Specialized ecological polygon as one of the tools to reduce pharmaceutical pollution of the environment

Vladimir Belov¹,³, Tatyana Komandresova² and Alexander Samarkin¹

¹Pskov State University, Department of Medical Informatics and Cybernetics, Pskov, Russia
²Pskov State University, Department of Fundamental Medicine and Biochemistry, Pskov, Russia
E-mail: ³vsbb@yandex.ru

Abstract. The article discusses the problems of pollution of natural objects of the environment by medicines. The main sources of pharmaceutical waste, the causes of their occurrence, as well as the ways of penetration of drugs, the results of their metabolic transformation in the bodies of patients into environmental systems are characteristic. It has been shown that the main suppliers of pharmaceutical waste are medical organizations, chemical and pharmaceutical companies and the population. It is noted that the main channels of penetration of medicines into the environment are wastewater and landfills. Some data on the emergence of pharmaceutical substances in the natural environment are analysed. The composition of the recommendations and measures necessary to reduce the level of environmental risks associated with pollution is described. Particular attention is paid to the Environmental Monitoring Service, which provides laboratory support for environmental monitoring of environmental facilities, including hydro- and geochemical analysis of water, soil and air environment. It is proposed to improve the effectiveness of the environmental monitoring service in view of the degree of impact of controlled drugs on the natural environment by deploying a specialized ecological polygon.

1. Introduction
It is impossible to provide effective treatment for various diseases without pharmaceuticals, such as the drugs, that allow in many cases to carry out the recovery of patients without surgery, without complicated and expensive medical and technological procedures. However, using pharmaceuticals in medical practice is accompanied by rather serious negative consequences of a planetary scale. This is nothing more than pollution of the environment (soil, water environment (surface and ground waters), partly air) with medicinal wastes of the population; products of metabolic processing of drugs in the bodies of patients; expired and unnecessary non-utilized pharmaceuticals of medical institutions; waste and emissions from chemical and pharmaceutical industries. Naturally, the issues of destruction by medical institutions of unused and expired medicinal and related chemicals; the tasks of organizing the most harmless pharmaceutical production; a lot of attention and efforts are paid to the schemes of creation, testing, introduction, use of new medicines, taken by humans or used in veterinary medicine. The regulations of industrial waste for the election of pharmaceutical industry enterprises have been carefully and in detail worked out; rules and forms of accounting for the use in medical institutions of medicines and pharmaceuticals as prescribed; procedure, technology and other issues of organizing the processes of disposal of expired and unused drugs and related chemicals in medical institutions. International standards on environmental safety are actively discussed and implemented in Russian
laws and by-laws on environmental protection (of which there are more than 7 thousand), include in the field of protection against pharmaceutical contamination [1, 2]. At first glance, such a state of regulatory and organizational support for environmental management, technogenic relationships of legal entities and individuals with the environment, should effectively affect the environmental situation in the country and its regions, including on the state of pharmaceutical pollution. However, numerous studies in Russia and other countries – see, for example, [3-10] show that drugs already produced and used in medical practice inevitably end up in the environment, first of all, in surface and underground waters, as well as in the soil, and, to a lesser extent, in the atmosphere and have rather serious biological effects on the biota, and then, having completed the cycle, they return to humans back with food, with water, and finally with air. Ultimately, the effects of re-use of medicinal principles by humans are formed due to the emergence of a closed-loop “man - pharmaceuticals - medicinal waste in sewage and landfills - surface water bodies and groundwater - sources of irrigation for food plants - accumulation of metabolites and fragments of pharmaceuticals in plants - meat and dairy products with the inclusion of fragments of veterinary medicinal substances (obtained using infected plants and contaminated water) and drinking water (often insufficiently purified from secondary medicinal principles) - a person and then in a circle.” This system of circulation of derivatives of medicinal substances shows what a huge chemical-pharmaceutical load falls on the environment (primarily on its water resources) due to its pollution with pharmaceutically active substances, metabolites, and their derivatives.

In this case, the question inevitably arises of how it is possible to reduce the scale of medicinal pollution of the environment and thereby reduce the factor of the negative impact of pharmaceutical pollution on humans and, as a consequence, preserve (and if the opportunity presents itself, then increase) the level of bioecological safety of natural agglomerations. at the permissible value.

2. Materials and methods
As already mentioned, there are a large number of publications, in particular, the already noted works [3-10], which describe in sufficient detail the sources of medicinal contamination, the ways of their penetration into the environment, the concentration of medicinal, pharmaceutically active, metabolic, xenobiotic and other chemicals in controlled natural recreation and other data. This publication based on research materials set out in the aforementioned articles, international and Russian regulatory legal acts on environmental protection, waste recycling, regulation of drug pollution, sanitary-epidemiological and sanitary-hygienic standards and rules.

The methodological basis of the research was a complex of general scientific methods, such as expert-analytical, system-structural methods, methods of content analysis, comparative analysis and generalization of information.

3. Results
Study of the composition of organizational structures and formations, small communities of people and individual entities that form a systemic set of legal entities and individuals, in one form or another associated with the creation, testing, implementation, use, disposal of medicinal and related medicinal and chemical substances, allow to establish the following main sources of pharmaceutical pollution of the environment [9]:

- pharmaceutical industry enterprises;
- medical research centres;
- pharmacies and pharmacy organizations;
- medical institutions of outpatient, polyclinic and inpatient types;
- population (urban and rural);
- livestock complexes and poultry farms.

Chemical and pharmaceutical enterprises that provide the production of medicines, as well as research centres involved in the creation and testing of new pharmaceuticals, pollute the environment due to poor sewage treatment, insufficient efficiency of measures for the disposal of solid
pharmaceutical waste and their derivatives, as well as in case of accidents and emergency situations [11].

Pharmacy organizations and medical institutions are, perhaps, one of the main suppliers of medicinal substances to the environment, primarily to near-surface water basins. At the same time, the main channels of pollution are household wastewater from hospitals and clinics, in which the environmental toxicity factor is more than 15 times higher than the toxicity of sewage wastewater from residential and public buildings [12].

Significant amounts of pharmacological substances enter the environment from the population. At the same time, the main ways of penetration of bioactive substances into the natural ecosystem are not only sewage drains, into which the results of metabolism and drug residues with natural excretion products of the human body enter, and where liquid and soluble drugs, expired, spoiled due to improper storage or simply become unnecessary; as well as channels for the export of solid unnecessary, expired and become unusable pharmaceuticals arriving at landfills and landfills together with the household waste of the population. So only on a US scale, the population gets rid of medicines annually by throwing them into a landfill or draining them into the sewer in the amount of more than 100 thousand tons [10].

Another fairly capacious channel for the entry of medicinal principles and their derivatives into the aquatic and soil environment is associated with agriculture, primarily with animal husbandry and poultry farming. According to the data of [6], about 3.5 thousand tons of antibiotics are used annually in animal husbandry alone in Russia.

It is obvious that the drug pollution of near-surface water bodies, groundwater, and the soil layer leads to a large number of problems. Here are some of the most serious and pressing ones.

Accumulation of the pollution of pharmaceutical origin in ecosystems and their long-term effect on living organisms is often accompanied by the development of neoplasms and impaired renal function in domestic mammals and birds, a decrease in reproductive functions in fish, and some other pathological changes [13, 14]. As a result, food products produced by livestock, poultry, and fish farming enterprises may turn out to be of poor quality and environmentally unsafe.

Another of the significant environmental risks from pharmaceutical pollution that can cause serious diseases in humans is the risk of being exposed to the complex effects of a large number of pharmaceutically active substances and their metabolites that have entered into chemical reactions with each other. Often, in such situations, the effects of mutual "reinforcement" of substances appear, the dose-effect relationship for a specific pharmaceutical compound changes, the type, and nature of the therapeutic effect change hundreds or more times due to the mixing of different medicinal substances. Such undesirable effects drastically reduce the level of ecological safety of a pharmaceutically contaminated environment.

We must also note, that the presence of antibiotics and other pollution, associated with the use of pharmaceuticals, may lead to disrupting the processes of self-purification and detoxification of organic compounds in the soil and water bodies, and thus secondary pollution affected environment, like as bacteria resistant to antibiotics can appear in it also capable of causing disease in humans.

Here it is necessary to pay attention to the fact that at present there are no qualitative studies in the field of predictive assessment of the complex effect of pharmaceutically active compounds and their metabolites present in the surrounding biosphere on humans. The main reasons for this situation are that the collection of reliable and adequate experimental data is extremely difficult and, in many cases, practically impossible due to the high temporal and spatial variability of the concentrations and names of medicinal substances in the water or soil environment [5, 15].

Some scientists had carried out studies about environmental safety and related to the control of the consequences of the ingress of pollution of pharmaceutical origin and medicinal compounds into the aquatic environment of near-surface water bodies in Russia. Certain conclusions are drawn and specific systemic recommendations are formed.

For example, the work [16] describes the results of control measures to assess the medicinal pollution of water bodies in the North-West of Russia. Betting on this, it was found that almost all
water samples from the studied reservoirs contained the drug "Caffeine" at concentrations of 3.8–446 ng / dm3; in many samples, traces of the drugs "Ketoprofen", "Diclofenac", "Ciprofloxacin" tens to hundreds of ng / dm3.

There are also publications - see, for example, [7, 8, 17], devoted to the study and assessment of the level of pharmaceutical pollution of the Moscow region water bodies and rivers, including the study of not only the aquatic environment but also bottom soil sediments. As a result, traces of 23 active drugs were found in the water and bottom sediments of the studied objects, in particular, such as: "Ofloxacin", "Sulfamethoxazole", "Erythromycin", etc., 9 auxiliary dosage forms, 5 pharmaceutical substances included in vitamins complexes and biologically active additives.

Thus, the noted negative environmental consequences from medicinal pollution of the environment significantly reduce the level of its environmental safety for the population living in the vicinity of the contaminated area, forcing them to perceive pharmaceutical pollutants through the gastrointestinal tract, skin, and respiratory system. Medicinal substances, metabolites, and their derivatives, entering the human body, including through food chains of the type "plant food - man", "plants - animals - meat and dairy products - man", "fish - man", "water - water treatment system - a person ", interact intensively in the body both with each other, often sharply increasing the therapeutic effect of the pharmaceutical complexes formed in this process, and with functionally significant molecular formations of internal organs, into which they enter, causing undesirable physiological and biochemical processes in the latter.

4. Discussion

The value of saturation of the environment with medicinal impurities varies significantly in different territorial enclaves of the Russian Federation. The level of pharmaceutical contamination of regions is influenced by many factors, in particular, such as the presence or absence of enterprises of the chemical and pharmaceutical industry in the constituent entities of Russia: the concentration of the population in the regions, the presence of megalopolises, urban agglomerations, the peculiarities of the territorial settlement of people; the number of medical organizations in a particular territory, including scientific and medical centres, pharmacies, hospitals, clinics; the geographical features of the regions, first of all, the degree of their saturation with water bodies and the degree of their sensitivity to the injection of pollutants into the ecosystems.

A wide variety of states of the listed factors leads to the fact that the concentrations of pollution caused by pharmaceuticals, in different territorial enclaves of even one subject of Russia (and even in different regions and even more so) can differ hundreds and thousands of times. This complicates, to a certain extent, the formation of uniform recommendations and systemic solutions aimed at controlling and, if possible, reducing the negative impact of pharmaceutically-induced pollution on ecosystems.

It can be mentioned here that certain recommendations and measures to reduce the environmental risks associated with drug pollution in the Russian Federation have been developed and are being implemented. Thus, work [8] mentions many general recommendations for reducing xenobiotic and pharmaceutical pollution of the aquatic environment, including near-surface and ground waters, in particular, such as:

- development of systems for monitoring water basins and rivers, as well as wastewaters for assessing the degree of their pollution with pharmaceutical pollution;
- cataloging and mapping sources and water bodies with a high anthropogenic xenobiotic, pharmaceutically active load, for the preparation and implementation of preventive environmental remediation measures;
- preparation of legislative and normative-legal acts regulating the composition of measures and the procedure for their application to reduce the level of medicinal pollution of the environment, primarily natural waters, as well as taking into account the experience of lawmaking in this area of foreign countries;
- improvement and implementation of modern technologies for water treatment of drinking water and water disposal and treatment of sewage household water.
In work [6], interesting proposals were also formed in the areas of work related to reducing the pathways of drugs entering the environment, among which the following can be noted:

- development of measures and methodological materials to reduce the possibility of drug residues (expired, unnecessary, unusable, spoiled by improper storage and transportation) from the activities of pharmaceutical manufacturers and the activities of medical and pharmacy institutions;
- development and improvement of schemes for the use of diagnostic and disinfectants, methods of decontamination and disposal of medicinal waste to prevent it from entering the sewerage system and landfills;
- determination of the composition of marker pharmaceutical pollution for basic objects of the environment, according to the concentration of which in the water, soil, or air environment, it would be possible to judge the degree of pharmaceutical pollution of controlled natural objects and conduct constant monitoring of the state of environmental ecosystems.

However, the analysis of the listed proposals for reducing environmental risks from drug pollution of the environment showed that among the mentioned recommendations and measures one of the most important links fell out - a system of proactive control of environmental consequences from the release of controlled and new pharmaceuticals used in clinical practice into the environment.

Here, one of the possible solutions to improve the system of environmental monitoring of the state of the environment is to create, within the framework of existing regional centers for environmental monitoring of the quality of natural environments [18], organized in each constituent entity of the Russian Federation on the basis of Article 6 of the Federal Law No. an ecological laboratory or a special ecological polygon for targeted studies of the effect of pharmaceutical pollutants on the environment.

By recreating controlled chemical and ecological experiments in laboratory or field conditions, in the chambers of which the final stage of the "life cycle" of a pharmacological preparation is artificially imitated - the stage of its disposal and deactivation, intentional or unintentional entry into the environment as a pharmaceutical impurity. By simulating various ecological situations (by the composition of pharmaceutical pollution, bioactive substances, metabolites, xenobiotics, chemicals, household waste) in a laboratory or at an ecological polygon it is possible to study in sufficient detail the degree of influence on environmental ecosystems not only of new drugs, but also of any pharmaceutical preparations, medicinal substances, and forms, their combinations and thereby assess and predict the level of negative consequences for the environment and, ultimately, for humans in the event of pollution of the biosphere with controlled drugs and forms.

It should also be noted here that the introduction into clinical practice of pharmaceutically active drugs, the appearance of drugs selectively acting only on "harmful" cells or endoparasites greatly increases the bioactivity of not only drug substances and derivatives from pharmacy active drugs, but also metabolic products of the human body after them. application. The increased chemical activity of medicinal substances in the aquatic environment and other natural environments leads to increased chemical and ecological stress of ecosystems and, as a consequence, to a noticeable increase in environmental risks and a significant increase in the negative impact of the affected ecology on humans. For these reasons, timely identification of negative factors from the pollution of environmental ecosystems with pharmaceutically active drugs becomes urgent and urgent.

5. Conclusion
A high-quality organization of public health protection, an increase in the level of accessibility of medical services, including high-tech ones, the availability of proven medicines, as well as new pharmaceutically active drugs and dosage forms, contributes to an increase in the average life expectancy of people. However, at the same time, these factors, together with a high concentration of the population in megalopoles and urban agglomerations, where, also, medical organizations of all types, pharmaceuticals, and pharmacies are inevitably concentrated, leading to a noticeable annual increase in the level of environmental pollution with waste and residues of pharmaceuticals and their mutagens. This anthropogenic phenomenon is observed in almost all countries of the world and is
actively being studied in many of them. Based on the results of such studies, various measures and measures are developed and implemented to protect the water, soil, and air ecosystems of the environment from such a "scourge" of a planetary scale.

The implementation of the measures and systemic recommendations mentioned in this work, aimed at reducing the concentration of pharmaceutical substances in household waste and sewage, in solid and liquid waste of the population, medical and pharmaceutical institutions, will help improve the state of environmental ecosystems, preserve the homeostasis of ecosystems, lowering the level of environmental risks.

Ensuring total control of the ways of penetration of medicinal substances and their derivatives into the natural environment, proactive research (within the framework of the environmental monitoring service for the quality of natural environments) of environmental consequences when new and controlled drugs and dosage forms, primarily bioactive and selective, enter the natural environment, implementation measures for the timely disposal and deactivation of medicinal waste, as well as the implementation of high-quality reclamation and restoration of the affected environmental objects, will ultimately reduce the quantitative and qualitative aspects of the concentration of medicinal substances and xenobiotics in environmental ecosystems.

Improving the ecological situation in the environment in terms of increasing the level of controllability of the degree of its damage by pharmaceutical pollution makes it possible to reduce the concentration of secondary medicinal substances that enter the human body from the ecosystems of the environment through food channels (with water, food plants, food products of the agro-industrial and fish-processing complexes).

6. References
[1] Kuznetsov D A 2010 Approaches to the assessment of environmental safety in pharmacy XVII Bulletin of new medical technologies vol 4 pp 202–205
[2] Yankovskaya A A and Kuznetsov L M 2017 Eco-potential Mechanisms and tools for ensuring the environmental safety of the region vol 3 pp 32–37
[3] Kolpin D W, Furlong E T, Mayer M T and Thurman E M 2002 1999–2000: a national reconnaissance Environmental Science & Technology, Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams vol 36 no 6 pp 1202–1211
[4] Santos L, Arauio A, Fachini A and Pena 2010 Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic environment A Journal of Hazardous Materials vol 175 pp 45–95
[5] Richards S M, Wilson C J, Johnson D J and Castle D M 2004 Effects of pharmaceutical mixtures in aquatic microcosms Environmental Toxicology and Chemistry vol 23 no 4 pp 1035–1042
[6] Novikova Yu A, Markova O L and Fridman K B 2018 Main aspects of minimization of population health risks caused by pharmaceutical pollution of surface sources of drinking water supply Gigienai and Sanitaria (Hygiene and Sanitation, Russian journal) vol 97 no 12 pp 1166–1170 doi: http://dx. doi. org/1018821/0016-9900-2018-97-12-1166-1170
[7] Kozlova M A 2020 Pharmaceutical pollution of natural and waste waters: treatment methods and research results Ecological Bulletin of the North Caucasus vol 16 no 1 pp 77–80
[8] Barenboim G M and Chiganova M A 2014 Pollution of water bodies in the Moscow Region with drugs, their metabolites and other xenobiotics with pharmacological activity: Problems and solutions Bulletin of the Russian Academy of Natural Sciences vol 2 pp 97-103
[9] Barenboim G M and Chiganova M A 2015 Pollution of natural waters with pharmaceuticals (Moscow: Nauka) 283 p
[10] Kozyrev S V, Korablev V V and Yakuceni P P 2012 New environmental risk factor: medicinal substances in the environment and drinking water SPbSPU Scientific and Technical Bulletin Science and Education vol 4 pp 195–201
[11] Eremin G B, Lomtev A Yu, Mozhhukhina N A, Sinilshchikova I A and Nikonov V A 2017 Ecological Problems of the Present: Identifying and Preventing the Adverse Impact of Anthropogenically Deterministic Factors and Climate Change on the Environment and Public Health Materials of the International Forum of the Scientific Council of the Russian Federation on Human Ecology and Environmental Hygiene, Questions of functional zoning when placing pharmaceutical enterprises pp 146–148

[12] Felicity T 2017 Pharmaceutical waste in the environment: a view from the standpoint of culture Panorama of public health vol 3 no 1 pp 1–140

[13] Lalumera G M 2004 Preliminary investigation on the environmental occurrence and effects of antibiotics used in aquaculture in Italy Chemosphere vol 54 pp 661–668

[14] Calisto V and Esteves V 2009 Psychiatric pharmaceutical in the environment, Chemosphere vol 77 pp 1–4

[15] Cleuvers M 2003 Aquatic ecotoxicity of pharmaceuticals including the assessment of combination effects Toxicol Lett vol 142 pp 185–194

[16] Russian Ya V, Chernova E N, Nikiforov V A and Zhakovskaya Z A 2014 Regional’naya ekologiya Medicinal compounds in water bodies of the North-West of Russia vol 1-2 no 35

[17] Barenboim G M and Chiganova M A 2012 Water: Chemistry and ecology Pollution of surface and waste waters by drugs vol 10 pp 40–46

[18] Volkova L S 2017 About the Republican Information and Analytical Center for Environmental Monitoring Arctic XXI Century Natural Sciences vol 1 pp 32–37