health. *International journal of epidemiology*, 2004, vol. 33, no. 4, pp. 650–667.

44. Kawachi I., Berkman L.F. Neighborhoods and Health. New York, Oxford University Press Publ., 2003, 368 p.

45. Kawachi I., Kennedy B.P., Glass R. Social capital and self-rated health: a contextual analysis. *American journal of public health*, 1999, vol. 89, no. 8, pp. 1187–1193.

46. Villalonga-Olives E., Kawachi I. The dark side of social capital: a systematic review of the negative health effects of social capital. *Social science and medicine*, 2017, vol. 194, pp. 105–127.

47. Marsh C. Social capital and grassroots democracy in Russia's regions: evidence from the 1999–2001 gubernatorial elections. *Demokratizatsiya: the journal of post-soviet democratization*, 2002, vol. 10, no. 1, pp. 19–36.

48. Vasil'eva E.N., Poltavskaya M.B. Ekonomicheskaya i sotsial'naya aktivnost' naseleniya kak indikator formirovaniya sotsial'nogo kapitala [Economic and social activity of population as an indicator of social capital formation]. *Izvestiya VUZov. Povolzhskiy region. Obshchestvennyye nauki*, 2015, vol. 36, no. 4, pp. 113–119 (in Russian).

49. Turner B. Social capital, inequality, and health: The durkheimian revival. *Social theory and health*, 2003, vol. 1, no. 1, pp. 4–20.

50. Kawachi I., Kennedy B.P., Lochner K. Long live community: social capital as public health. *The American prospect*, 1997, vol. 35, pp. 56–59.

51. De Silva M.J., Huttly S.R., Harpham T., Kenward M.G. Social capital and mental health: a comparative analysis of four low income countries. *Social science and medicine*, 2007, vol. 64, pp. 5–20.

52. Harpham T., Grant E., Thomas E. Measuring social capital within health surveys: key issues. *Health policy and planning*, 2002, vol. 17, no. 1, pp. 106–111.

53. Rusinova N.L., Safronov V.V. Znacheniye sotsial'nogo kapitala dlya zdorov'ya v stranakh Yevropy [The importance of social capital for health in Europe]. *Zhurnal sotsiologii i sotsial'noy antropologii*, 2014, no. 3, pp. 112–133 (in Russian).

54. Belov V.B., Rogovina A.G. Sotsial'nyy kapital i zdorov'ye naseleniya [Social capital and public health]. *Problemy sotsial'noy gigiyeny, zdravookhraneniya i istorii meditsiny*, 2013, pp. 3–5 (in Russian).

55. Karhina K., Ng N., Ghazinour M., Eriksson M. Gender differences in the association between cognitive social capital, self-rated health, and depressive symptoms: a comparative analysis of Sweden and Ukraine. *International journal of mental health systems*, 2016, vol. 10, no. 37, pp. 1–14. DOI 10.1186/s13033-016-0068-4

56. Iversen T An exploratory study of associations between social capital and self-assessed health in Norway. *Health economics, policy, and law*, 2008, vol. 3, pp. 349–364.

57. Rocco L, Suhrcke M. Is social capital good for health? A European perspective. Copenhagen. WHO Regional Office for Europe, 2012, 24 p.

Lebedeva-Nesevrya N.A., Eliseeva S.Yu. Social capital as a factor that contributes into population health: analytical review. Health Risk Analysis, 2018, no. 3, pp. 156–164. DOI: 10.21668/health.risk/2018.3.17.eng

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NEW LEGAL, REGULATORy AND METHODOLOGICAL DOCUMENTS ISSUED IN THE RF IN THE SPHERE OF HEALTH RISK ANALYSIS

July – September 2018

The Decision by The Board of the Eurasian Economic Commission No.44 dated April 18, 2018 "On typical schemes for assessing conformity"

The decision fixes typical schemes that can be applied to assess conformity of products and product-related processes of designing, manufacturing, construction, erecting, setups, operation, storage, transportation, sales, and utilization to the requirements set forth by technical regulations. The document contains typical schemes for validating conformity (typical certifications schemes and typical schemes for declaring conformity) and typical schemes for state registration; technical regulations, taking into account peculiarities of products, can fix other schemes and procedures for assessing conformity.

The Decision by The Board of the Eurasian Economic Commission No.100 dated June 13, 2018 "On making alterations into the Decisions by the Board of the Eurasian Economic Commission No.30 dated April 21, 2015 "On non-tariff regulations"

The document fixes the order for imports of plants protectors and other persistent organic pollutants (POPs) which are to be applied in laboratory research or as a reference standard on the EAEU customs territory. It is envisaged by the order that the above-mentioned substances are to be imported in hermetically closed vials or bottles with their volume being from a to 10 ml (g) and in quantities required for laboratory research and/or as a reference standard, including laboratory research and control over safety of food products, water, air, performance of inter-laboratory comparative tests, working out measuring techniques, accomplishment of scientific-research works. Imports of samples on the EAEU customs territory require permission that should be given by a document issued in a form approved by the EAEU Board Decision No. 45 dated May 16, 2012. Imports of samples for private purposes by physical persons are strictly prohibited. The document contains a list of plants protectors and other POPs that can be applied in laboratory research and/or as a reference standard.

The Decision by The Council of the Eurasian Economic Commission dated July 13, 2018 No. 49 "On Approval of rules for determining origin of products imported on the EAEU customs territory (non-preferential rules for determining origin of products)"

The rules are to be applied when products are imported onto the EAEU customs territory from countries that are not the EAEU members. The rules, among other things, include criteria and peculiarities of determining origin of goods and fix the order for determining origin of products. They also contain requirements to a certificate of origin.

The Decision by The Council of the Eurasian Economic Commission dated June 14, 2018 No. 64 "On making alterations into the Section II Of the Unified list of products (goods) that are subject to sanitary-epidemiologic surveillance (control) on the EAEU customs border and customs territory"

The decision excludes item 2 "Products for children nutrition 03 EAEU CN FEA" from the list; groups 03, 16, and 21 are excluded from the table in the above-mentioned section.

The Federal Law No. 208-FL dated July 19, 2018 "On making alterations into some RF legislative acts as regards exclusion of duplicated authorities of the federal executive bodies in labor protection sphere"

The law states that when industrial control fixed by the Federal Law "On sanitary-epidemiologic welfare of the population" is being performed, experts can use results obtained in research on hazardous (dangerous) factors accomplished within specific assessment of working conditions by a laboratory (center) certified as per conventional order, but not more than 6 months prior to the moment when the above-mentioned industrial control is being performed. The Federal Law "On basics of the citizens health protection in the Russian Federation" excludes surveillance over safe working conditions out of Roszdravnadzor responsibilities in order to eliminate duplications of Rostrud authorities.

The Federal Law No. 244-FL dated July 29, 2018 "On making alterations into the Federal Law "On basic principles of local government organization in the Russian Federation" as regards rights belonging to local governments of a city or a rural settlement, municipal district, city county, a city county with an intra-city division, intra-city

district, to perform activities aimed at consumer rights protection"

The Law fixes the authority belonging to local governmental bodies (a city or a rural settlement, municipal district, city county, city county with intra-city division, intra-city district) to perform activities aimed at consumer rights protection.

The Federal Law dated July 29, 2018 No. 252-FL "On making alterations into the FL "On environmental protection" and Clause 1 and Clause 5 of the FL "On making alterations into the FL "On environmental protection" and some legislative acts of the RF " as regards creation of systems for automated control over emissions and discharges of contaminants"

The law states that all the objects that belong to the 1st category and exert negative influence on the environment, the types of such objects being fixed by the RF Government, should be equipped with automated devices for measurement and control over emissions and (or) discharges of contaminants as well as with technical devices for fixing and transmitting information on emissions and discharges into the state register of objects that exert negative impacts on the environment. The law also introduces requirements to programs of creating automated control systems, and the RF Government are granted authority to approve on rules for creation and operation of automated control systems.

The Federal law dated August 03, 2018 No. 316-FL "On making alterations into the FL "On protecting rights of juridical persons and private entrepreneurs when performing state control (surveillance) and municipal control" and Clause 19 of the FL "On licensing of certain activities "

The law fixes authority that belongs to the highest executive bodies in the RF regions as regards determination of types of regional state control (surveillance) which are subject to risk-oriented approach, as well as criteria for assigning activities performed by juridical persons, private entrepreneurs, and (or) their industrial objects into a specific risk category or a specific hazard class (category).

Unscheduled inspections which are accomplished in relation to submission of applications for granting a legal status, special permission (license) to perform specific activities, or permission (agreement) to perform other juridically significant actions, are to be excluded from the list of inspections information on which is to be included into the unified inspections register. The law also fixes that risk indicators related to possible violation of obligatory requirements can be considered by authorities that perform state control as a reason for an unscheduled inspection. It also gives a larger list of situations in which scheduled inspections can be omitted when licensing control over a concrete activity is performed.

The Federal Law dated August 03, 2018 No. 280-FL "On organic products and on making alterations into some RF legislative acts"

The law fixes standards for manufacturing, storage, transportation, marking and sales of organic (ecologically clean) products. It is fixed that some requirements are to be met when organic products are manufactured; these requirements include prohibition to use agrochemicals, pesticides, antibiotics, growth and fattening promoters for animals, hormones, excluding those permitted in the Russian Federation by the standards in the sphere of organic products manufacture; prohibition of embryo transplantation, cloning, and genetic engineering techniques, genetically modified and transgenic organisms, prohibition to apply hydroponic plants cultivating; prohibition to apply ionizing radiation etc. In order to provide free-of-charge informing for customers about manufacturers and types of organic products, a unified state register of organic products manufacturers has been created. Data contained in the unified state register of organic products manufacturers can be found on the RF Ministry for Agriculture official web-site.

The Federal Law dated August 03, 2018 No. 281-FL "On ratification of the Agreement on marking of goods with identification means in the Eurasian Economic Union"

The Law ratifies the Agreement on marking of good with identification means in the EAEU signed on February 2, 2018 in Almaty. In accordance with the Agreement, the Board of the Eurasian Economic Commission (EEC) decides on implementation of marking on the basis of well-grounded proposals submitted to the EEC by the member-states, analysis of practicability of goods marking introduction, information about influence exerted by introduction of marking on businesses, technological possibilities to mark goods, as well as information about other systems of control over distribution of goods. Goods are marked via application of identification means or material carriers that contain such means directly on goods or their package. Data on identification means are introduced into a unified register that is to be created and kept as an electronic database by the EEC.

The Agreement distributes authority on marking system creation among the EEC and the EAEU member-states.

The RF Governmental Regulation dated June 26, 2018 No. 731 "On standards fixing permissible emissions of radioactive substances and standards fixing permissible discharges of radioactive substances, as well as on granting permissions to emit or discharge radioactive substances"

The Rules for designing and fixing standards for permissible emissions and discharges of radioactive substances, as well as for granting permissions to

emit and discharge them, come into force on January 1, 2019. Standards for emissions or discharges are designed in relation to new economic or other objects that are being put into operation or reconstructed objects on the basis of construction documentation and inventory data on radioactive substances emissions into the atmosphere of radioactive substances discharges into water objects.

Standards for emissions or discharges are fixed in a permission to emit or discharge radioactive substances provided that such permissions are agreed on with Rospotrebnadzor that confirms standards for emissions or discharges being designed in conformity with sanitary rules. Permissions to emit or discharge radioactive substances are granted for 7 years. Those permissions to emit radioactive substances into the atmosphere and to discharge radioactive substances into water objects that were earlier granted by Rospotrebnadzor remain in force till their validity expires.

The RF Governmental Regulation dated July от 18, 2018 No. 840 "On making alterations into the Regulation on unified state system for prevention and elimination of emergencies"

The list of primary activities performed by governmental authorities and bodies acting within the unified state system for prevention and elimination of emergencies in case of red alert includes informing population about emergencies, their parameters and scales, damaging factors, measures aimed at providing safety of population and territories, protection means and techniques, necessary actions, rules of behavior in an emergency zone, and on citizens' rights in the sphere of protection of population and territories from emergencies and social protection of injured, including the right to receive compensations fixed in the legislation, and a procedure for recovering documents that were lost due to an emergency.

The RF Governmental Regulation dated August 13, 2018 No. 935 "On introduction of temporary quantitative limitation on imports of ozone depleting substances into the Russian Federation in 2018"

From September 7 till December 31, 2018, a quantitative limitation on imports of ozone depleting substances into the Russian Federation is valid; it regards substances from the Group I, list C, Section 2.1 of the list of goods that can be imported onto the customs territory of the EAEU or exported from it only on permission, fixed in the Appendix No. 2 to the Decision by the board of the Eurasian Economic Commission dated April 21, 2015 No. 30 "On non-tariff regulation".

The RF Governmental Regulation dated August 13, 2018 No. 934 "On acknowledgment of some RF Governmental acts as being no longer valid"

The following RF Governmental acts are no longer valid: The Rules for fixing standards of permissible contaminants discharges into water objects via centralized sewerage systems and limits on discharges for sewerage organizations (approved by the RF Governmental Regulation dated April 30, 2013, No. 393); The Regulation on a planned decrease in discharges of contaminants, other substances, and microorganisms into surface water objects, underground water objects, and on water-collecting areas (approved by the RF Governmental Regulation dated April 10, 2013, No. 317).

The RF Governmental Regulation dated August 18, 2018 No. 967 "On making alterations into some RF Governmental Acts"

The regulations on the federal state surveillance over consumer rights protection and on the federal state sanitary-epidemiologic surveillance are supplemented with a directive on a possibility of test purchases.

The RF Governmental Regulation dated August 31, 2018 No. 1039 "On Approval of Rules how to arrange grounds for accumulation of solid communal wastes (SCW) and enlist them in a unified register"

The document fixes the procedure for arranging grounds where solid communal wastes are to be accumulated, forming and keeping a unified register of such grounds. It is stated that grounds where solid communal wastes are accumulated are to be in full conformity with the RF legislation in the sphere of sanitary-epidemiologic welfare of the population and other RF legislative acts, as well as to the rules for municipal settlement improvement. A unified register of SCW accumulation grounds is a database that contains data on all the grounds where solid communal wastes are accumulated. The register is to be kept by an authorized body both on paper and as an electronic database.

The Order by the RF Chief Sanitary Inspector dated May 31, 2018 No. 37 "On making alterations into the Order by the RF Chief Sanitary Inspector dated December 22, 2017 No. 165 "On Approval of Hygienic Standards HS 2.1.6.3492-17 "Maximum permissible concentrations (MPC) of contaminants in the atmospheric air in cities and rural settlements" Registered in the RF Ministry of Justice on June 18, 2018 No. 51367.

The document adjusts maximum permissible concentrations (MPC) of contaminants in the atmospheric air in cities and rural settlements; in particular, for such contaminants as "Hexahydro-2H-azepine-2-on", Hex-1-en", 1-Hydroxy-4-chlorobenzene, 1,2-dibrompropane,

, "Propylpantanoate", and some others.

The Order by the RF Chief Sanitary Inspector dated April 18, 2018 No. 30 "On additional measures for preventing hydrophobia in the Russian Federation" Registered in the RF Ministry of Justice on August 08, 2018 No. 51814.

Heads of Rosporebnadzor regional offices are to determine exact volumes and dates for immunization of population against hydrophobia. The RF Chief Sanitary Inspector indicates that epidemiologic situation as regards hydrophobia is not stable on the RF territory.

The document also contain recommendations on prevention of hydrophobia and morbidity with the diseases among people.

Recommendations by The Board of the Eurasian Economic Commission dated July 31, 2018 No 13 "On collecting samples to perform examinations (tests) and measurements of food products when applying and meeting requirements fixed by the Technical regulations of the Eurasian Economic Union"

The document proposes specific rules and procedures for the EAEU member states as regards samples collection for examining food products when applying the EAEU technical regulations (EAEU TR) and meeting requirement set forth by them. These rules and procedures are recommended to be applied starting from October 1, 2018. The rules and procedures determine overall sequence of actions for collecting samples of food products, basic requirements to storage, transportation, and delivery of samples, and they are to be applied in the process of obligatory assessment of food products conformity to the requirements set forth by the EAEU technical regulations and state control (surveillance) over meeting the requirements set forth by the EAEU technical regulations. The said rules and procedures are to be applied in case there are no procedures that fix collection of samples in international, inter-state, or national (state) standards that contain rules and procedures for examinations (tests) and measurements, including rules for collecting samples that are necessary for application and meeting requirements set forth by technical regulations and performing assessment of conformity for objects of technical regulation.

Recommendations by The Board of the Eurasian Economic Commission dated June 19, 2018 No. 9 "On interaction between state control (surveillance) bodies in the EAEU member states when performing control (surveillance) activities in relation to meeting requirements fixed by the EAEU technical regulations"

The EAEU member states are offered some recommendations on how to perform state control (surveillance) over meeting requirement fixed by the EAEU technical regulations. The recommendations contain an algorithm of standard activities accomplished by state control (surveillance) authorities when they detect products that don't conform to the requirements fixed by the EAEU technical regulations; a typical notification on detected products that don't conform to the requirements fixed by the EAEU technical regulations and on measures taken as regards this situation.

The Information Letter by the RF Federal Biomedical Agency dated August 24, 2018 No. 32-024/646 "On establishing sanitary-hygienic zones of industrial enterprises and radiation objects"

The RF Federal Biomedical Agency clarify the order for agreeing on sanitary-hygienic zones and observation zones on areas where a nuclear plant, a source of radiation or a storage facility with radiation materials is located; such zones are to be established in full conformity with the RF legislation in the sphere of nuclear power application and the RF land laws. Sizes and boundaries of a sanitary-hygienic zone near an object where nuclear power is applied are to be determined by a project of a sanitary-hygienic zone in conformity with standards and rules for nuclear power application; the project is to be agreed upon by state sanitary-epidemiologic surveillance authorities. A regulation on such sanitary-hygienic zones is to approved by the RF Government.

Methodical Guidelines MG 4.2.2.0127-18. 2.4.4. Children and teenagers hygiene. A procedure for assessing efficiency of health-improving activates performed by stationary facilities for children's rest and recreation. Methodical guidelines" (approved by the RF Chief Sanitary Inspector on May 11, 2018)

Methodical guidelines cover stationary facilities for children's rest and recreation with a shift duration being not less than 21 days and are aimed for bodies that perform federal state sanitary-epidemiologic surveillance, executive bodies of the RF regions, heads and medical personnel employed at stationary facilities for children's rest and recreation that are located in the countryside. These methodical guidelines replace MG 2.4.4.0011-10 "A procedure for assessing efficiency of health-improving activities performed by stationary rest and recreation facilities for children located in the countryside ".

The Information letter by Rospotrebnadzor "Rospotrebnadzor recommendations for workers who perform their work tasks under increased air temperature"

Rospotrebnadzor remind how to properly organize work processes at workplace with increased air temperature. When air temperature in a working area reaches 28.5^{o}C, it is recommended to make a workday 1 hour shorter; when it reaches 29^{o}C, 2 hours shorter; when it reaches 30.5^{o}C, 4 hours shorter. When work is

performed on open air with air temperature being 32.5°C and higher, uninterrupted working period should last for 15-20 minutes and then there should be a breaks for not less than 10-12 minutes in cooling rooms; the total duration of work under thermal loads should not exceed 4-5 hours per a working shift for workers who wear heatproof clothing, and 1.5-2 hours for workers without any heatproof clothing.