RISK ASSESSMENT PRACTICE IN HYGIENIC AND EPIDEMIOLOGICAL STUDIES

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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).

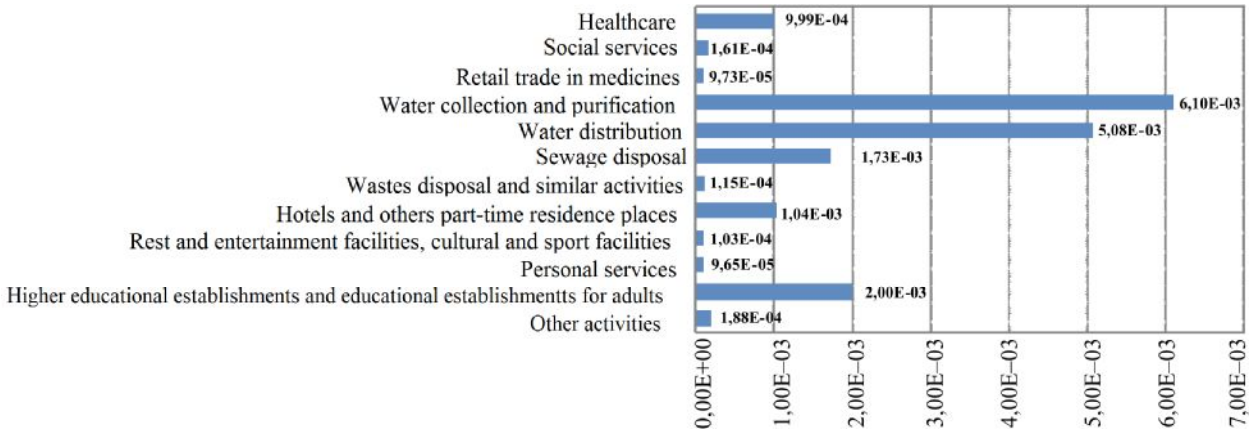

Figure 1. Average potential health risk per one economic entity as per activities performed in the sphere of "Healthcare, communal, social, and personal services"

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

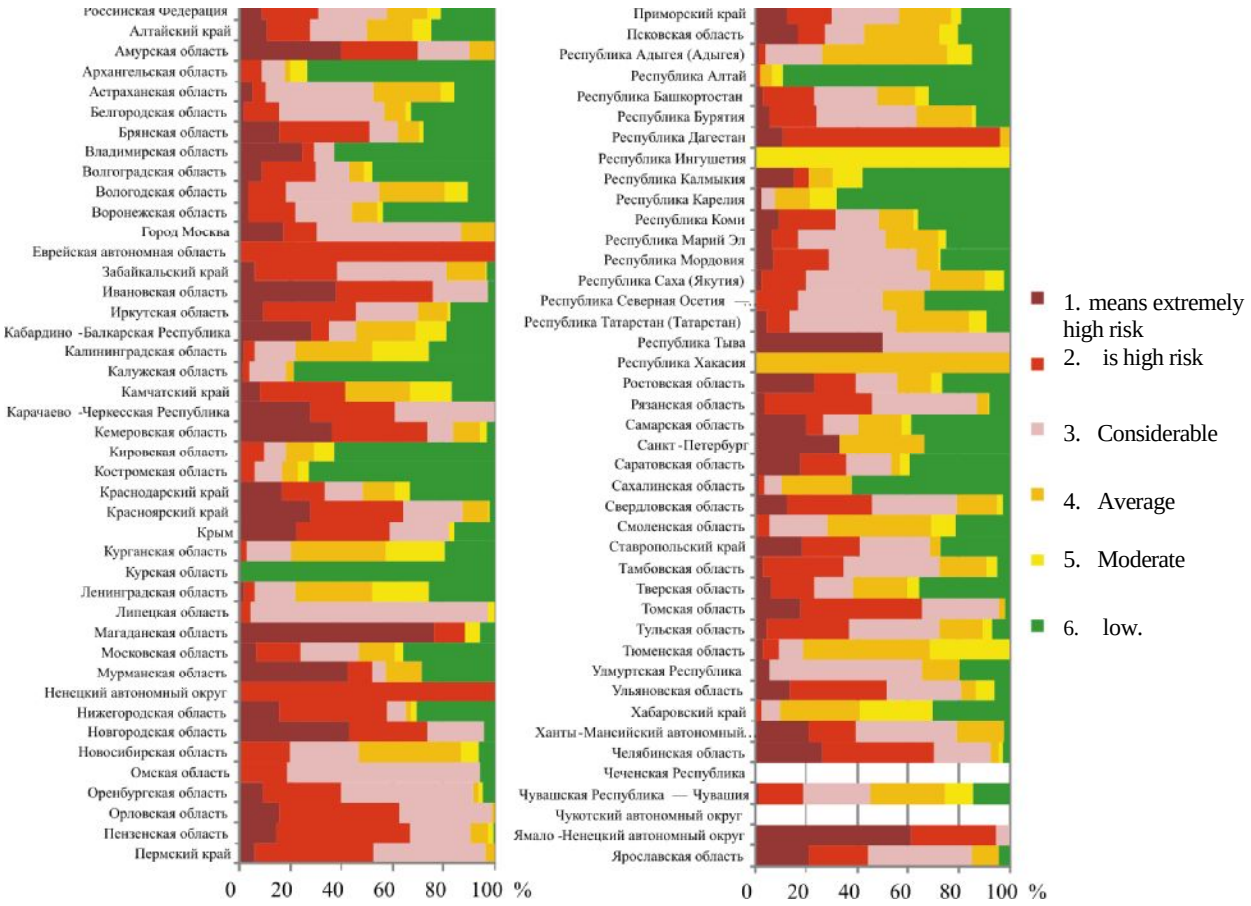

Figure 2. Distribution of economic entities (juridical persons and private entrepreneurs), who deal with water collection and purification (41.00.1), as per health risk categories in all the RF regions (The RF regions are enlisted in the alphabetical order)

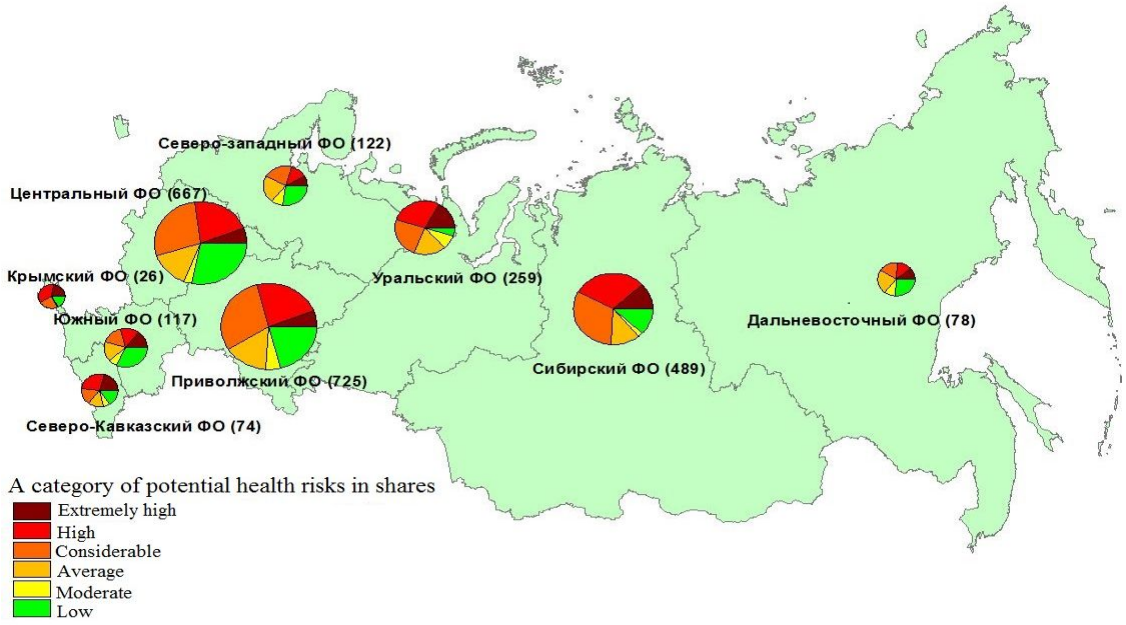

Figure 3. Distribution of economic entities (number and shares) that deal with water collection and purification as per health risks in the RF Federal Districts (the size of a diagram and figures in brackets correspond to the number of economic entities that belong to the 1st and 2nd categories as per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