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Standardization in regulating artificial intelligence systems in Russian healthcare

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Abstract

Artificial intelligence technologies in medical practice are a promising direction in the world. Artificial intelligence medical decision support systems, diagnostic and screening programs can help medical personnel in routine and complex tasks and improve the level of medical care provided to patients. At the same time, the development, production and distribution of artificial intelligence systems must be regulated without fail. Registration and subsequent control (post-registration monitoring) of artificial intelligence systems in medicine require the creation, adjustment of the legal framework and technological regulation. The Russian Federation has developed a promising development strategy in this area. Seven national standards have been developed by experts in the field of Artificial intelligence in healthcare. These standards establish the procedures for conducting clinical and technical trials, performance requirements and the concept of life cycle, a quality management system and risk management. A separate standards is devoted to dataset creation for training and testing the developed algorithms, requirements for them and a metadata format. There are plans to bring the developed national standards to the international level, which will allow Russian manufacturers of artificial intelligence systems implemented these national standards to comply with foreign counterparts and become more competitive at the international level. The international community has already supported the development of an ISO standard based on the national standard for clinical trials. The development will be performed based on the technical committee ISO/TC 215 (Health informatics) in conjunction with ISO/IEC JTC 1/SC 42 (Artificial intelligence), this will allow bringing the national requirements for the Artificial intelligence to the international level. The cycle of these standards will summarize recognized methodologies, helping both manufacturers and medical organizations, doctors and patients to produce and use a quality, safe and effective product.

Keywords: standardization, medical artificial intelligence, artificial intelligence-based software as a medical device, medical software.

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Introduction. More and more evidence has been reported that artificial intelligence (AI) technologies have the potential to become an effective assistant to the doctor in the diagnosis of lung diseases (lung cancer [1], tuberculosis [2], and other pulmonary diseases [3]), breast cancer [4], cardiovascular diseases [5], and many other types of pathologies [6–10]. Directions for AI technology implementations in the Russian Federation have been developed, including solutions in the field of patient navigation in the healthcare system and decision support in the field of healthcare management, as well as in the field of medical decision support [11–13].

Additionally, AI-based systems (AIS) are already used in practice. In the Russian Federation, medical decision support and screening systems have already been registered as medical devices and are introduced into medical practice.

However, the problems that hinder the widespread use of AIS in healthcare practice remain relevant [14].

First, there may be errors in the operation of AI models in real clinical practice, which may be due to the insufficient quality of the data sample that the developers use to train AIS. At the moment, requirements for the completeness and transparency of the

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AIS documentation are unavailable, thus users cannot verify the correspondence between the training set of data and the patient data of the real population.

Secondly, the protection of personal data in the era of information technology is actively discussed since information about patients is used both for training and testing AIS, as well as their operation [15].

Thirdly, the biggest problem with the widespread introduction of AIS is the lack of complete trust in them by doctors and patients [16].

AIS is a kind of "black box," that is, the decision-making algorithm is not transparent for both the medical specialist and the patient because the doctor cannot fully disclose the treatment information due to the opacity of the AIS decision.

Particular attention to the development and use of AIS should be given for patient safety, and this aspect directly affects the credibility of the technology. A procedure is established for assessing the quality, efficiency, and safety of software operation as a medical device, including AIM to increase confidence. By the order of the Ministry of Health of the Russian Federation dated July 7, 2020, No. 686n, IIS are assigned to the third class: software with a high degree of risk. Thus, control and supervision measures should be built considering all the features and problems of this area.

The above-mentioned aspects indicate the need to improve the regulatory documents [17] and regulatory legal acts that will establish uniform provisions for the formation of operational documentation of the AIS, regulate the procedure for testing the AIS, and determine the parameters of data sets used in training and testing.

His literature aimed to review the currently existing regulatory framework in the field of AI regulation worldwide and present the Russian experience in creating the first national standards that will establish technical standards for the development and application of AI technologies in healthcare.

The literature search was carried out in PubMed, Google Scholar, and eLibrary databases in English and Russian. The international regulatory documents from the International Medical Device Regulators Forum (IMDRF), Health Sciences Authority, Food and Drug Administration (FDA), international reviews, and national strategies in the field of AI of several states were used. For searches in PubMed and Google Scholar, the following queries were used: "artificial intelligence/standardization," "artificial intelligence/legislation and jurisprudence," (systematic reviews), "artificial intelligence/clinical assessment."

The eLibrary was searched for the keywords "AI medical device," "AI medical device clinical trials," "AI technical testing of medical devices," and "clinical evaluation of medical devices" in connection with the specifics of legal regulation in Russia.

Inclusion criteria are as follows: up-to-date reviews and normative documents on the use of AIS in the healthcare system in English or Russian.

Exclusion criteria are as follows: the full text of the document is unavailable or the data given in the text has lost its reliability/relevance, and scientific articles were published >5 years ago.

International regulation of AI-based systems in medicine. Currently, a full-fledged regulatory framework, control systems, and sufficient experience in the field of AI technologies are unavailable worldwide. The directives of the world's leading community of competent authorities in the field of medical device regulation worldwide (IMDRF) [18], as well as the regulatory guidance of the Health Sciences Authority (Singapore), describe the life cycle and approaches to assessing software as a medical product, but they do not consider the features of AI technologies [19].

Regarding national strategies in the field of AI, several states have developed their documents. In the United States, a discussion paper in the field of AIS "The national artificial intelligence research and development strategic plan: 2019 update" was submitted, which indicates a strategic development plan in the following areas [20]:

– calling for long-term investment in AI research;

– developing effective methods of interaction between humans and AI;

– understanding and addressing the ethical, legal, and social implications of AI;

– ensuring AI safety;

– developing publicly available datasets for AI training and testing;

– calling for the measurement and evaluation of AI technology through standards and norms;

– understanding the national needs of employees in research and developing institutions in the field of AI;

– expanding public-private partnerships to accelerate progress in the field of AI [21].

The implemented new approach to software regulation, which is a medical device, in the FDA suggests paying more attention, not to the final product, but the manufacturer (developer) [22]. Thus, the FDA can pre-certify a software developer (including in the field of AI) who has previously demonstrated a "culture of quality and organizational excellence based on objective criteria," and enter the market with a low-level risk without extensive FDA approval.

The South Korean document presents all the national strategies, labeled as follows: "If we focus our national support on the strengths of our policies, we can close the gap with the world leaders in AI. To this end, the government is presenting a national vision and national action plans for a new leap forward in our economy and the improvement of society, taking advantage of AI-assisted civilizational change as a golden opportunity" [23].

In 2020, the European Union (EU) published the book "On Artificial Intelligence: A European approach to excellence and trust" [24], which proposes a common EU approach to the development of AI and ways to build trust in this technology. Experts see great potential in advancing the concept of building trust in AI by informing patients and clinicians about the functionality of AI, how the data will be used, and so on [25]. The document "New Generation Artificial Intelligence Development Plan" [26] was presented in 2017 by China. The document outlines a high-level project framework that reflects the country's approach to AI technology development and applications and defines common goals until 2030. Separately, the issue of ensuring legal and ethical standards for the use of AI [27] is raised, which is beyond the scope of this work.

Regulatory documents for AIS in healthcare in Russia; the experience of creating the first national standards. Russia's regulatory framework for AI and medical devices is also just beginning to take shape. According to the Decree of the President of the Russian Federation of October 10, 2019, No. 490 "On the development of artificial intelligence in the Russian Federation," the National Strategy for the Development of AI up to 2030 defines the tasks of AI development in Russia, which include the following:

1) support for scientific research to ensure the advanced development of AI;

2) development of software that uses AI technologies;

3) increased availability and quality of necessary data for AI technology development;

4) increased availability of needed hardware to solve problems in the field of AI;

5) increased level of providing the Russian market of AI technologies with qualified personnel and the level of public awareness of the possible areas of use of such technologies;

6) creation of an integrated system for regulating social relations arising in connection with the development and use of AI technologies.

In pursuance of the above strategy, the Government Commission for Digital Development approved the passport of the developed federal project "Artificial Intelligence" as part of the national program "Digital Economy" on August 31, 2020 [28]. Additionally, within the framework of standardization in the field of AI, technical committee 164 was created as a "mirror body" of the international technical subcommittee SC42 "Artificial intelligence," which is part of the international joint technical committee ISO/IEC JTC1 "Information technologies" [29].

By order of Rosstandart No. 3471 dated December 31, 2019, based on technical committee 164, subcommittee 01 "Artificial intelligence in healthcare" (PC 01) was created [30].

The SC 01, which included both researchers from various scientific and clinical departments and AIS developers, aimed to coordinate work on the unification and standardization of requirements used in the development, testing, and operation of AIS in healthcare. In 2020, SC 01 initiated the development of the first seven national standards that will regulate the key aspects of the use of AI in healthcare and its role in medical decision-making as follows:

– Artificial intelligence systems in clinical medicine. Part 1: Clinical trials.

– Artificial intelligence systems in clinical medicine. Part 2: Program and methodology of technical tests.

– Artificial intelligence systems in clinical medicine. Part 3: Change management in artificial intelligence systems with adaptive algorithms.

– Artificial intelligence systems in clinical medicine. Part 4: Evaluation and control of operational parameters.

– Artificial intelligence systems in clinical medicine. Part 5: Requirements for the structure and order of using a data set for training and testing algorithms.

– Artificial intelligence systems in clinical medicine. Part 6: General requirements for operation.

– Artificial intelligence systems in clinical medicine. Part 7: Life cycle processes.

The standard "Artificial Intelligence Systems in Clinical Medicine. Part 1: Clinical Trials" (on behalf of SC 01 experts) initiated the development of an international standard for clinical evaluation of AI-based software ISO "Artificial Intelligence (AI)—Software testing of AI medical devices. Part 1: Clinical evaluation. The initiative was included in the agenda of the plenary session held from October 19–30, 2020. A unanimous decision was made to develop the above standard due to the consideration by ISO member countries. The work will be based on the technical committee ISO/TC 215 (Health informatics) in conjunction with ISO/IEC JTC 1/SC 42 (Artificial intelligence). Figure 1 pre-

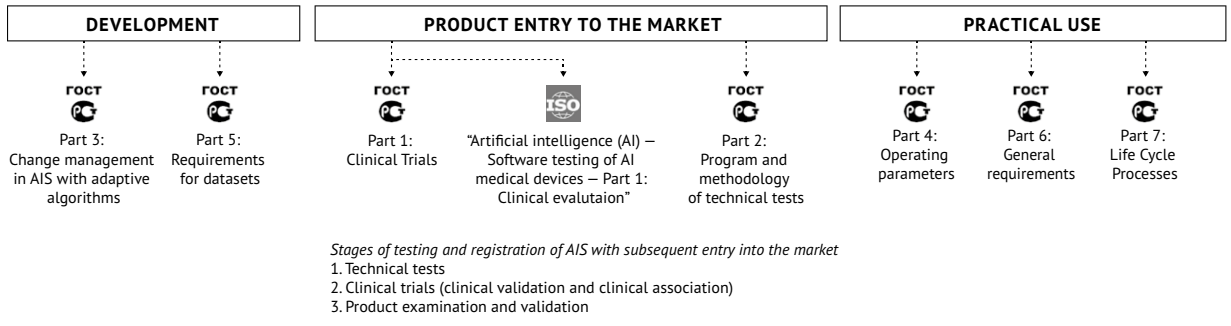

Fig. 1. Seven emerging standards in the field of artificial intelligence systems (AIS) regulation; GOST-state standard (Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health)

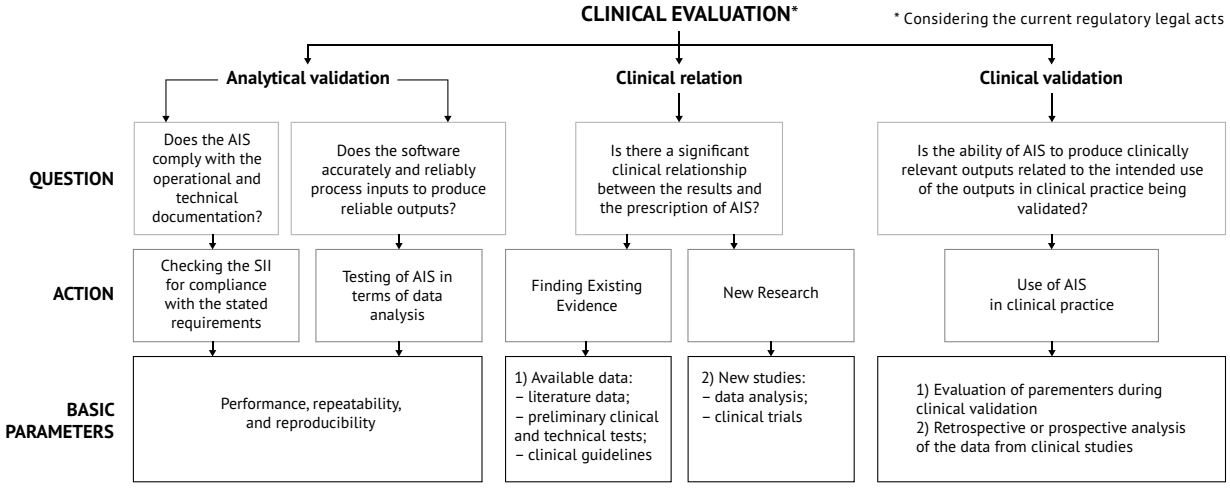

Fig. 2. Stages of clinical evaluation of artificial intelligence systems (AI); NLA: regulatory legal acts (Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health)

sents the current stages of work on the seven foundational standards.

The standard will establish the rules for conducting clinical trials (CT) to register AIS as a medical device; only medical organizations that are included in the register of Roszdravnadzor, with a license for this type of activity, can conduct the tests. The standard details the methodology for conducting CT, which is part of the clinical AIS evaluation. When compiling and developing the document, the experts of SC 01 relied on international documents and projects in the field of FDI regulation, as well as the Russian regulations and other works [25–27, 31–33]. Figure 2 presents the methodology for assessing AIS within the framework of technical tests (TT) and CT.

According to the presented methodology, the clinical assessment includes the following three components:

1) Clinical connection: confirmation of the scientific validity between the results and the appointment of AI;

2) Analytical Validation: Confirmation accurately, reproducibly, and reliably whether the AIS processes input data to create reliable output data;

3) Clinical validation: confirmation of the AIS ability to produce clinically significant outputs associated with the intended use of the output in clinical practice.

Within the framework of this standard and following the regulatory requirements, developing and evaluating AIS according to safety and quality requirements is necessary, especially for doctors and other representatives of medicine. The AIS should be "transparent" in understanding the medical professionals and protect the interests of doctors and patients in the field of confidentiality of personal information. Only in this case will it be possible to establish trusting relationships between doctors, patients, and developers [28–30, 34–36].

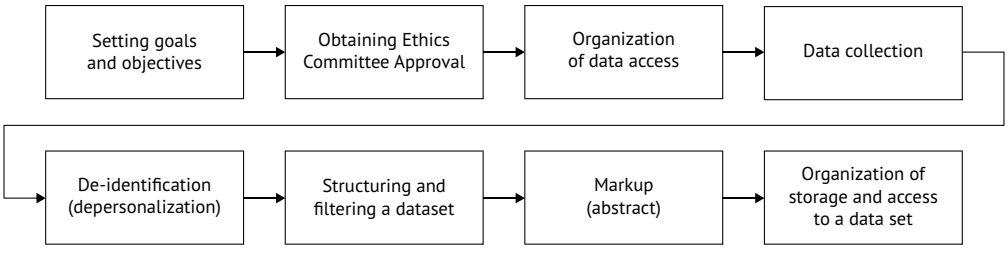

Fig. 3. The process of preparing a data set for training and testing artificial intelligence systems (Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health)

Moreover, the requirements for data sets used in testing AI should be clearly articulated to increase the credibility of AI. The Part 5 standard is fully devoted to this aspect, thus Part 1 briefly describes the requirements for data set formation for testing, as well as a standard set of indicators for assessing the effectiveness of AIS in clinical validation. Sensitivity, specificity, the predictive value of a positive result, the predictive value of a negative result, etc., are the main indicators in the field of assessing AIS within a clinical trial [18].

The concept of a quality management system is considered, which should be introduced into the work of the AIS developer following the current regulatory legal acts and confirmed by the relevant certificates. The presence of a quality management system for the registration authority (Roszdravnadzor) and medical organizations that purchase medical devices (consumers) after entering the market is an important indicator of confidence in the developed product.

GOST R "Artificial intelligence systems in clinical medicine. Part 2: Program and methodology of technical tests. The manufacturer must go through several stages, the first of which is the TT, to register an AI as a medical device and obtain a registration certificate. In the course of TT, AIS are checked for quality, as well as compliance with the declared regulatory documentation. They study the operational and technical documentation from AIS manufacturers and conduct or check tests according to the TT methodology for specific AIS. In the course of the TT, the AIS performs verification of compliance with safety, quality, risk management, and quality management system standards. Successful passing of the TT enables the manufacturers of AIS to proceed to the stage of passing the CT.

GOST R "Artificial intelligence systems in clinical medicine. Part 5: Requirements for the structure and procedure for using a data set for training and testing algorithms. Developing a test design and creating a data set for testing is necessary for reliable and high-quality TT and CT. In "Part 5," the requirements for the content of the data set, its creation, and the importance of data de-identification, as well as quality control and state registration of the verified data set, are indicated step by step. A separate chapter is devoted to the quality management system in the development, testing, and training of a data set. The annexes to the standard provide a developed list of metadata to assist in the dataset creation for both medical organizations for testing AIS, conducting trials, and training algorithms by manufacturers.

Figure 3 shows the process of preparing a data set, which can be changed in the conditions of specific tasks.

Standardizing approaches have been developed for managing changes in AIS with adaptive algorithms, assessing and monitoring operational parameters, in general, the concept of the life cycle of AIS (Fig. 4), and other fundamental points, except for the above standards. All the above-mentioned standards are necessary to ensure the proper quality, efficiency, and safety of the work of AIS, the reproducibility of results, on which, among other things, and the further development of healthcare.

In February 2020, Rosstandart adopted the "Prospective standardization program for 2020–2027." According to which, over 7 years, SC 01 experts plan to develop approximately 50 standards in the field of medicine and healthcare in ten main areas (Fig. 5).

According to the plan, fundamental standards will first be developed that govern the general requirements for AIS in healthcare. Experts have begun creating several national standards for specific areas of medicine: radiation and functional diagnostics, histology, remote monitoring systems, medical decision support systems, big data processing, image reconstruction, analytics, and forecasting, as well as educational healthcare programs.

Previously, such documents were shown to play an important economic role, and they become catalysts for innovation [37]. Standards create conditions for the development of innovative products and facilitate their entry into the markets, thereby facilitating distribution to the target audience.

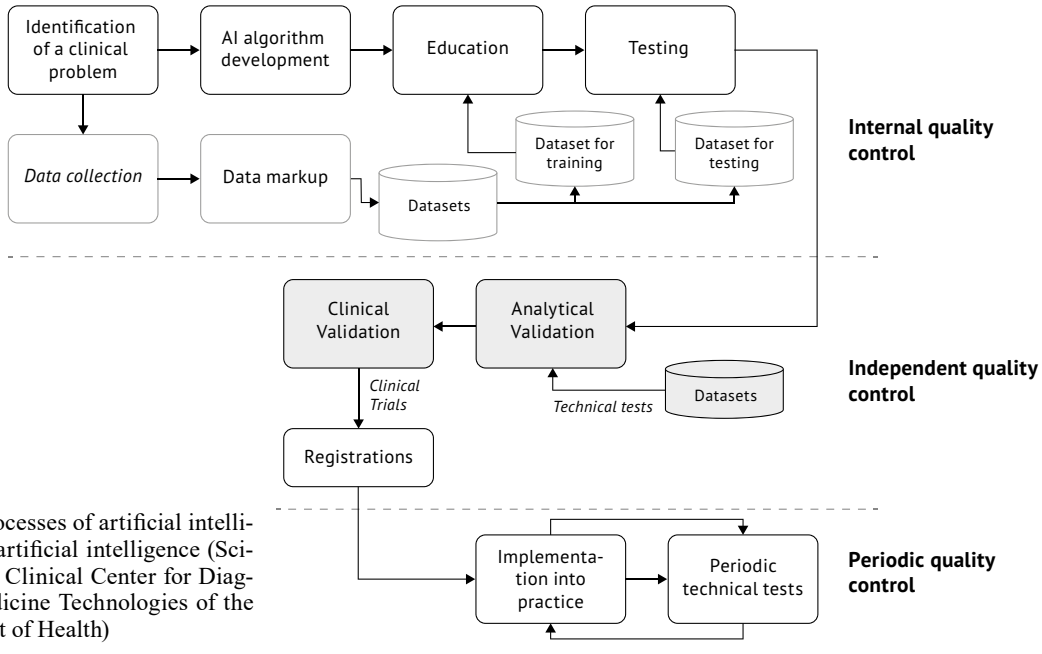

Fig. 4. Life cycle processes of artificial intelligence systems; AI: artificial intelligence (Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health)

Block **1** **General requirements**
Clinical and technical tests (2 GOST R). Estimation and control of parameters, adaptive algorithms, general requirements, and life cycle processes (4 GOST R). Glossary of terms, classification, QMS, risk management system, and ethical aspects (5 GOST R)

Block **2** **Radiation diagnostics**
General provisions (1 GOST R)
Development planned for 2021

Block **3** **Functional diagnostics**
General provisions (1 GOST R). SII for quality control of diagnostic data (1 GOST R). AIS for monitoring and optimizing the parameters of research protocols (1 GOST R).

Block **4** **Remote monitoring systems**
General requirements (1 GOST R). Remote monitoring of physiological functions. Requirements for processing, storage, and interpretation (1 GOST R). Remote monitoring of anthropometric data, the patient's motor activity, the severity of pain, and the degree of functional limitations (1 GOST R).

Block **5** **Histology**
Classification, sorting, and differential analysis of tissue and liquid samples (1 GOST R)

Block **6** **MDSS in health care**
General provisions (1 GOST R).

Block **7** **Image reconstruction**
Application of AI algorithm for image reconstruction. General provisions (1 GOST R).

Block **8** **Big data in healthcare**
General requirements. Format for presenting the results of analysis and forecast (3 GOSTR). Requirements for the transfer and storage of the algorithm results (1 GOST R)

Block **9** **Analytics and forecasting**
General requirements (1 GOST R). Routing and optimization of patient flow (1 GOST R). Analytics for segmentation and profiling of patients (1 GOST R).

Block **10** **Educational programs in healthcare**
Development of educational digital platforms (simulators) for obtaining practical skills in clinical disciplines (1 GOST R).

Block **11** **Metrological standards**
13 GOST R

Fig. 5. Forward-looking program for standardization in the field of medical devices for 2020–2027; GOST: state standard; LC: life cycle; QMS: quality management system; AIS: artificial intelligence system; MDSS: medical decision support system (Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health)

Additionally, they regulate the rules of innovation "competition," leveling small companies and large technology corporations.

Moreover, as previously shown [38], the introduction of standards can increase the trust in the "customer-supplier" chain and improve the relationships between developers and users of innovative products.

Discussion: the importance of the national health standards: prospects for legal regulation. The legal and regulatory framework for the development and application of AIS in healthcare is in its early stages of development. The current lack of standardization makes it difficult and sometimes impossible to compare different training datasets, as well as the characteristics of the AISs themselves. Currently, none of the foreign regulatory bodies has the proper expertise in the field of AI technologies. Thus, the experience of Russia is recognized by the international community in the face of ISO as the best since the development of a regulatory framework and fundamental standards are currently underway, directly for SII.

The use of standards by AIS developers has several important advantages. Firstly, it supports competition: ensuring equal conditions for all access to the necessary data for AIS development, opportunities for the application of experimental legal regimes, and government support measures. Secondly, a reduction in production costs, increased company image, production of high-quality and safe products, and socially-oriented nature of AIS:

the priority of human well-being (the goal of ensuring human well-being and security should prevail over other goals of AIS development and usage).

The standards will make it possible to minimize the likelihood of harm due to poor-quality or harmful work of AIS (the development, circulation, and use of AIS that is capable of causing harm to a person on their initiative, purposefully by action or inaction, should be prevented) and ensure the controllability of a person to the extent possible, considering the required degree of autonomy of AIS. They will also regulate the prevention of illegal AIS manipulation with human behavior.

Participation in the development of AIS manufacturer standards provides several advantages. They can design their service following the law, including security requirements, as well as apply their applied experience to develop the product and the infrastructure for their development.

Other benefits include the following:

– improving the performance and quality of IT products and systems;

– improving the security of IT systems and information;

– developing portable application software;

– improving the interoperability of IT products and systems;

– improving the unification of tools and development tools;

– improving the harmonization of the AI vocabulary in healthcare;

– improving the ergonomics of user interface design.

Conclusion. Currently, in Russia, regulatory and technical regulation in the field of AI is just beginning to take shape. Standardization in the field of AI in healthcare aimed to establish a trial process for AI that evaluates their safety, effectiveness, and quality. Additionally, the unification of best practices will structure the development, assessment, and control of security in the field of AI technologies and increase public confidence.

The standards will prescribe not only the development and testing stages of AIS but the entire life cycle to help the manufacturers, which will be applicable both in the work of accredited testing laboratories during the TI and the clinical trial to register the relevant MI as medical devices.

The methodologies underlying the standards represent the convergence of scientific and medical decisions in various fields. They will make it possible to give certainty in the order of clinical evaluation of AIS, give a structured answer in the field of reference data set formation, including metadata for them, as well as the quality management system and risk management concerning AIS.

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