Current issues of registration of medical devices

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CEO
FSBI "VNIIIMT" of Roszdravnadzor,
Doctor of Medical Sciences

OVER 34.5 THOUSAND REGISTERED IN TOTAL. MEDICAL DEVICES
(of which about 13 thousand are domestic production and more than 21 thousand are foreign production)

REGISTRATION PROCEDURES IN THE RUSSIAN FEDERATION

Decree of the Government of the Russian Federation **№ 1416**

Decree of the Government of the Russian Federation **№ 552**

Decree of the Government of the Russian Federation **№ 299**

Decree of the Government of the Russian Federation **№ 430**

* *Introduced in 2022 in connection with the introduction of restrictive economic measures against the Russian Federation*

* *Introduced in 2020 as part of measures to prevent the spread of a new coronavirus infection*

REGISTRATION PROCEDURE WITHIN THE EEC

Decision of the Council of the Eurasian Economic Commission № 46

More than 3.5 thousand medical devices have been registered under accelerated procedures

"ON APPROVAL OF THE RULES FOR ORGANIZING AND CONDUCTING INSPECTION OF PRODUCTION OF MEDICAL DEVICES FOR COMPLIANCE WITH IMPLEMENTATION REQUIREMENTS, MAINTENANCE AND EVALUATION OF THE QUALITY MANAGEMENT SYSTEM FOR MEDICAL DEVICES DEPENDING ON THE POTENTIAL RISK OF THEIR USE"

from 01.09.2022
took effect

29.12.2022 amendments were made to Decree of the Government of the Russian Federation No. 135
(approved by RF GD No. 2517)

from 01.01.2023 Edition No. 2 of the Decree of the Government of the Russian Federation No. 135 is in effect

Decree of the Government of the Russian Federation No. 135 **is proceed until 01.09.2028**

Manufacturing inspection is carried out in the next cases:

- carrying out examination of quality, efficiency and safety
- changing the address of the place of production of medical devices
- manufacture of medical devices that are made to individual orders (implantable medical devices)

EXCEPT:

Decree of the Government of the Russian Federation № 552

Decree of the Government of the Russian Federation № 430

Current problems of manufacturers during registration of medical devices

- Difficulties in choosing the optimal procedure for registration of medical devices by the manufacturer (RF GD 1416, RF GD 299, RF GD 430, RF GD 552, EEC Decision No. 46)
- Long terms of the process of preparing a package of documents for medical device registration (the average time for preparing a registration file by consulting companies is 1.5-2 years)
- High costs for preparing a registration file due to the inability to obtain all the necessary services in one place (development of documentation, technical tests, toxicological and clinical studies)
- The problem of choosing testing centers and medical institutions (27 TC (technical tests), 10 TC (toxicology research), > 300 medical organizations)

COMPLEX SERVICE-SUPPORT FOR MANUFACTURERS FOR BRINGING MEDICAL DEVICES TO THE MARKET "FAST TRACK"

PROCESS

STEP 1 DOCUMENTS DEVELOPMENT

STEP 2 CONDUCTING TESTS

STEP 3. PRELIMINARY ANALYSIS AND EVALUATION

apply for «Fast Track»

(on the website https://www.vniiimt.ru)

ADVANTAGES

9 Agreements on cooperation with testing laboratories

42 Cannouncements with National Medical Research Center and University

STRATEGY FOR WORKING WITH APPLICANTS "TURNKEY"

✓ the ability to carry out a full cycle of tests according to standards that are not available in the field of accreditation of VNIIIMT

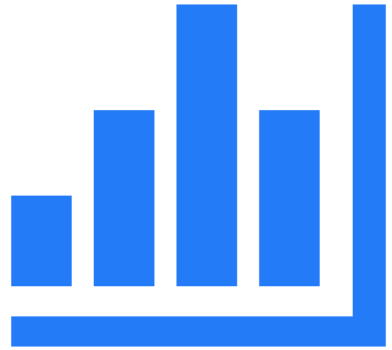
"FAST TRACK" – THIS IS A COMPLEX SERVICE SUPPORTING MANUFACTURERS FOR BRINGING MEDICAL DEVICES TO THE MARKET

The service may include:

- Finalization/development of technical/operational documentation
- Organization and conduct of technical tests
- Organization and conduct of toxicological studies
- Organization and conduct of clinical diagnostic researches in vitro
- Organization and conduct of tests to approve the type of measuring instruments
- Organization and support of clinical trials
- Preliminary analysis and evaluation of registration file
- Diagnostics of medical device manufacture — New service
- Finalization/development of quality management system/quality management system documentation — New service
- Implementation of quality management system/quality management system documentation — New service
- Instructing employees on the requirements of the quality management system/quality management system — New service
- Confirmation of compliance with quality management system/quality management system documentation — New service

STATISTICS OF COMPLEX SERVICE "Fast Track"

Average time from the moment of concluding the contract to receiving the registration certificate	≈5 months
Development of a set of technical and operational documentation	31 workday
Carrying out technical tests	26 workday
Conducting toxicological studies	28 workday
Preliminary analysis and evaluation of registration file	10 workday



RESULT

Contacted for – **692** MD

Received – **152** RC

Contact details

Please apply via email: **test@vniiimt.ru**

https://www.vniiimt.ru

info@vniiimt.ru

115522, Russian Federation,
Moscow, PO Box 135

Moscow, Kashirskoye highway, 24, building 16

VNIIIMT

Complex support service on introduction to the market of medical devices - Service «FAST TRACK»

Olga Isaeva,
Head of Center for Scientific Research and Advanced Developments

Problems and solutions

Manufacturer's problems during registration of medical devices

- lack of awareness of process of registration of medical devices
- Options of registration procedure
- Long registration period
- Inability to provide services on the principle of «One window» *(all services in one place)*
- High costs for the preparation of a registration file
- Low quality of a registration file's documents
- Difficulty to choose Testing Centers and medical organizations
- Sanctions policy
- Misunderstanding and disagreement with the opinion of the expert
- Stress due to potential changes and fear of missing a deadline

Ways of solving problems:

- State support programs
- Simplifying the registration procedure
- Interaction with manufacturers
- Turning to Professionals for Help

→ Reducing the time of medical device registration procedure

→ Reducing the registration procedure cost

→ Choice of Testing Centers and medical organizations

→ Training

Service «FAST TRACK»

service request, definition of a list of services

technical documentation, operational documentation, other documents

drawing up a contract, calculating the cost, invoicing

appointment of curator

finalization of documentation

providing samples for testing

organizing tests, registration of protocols

clinical trials, clinical laboratory trials

registration file analysis, formation of registration file

apply for the service FAST TRACK
(https://www.vniiimt.ru)

«Fast Track» application procedure

apply online on the website, write an official letter

attach the required documents

contract price calculation within 5 working days

agreement of contract price and terms

drawing up a contract, invoicing

apply for the service FAST TRACK
(https://www.vniiimt.ru)

How to apply:

- https://www.vniiimt.ru
- test@vniiimt.ru
- 115478, Россия, Москва, Каширское шоссе, д. 24, стр.16

Center for Scientific Research and Advanced Development

Long-term cooperation

- Contract for the long term
- All services in the framework of the one contract
- Individual approach to every applicant
- Any service in the field of circulation of medical devices on an individual basis

Cooperation expectations

- **Save time**
- **Free seminars** from experts
- **Budget Savings**
- **Obtaining a registration certificate** under the supervision of professionals and experts

Cooperation with national medical research centers and institutions of higher education

In accordance with the implementation of the Strategy for the Development of Medical Science in the Russian Federation for the period up to 2025 VNIIIMT concludes cooperation agreements on next issues:

- ✓ quality, efficiency and safety of medical devices being developed and put into circulation on the territory of the Russian Federation;
- ✓ development of the Russian circulation market, analysis of the state, equipment and use of medical devices
- ✓ quality control and safety of medical activities, including ensuring the safety of medical devices
- ✓ scientific research aimed at import substitution in the field of medical devices
- ✓ metrological support of healthcare

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Moscow, Kashirskoye highway, 24, building 16

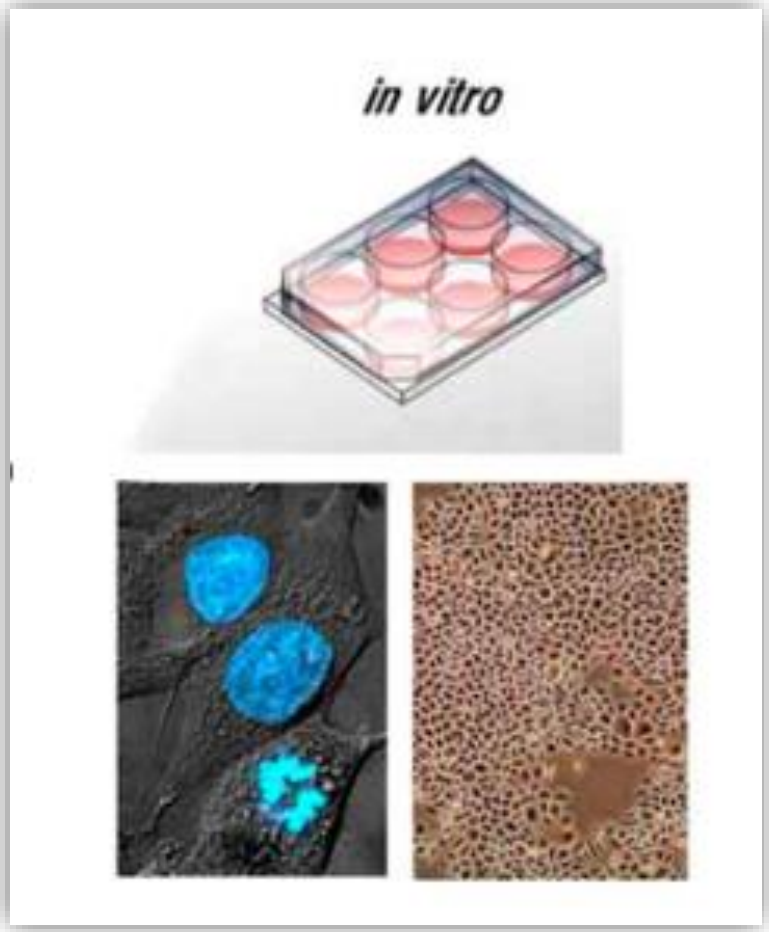
Kuvat Momynaliev
Assistant general manager
FBSI «VNIIIMT» of Roszdravnadzor

In vitro diagnostic medical devices (IVD) registration in Russia

In vitro diagnostic medical devices (IVD):

Medical device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.

IVD medical device include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological state



(ISO 18113-1:2009 «In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements»)

STATE REGISTRATION OF MEDICAL PRODUCTS

ORDER OF RUSSIAN GOVERNMENT № 1416 of December 27, 2012 «ON THE APPROVAL OF THE RULES STATE REGISTRATION OF MEDICAL DEVICES»

Registration certificate for a medical device issued indefinitely
Request if materials and information are insufficient (response to request within 50 working days)

ORDER OF RUSSIAN GOVERNMENT № 430 of April 3, 2020 «On certain specific features of the circulation of medical devices, including but not limited to the marketing authorisation of a batch (lot) of a medical device»

Registration certificate for a series (batch) of a medical device is issued until January 1, 2025
Request if materials and information are insufficient (response to request within 5 working days)

Government Resolution № 552 of April 1, 2022 «On the approval of specific features of the circulation, including specific features pertaining to the marketing authorisation, of medical devices in the event of deficiency or risk of possible deficiency which may occur due to the implementation of restrictive economic measures with regard to the Russian Federation»

Registration certificate for a medical device is issued until January 1, 2025
Request if materials and information are insufficient (response to request within 30 working days)

Government Resolution № 2026 of November 24, 2021 «About Unregistered *In Vitro* Diagnostic Medical Devices»

This Resolution entered into force on March 1, 2022 and valid until March 1, 2028

- ✓ rules for granting, re-issuing, confirming and canceling permission to use medical devices that are intended for diagnosing diseases by conducting studies of samples of human biological material outside the body, manufactured in a medical organization and applied in the medical organization that manufactured them
- ✓ requirements for medical organizations that manufacture and use medical devices that are intended for diagnosing diseases by conducting studies of samples of human biological material outside the body
- ✓ requirements for medical devices that are intended for diagnosing diseases by conducting studies of samples of human biological material outside the body, manufactured in a medical organization and applied in the medical organization that manufactured them

Decision № 144 of the Council of the Eurasian Economic Commission dated December 24, 2021
«On Amendments to the Rules of Registration and Examination of the Safety, Quality and Effectiveness of Medical Devices»
valid from July 18, 2022

«Second» level documents	*«Third» level documents*
○ Decision № 27 of the Council of the Eurasian Economic Commission dated February 12, 2016	○ Recommendation № 25 of the Board of the Eurasian Economic Commission dated November 12, 2018
○ Decision № 46 of the Council of the Eurasian Economic Commission dated February 12, 2016	○ Recommendation № 14 of the Board of the Eurasian Economic Commission dated May 21, 2019
○ Decision № 106 of the Council of the Eurasian Economic Commission dated November 10, 2017	○ Recommendation № 29 of the Board of the Eurasian Economic Commission dated October 08, 2019
○ Decision № 28 of the Council of the Eurasian Economic Commission dated February 12, 2016	○ Recommendation № 17 of the Board of the Eurasian Economic Commission dated September 04, 2017
○ Decision № 29 of the Council of the Eurasian Economic Commission dated February 12, 2016	○ Decision № 116 of the Board of the Eurasian Economic Commission dated July 24, 2018
○ Decision № 38 of the Council of the Eurasian Economic Commission dated May 16, 2016	○ Decision № 123 of the Board of the Eurasian Economic Commission dated July 24, 2018
○ Decision № 42 of the Council of the Eurasian Economic Commission dated February 12, 2016	
○ Decision № 173 of the Board of the Eurasian Economic Commission dated December 22, 2015	
○ Decision № 177 of the Board of the Eurasian Economic Commission dated December 29, 2015	
○ Decision № 174 of the Board of the Eurasian Economic Commission dated December 22, 2015	
○ Decision № 62 of the Board of the Eurasian Economic Commission dated April 16, 2019	
○ Decision № 26 of the Council of the Eurasian Economic Commission dated February 12, 2016	

According to Government Resolution № 1416 of December 27, 2012 «On the Rules State Registration of Medical Devices» for state registration of medical devices, the following documents:

✓ ***operational documentation*** *of the manufacturer (manufacturer) for the medical device, including the instruction manual or operating instructions of the medical device*

«Operation documents» *- documents intended to familiarize the user with the design of a medical device, subject to the terms and rules of operation (intended use, maintenance, repairs, storage and transportation), guaranteed by the manufacturer values of key parameters, the characteristics (properties) of the medical device warranties, as well as information about its disposal or destruction*

Decision № 27 of the Council of the Eurasian Economic Commission dated February 12, 2016 «On Approval of the General Requirements for the Safety and Effectiveness of Medical Devices, Requirements for Their Labeling and Operational Documentation for Them»

"instructions for use" - operational documentation containing information provided by the manufacturer to the user regarding the purpose, proper and safe use of a medical device, which may include, inter alia, an operating manual, a method of medical use, a passport, a form, installation and commissioning instructions , maintenance, repair, transportation, storage, disposal of a medical device

The concept of **"contraindications"** is not applicable to medical devices for *in vitro* diagnostics

Government Resolution № 2026 of November 24, 2021
«About Unregistered *In Vitro* Diagnostic Medical Devices»

OPERATIONAL DOCUMENTATION
APPLICATION NO. 4

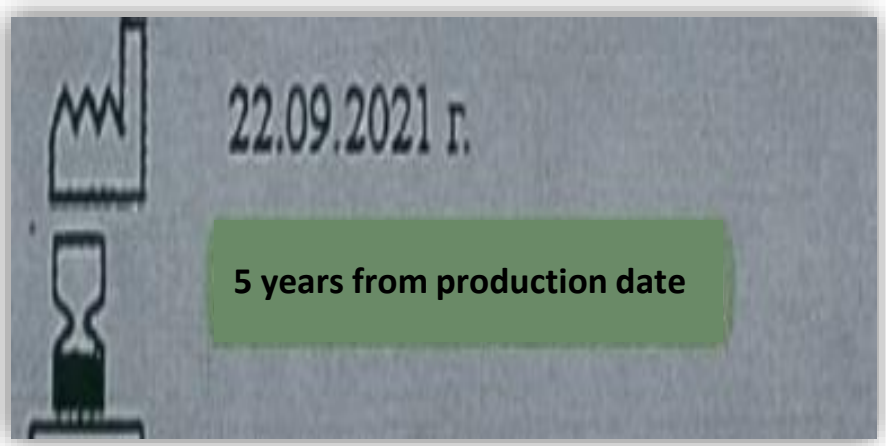
1. The name of a medical device, which is intended for diagnosing diseases by conducting research on samples of human biological material outside the body, is manufactured in a medical organization and is used in the medical organization that manufactured it *(hereinafter referred to as an unregistered medical device for in vitro diagnostics)*.

2. Full and abbreviated *(if available)* name of the medical organization, including business name, taxpayer identification number, address, location, and also telephone numbers and email address *(if available).*

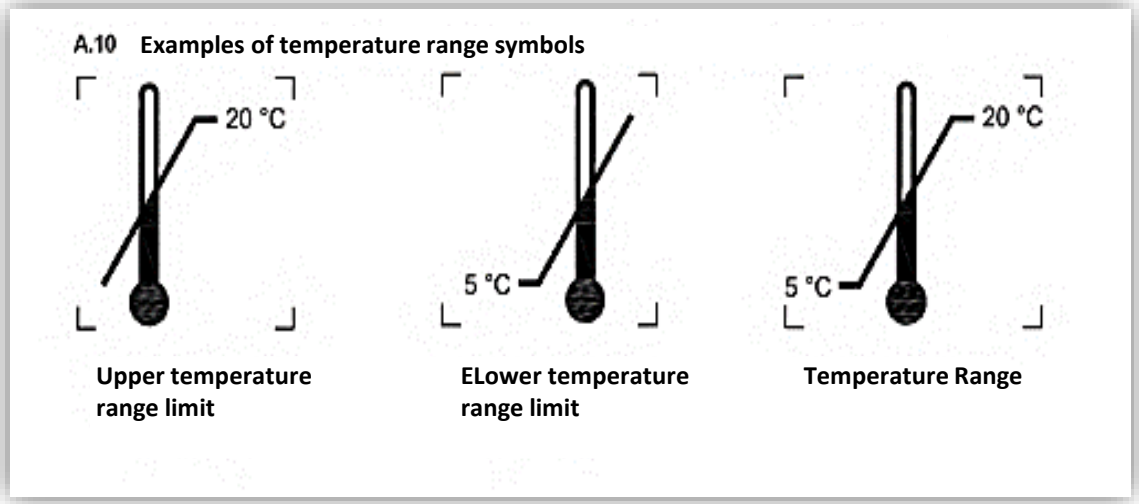
3. Place of manufacture of an unregistered medical device for *in vitro* diagnostics.

4. Type of medical device in accordance with the nomenclature classification of medical devices.

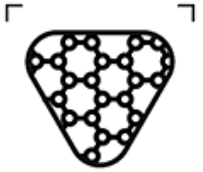
Examples of errors when preparing marking layouts for registration file



Examples of errors when preparing marking layouts for registration file



ISO 15223-1:2021(en) Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements

5.4.9		Contains human biological material	Indicates that the medical device contains biological tissues, human cells or their derivatives
5.4.10		Contains hazardous materials.	Indicates that the medical device contains carcinogenic, mutagenic, reprotoxic (CMR) substances or substances that disrupt the endocrine system
5.4.11		Contains nanomaterials	Indicates that the medical device contains nanomaterials
5.4.12		Multiple use per patient	Indicates that the medical device is intended for repeated use (multiple procedures) by a single patient

5.7.5		Medical center or doctor	Indicates the address of the medical center or doctor where patient information can be obtained	If used, the symbol should be placed next to the addresses of the medical center, doctor, or near the place intended for their notation
5.7.6		Date	Indicates the date the information was posted or the date of the medical procedure	If used, the symbol should be placed next to the relevant dates or near the space intended for their notation
5.7.7		Medical device	Indicates that this product is a medical device	-
5.7.8		Translation	Indicates that there is a translation of information about a medical device in addition to or instead of information in the original language	This symbol should be accompanied by the name and address of the person responsible for translating the information into another language, located next to the symbol

Examples of errors when preparing marking layouts for registration file (EEC)

- lack of full-color packaging layouts and labels with digital codes
- provision of information is not complete
- non-compliance with general requirements
- lack of registration certificate number
- the quantitative composition and volume of reagents are not indicated
- no special sign indicated

63	*It should be noted that this item is not stated in the information on the compliance of a medical device with general requirements.* *However, the label contains a sign* EAC MED

Government Resolution № 2026 of November 24, 2021 «About Unregistered *In Vitro* Diagnostic Medical Devices»

typical errors

- ✓ The name indicated in the application for permission does not correspond to the name in the technical and operational documentation
- ✓ The purpose specified in the application for permission does not correspond to the name in the technical and operational documentation
- ✓ The technical documentation does not contain information in full (application No. 3)
- ✓ The operational documentation does not contain information in full (application No. 4)
- ✓ Execution options are not defined
- ✓ Instead of a photographic image, marking layouts are presented
- ✓ The documents specified in clause 9 of the Rules are not presented in full (absent)

https://www.vniiimt.ru/

ОДНО ОКНО
Technical tests

ТЕХНИЧЕСКИЕ ИСПЫТАНИЯ
Technical tests

ТИПОВЫЕ ПРОГРАММЫ
Standard programs

СЕ МАРКИРОВКА
CE MARKING ILAC
Technical tests

КЛИНИКО-ЛАБОРАТОРНЫЕ ИСПЫТАНИЯ
Clinical and laboratory tests

ЭКСПЕРТИЗА
Expertise

ЭКСПЕРТИЗА КОМПЛЕКТУЮЩИХ МИ
Examination of MD components

МЕТРОЛОГИЯ
Metrology

Toxicological studies

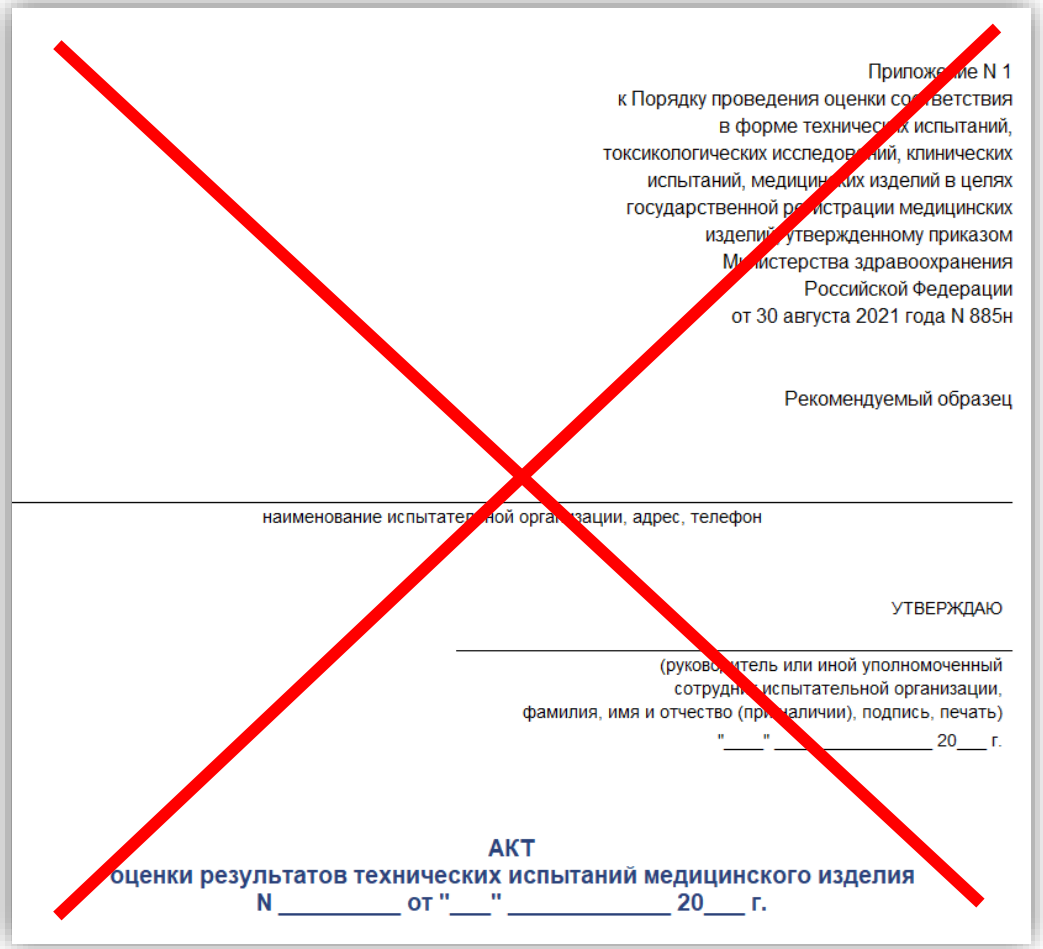
ТО И РЕМОНТ МТ
Maintenance and repair of medical equipment

Order of the Ministry of Health of the Russian Federation dated August 30, 2021 N 885n

«On approval of the Procedure for Conducting Conformity Assessments of Medical Devices in the Form of Technical Tests, Toxicological Studies, Test Results within the Framework of State Registration of Medical Devices»

into force on March 1, 2022 and valid until December 31, 2026

Conformity assessment of medical devices, which is carried out in the form of technical tests, toxicological studies, clinical trials of medical devices for the purpose of state registration of medical devices, including for the purpose of amending the documents contained in the registration dossier for a medical device, is carried out in accordance with this Procedure when compliance with the requirements of the current legislation of the Russian Federation on the circulation of medical devices, regulatory, technical documentation of the manufacturer (manufacturer) of the medical device, as well as documents of the national standardization system containing requirements, rules and methods of research (testing) and measurements of medical devices



Приложение N 1
к Порядку проведения оценки соответствия
в форме технических испытаний,
токсикологических исследований, клинических
испытаний, медицинских изделий в целях
государственной регистрации медицинских
изделий, утвержденному приказом
Министерства здравоохранения
Российской Федерации
от 30 августа 2021 года N 885н

Рекомендуемый образец

_____

наименование испытательной организации, адрес, телефон

УТВЕРЖДАЮ

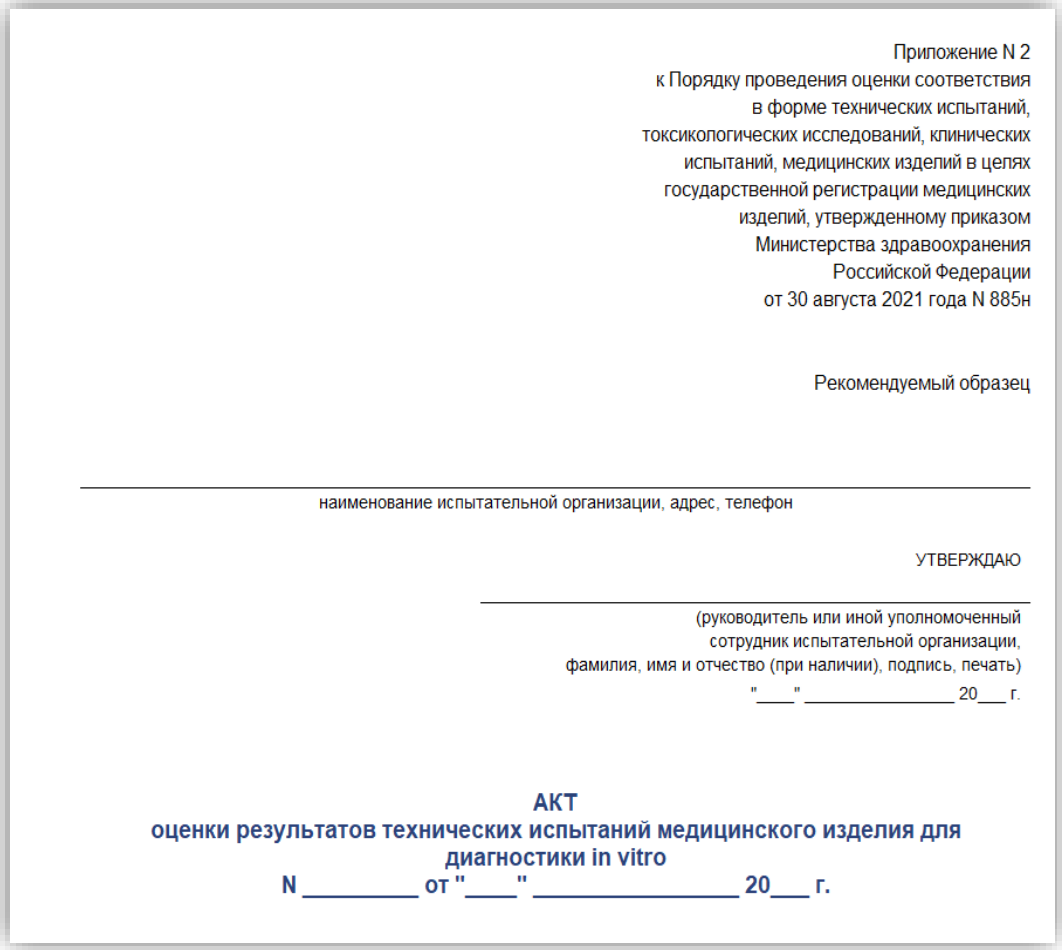
_____

(руководитель или иной уполномоченный
сотрудник испытательной организации,
фамилия, имя и отчество (при наличии), подпись, печать)

"____" _____ 20___ г.

АКТ
оценки результатов технических испытаний медицинского изделия
N _____ от "____" _____ 20___ г.

act of assessing the results of technical tests of a medical device



Приложение N 2
к Порядку проведения оценки соответствия
в форме технических испытаний,
токсикологических исследований, клинических
испытаний, медицинских изделий в целях
государственной регистрации медицинских
изделий, утвержденному приказом
Министерства здравоохранения
Российской Федерации
от 30 августа 2021 года N 885н

Рекомендуемый образец

_____

наименование испытательной организации, адрес, телефон

УТВЕРЖДАЮ

_____

(руководитель или иной уполномоченный
сотрудник испытательной организации,
фамилия, имя и отчество (при наличии), подпись, печать)

"____" _____ 20___ г.

АКТ
оценки результатов технических испытаний медицинского изделия для диагностики in vitro
N _____ от "____" _____ 20___ г.

act of assessing the results of technical tests of a medical device for *in vitro* diagnostics

Title of the document	Medical device of potential risk class				Medical device for in vitro diagnostics	
	1	2a	2б	3		
Document establishing requirements for the technical characteristics of a medical device	+	+	+	+	+	*certified by the manufacturer (authorized representative of the manufacturer)*
Protocols of technical tests carried out to prove the compliance of a medical device with the General Requirements, test programs or copies of these documents and (or) documents containing first-party evidence	+	+	+	+	+ *(excluding reagents, reagent kits, controls, calibrators, wash solutions and culture medium)*	*copies of the protocols are certified by the testing laboratory (center) or in accordance with the certification standards established by the legislation of the reference state; copies of programs are certified by the testing laboratory (center) or the manufacturer (authorized representative of the manufacturer);documents containing first party evidence are certified by the manufacturer*

Government Resolution № 552 of April 1, 2022 «On Approval of the Specifics of Circulation, Including the Specifics of State Registration, of Medical Devices in the Event of their Defectiveness or the Risk of a Defective Occurrence in Connection with the Introduction of Economic Restrictive Measures against the Russian Federation»

https://www.vniiimt.ru/

Typical test programs

Order of the Ministry of Health of the Russian Federation dated August 30, 2021 N 885n

«On approval of the Procedure for Conducting Conformity Assessments of Medical Devices in the Form of Technical Tests, Toxicological Studies, Test Results within the Framework of State Registration of Medical Devices»

To conduct clinical and laboratory studies of medical devices for in vitro diagnostics, the customer is:

a) an application for clinical and laboratory testing of medical devices for *in vitro* diagnostics

b) a sample (samples) of a medical device for *in vitro* diagnostics along with accessories necessary for using the medical device for its intended purpose

c) technical and operational documentation of the manufacturer (manufacturer) for the medical device for *in vitro diagnostics*

d) information on regulatory documentation for a medical device for *in vitro* diagnostics

e) documents confirming the results of technical tests of a medical device for *in vitro* diagnostics

Functional confirmation
Test methods:

- **Technical Documentation**
- **GOST R 51352-2013 «In vitro diagnostic medical devices. Test methods»**

5.2.7. Sensitivity assessment based on positive test results of certified positive seroconversion samples

5.2.7.1. The sensitivity of the diagnostic test during seroconversion must meet modern requirements. If further testing using the same or an additional seroconversion panel is performed by the testing authority, the results should confirm the original efficacy data. Seroconversion panels must begin with a negative blood sample(s) and have a minimum time interval between blood samples.

5.2.7.2. All positive samples must be confirmed as positive using the test article. A new product must have functional characteristics at least equivalent to those of a modern, previously tested product.

5.2.7.3. For products detecting antibodies to human immunodeficiency viruses, a minimum of 40 early HIV seroconversion samples must be analyzed. The results must meet modern requirements.

«Viam supervadet vadens» *(in Latin)*

Contact details

Please apply via email:

test@vniiimt.ru

https://www.vniiimt.ru

info@vniiimt.ru

115522, Russian Federation,
Moscow, PO Box 135

Moscow, Kashirskoye highway, 24, building 16

«Carrying out clinical tests during registration of a medical product»

Zinovieva Evgenia,
Deputy Head for Research Programs of the Center for Scientific Research and Advanced Development of the FSBI"VNIIIMT" of Roszdravnadzor, Ph.D.

Carrying out testing of medical devices

Carrying out tests within the Eurasian Economic Union

- Rules for conducting technical tests of medical devices, approved by the Council Decision Eurasian Economic Commission dated February 12, 2016 N 28
- Rules for conducting research (tests) to assess the biological effect of medical devices, approved by the Council Decision Eurasian Economic Commission dated May 16, 2016 N 38
- Rules for conducting clinical and clinical laboratory tests (research) of medical devices, approved by the Decision of the Council of the Eurasian Economic Commission dated February 12, 2016 N 29

The list of types of medical products subject to classification as measuring instruments upon registration, approved by Decision of the Council of the Eurasian Economic Commission dated February 12, 2016 N 42

Carrying out tests during state registration

The procedure for assessing the conformity of medical devices in the form of technical tests, toxicological studies, clinical trials for the purpose of state registration of medical devices, approved by order of the Ministry of Health of the Russian Federation dated August 30, 2021 N 885n

List of medical products related to measuring instruments in the field of state regulation of ensuring the uniformity of measurements, in respect of which tests are carried out in order to approve the type of measuring instruments, approved by Order of the Ministry of Health of August 15, 2012 N 89n

RF GD dated November 16, 2020 No. 1847 “On approval of the list of measurements related to the scope of state regulation of ensuring the uniformity of measurements (from January 1, 2021) pp. 1-3.

Clinical trial form

- *Decree No. 885n "On approval of the Procedure for assessing the conformity of medical devices in the form of technical tests, toxicological studies, clinical trials for the purposes of state registration of medical devices", section V:*

- *Clinical trials are underway*

- in the form of research (analysis and evaluation of clinical data)

- in the form of tests, including those involving humans, carried out to assess the safety and effectiveness of a medical device.

- *Please note that it is required to provide a sample(s) of the registered medical device, and in some cases, other medical devices to assess the functional qualities (for example, if consumables are registered).*

Clinical trial form

Clinical trials involving humans are carried out:

- New type of medical device
- The use of new complex, unique, special methods of prevention, diagnosis and treatment
- Application of new complex medical technologies
- During the analysis and evaluation of clinical data, the effectiveness and safety of the medical device are NOT confirmed
- The use of new materials that come into contact with the human body
- Contact of materials with the human body is longer than previously studied

- Clinical trials involving human participants are carried out in accordance with GOST R ISO 14155-2014 “Clinical trials. Proper clinical practice."

Clinical trial form

- ***Clinical trials in the form of research (analysis and evaluation of clinical data), the applicant provides to the Medical Organization:***
- *Statement*
- *Sample (MD samples)*
- *Permission to conduct clinical trials (except for low-risk medical devices, software, medical devices with features of state registration (430 and 552 RF PP), clinical trials when making changes to the Registration Dossier)*
- *Technical and operational documentation*
- *Information about regulatory documentation*
- *Color PHOTO 18x24 cm, labeling and packaging layouts (in Russian)*
- *Results of technical tests and toxicological studies*
- *Test results for the purpose of type approval of measuring instruments*
- *Data on the clinical use of MD outside the Russian Federation*
- *Notification of import into the territory of the Russian Federation*
- *Information about changes (when making changes to the Registration Dossier)*
- *Documents confirming the applicant's authority with a certified translation*

Clinical trial form

- ***Clinical trials in the form of research (analysis and evaluation of clinical data), the applicant provides to the Medical Organization:***
  - *The medical organization, within no more than 10 days, conducts a preliminary analysis to make a decision on the possibility of conducting a clinical trial.*
  - *The CO together with the applicant draws up the CI Program*
  - *When conducting a CT without human participation, the following is carried out:*

- Analysis and evaluation of clinical data presented by the applicant

- Assessment of information on clinically significant corrective actions taken, information on suspension of the use of medical devices, information on recalls of medical devices

- Analysis of scientific literature related to the intended use of the device and the intended method of its use

- Finalization of operational documentation

- Analysis and assessment of information about interchangeable medical devices (according to functional purpose, quality and technical characteristics and those capable of replacing each other)

- Registration and issuance of a Certificate of Evaluation of the Results of Clinical Trials.

Clinical trial form

During clinical trials, the following answers must be given:

- ❖Compliance of the medical device with regulatory, technical and operational documentation.
- ❖Completeness and reliability of the characteristics established by this documentation.
- ❖The quality of MD, clinical effectiveness and safety of its use (the use of MD must comply with existing treatment standards and clinical recommendations)

CT results are negative if:

- The MD does not correspond to the purpose and indications for use established in the operational documentation.
- Facts and circumstances have been established that create harm to the life of the patient and medical personnel when using MD.
- Severe actions and undesirable conditions that do not comply with operational documentation were identified.

Interchangeable medical devices

Federal Law of November 21, 2011 N 323-FL (as amended on December 28, 2022) “On the fundamentals of protecting the health of citizens in the Russian Federation” (with amendments and additions, which came into force on January 11, 2023)

Article 38 Medical devices

1. Medical devices are any instruments, devices, equipment, materials and other products used for medical purposes separately or in combination with each other, as well as together with other accessories necessary for using these products for their intended purpose, including special software , and intended by the manufacturer for the prevention, diagnosis, treatment and medical rehabilitation of diseases, monitoring the state of the human body, conducting medical research, restoration, replacement, changing the anatomical structure or physiological functions of the body, preventing or terminating pregnancy, the functional purpose of which is not realized through pharmacological, immunological , genetic or metabolic effects on the human body. Medical products can be recognized as interchangeable if they are comparable in functionality, quality and technical characteristics and are capable of replacing each other.

g) analysis and assessment of information about interchangeable medical products (medical products that are comparable in functionality, quality and technical characteristics and that can replace each other);

There are no concepts of equivalent medical devices or similar medical devices in the national legal framework!

Interchangeable medical devices

Approved
By decision of the council
Eurasian Economic Commission
dated February 12, 2016 N29

Rules
conducting clinical and clinical laboratory tests
(research) of medical devices

List of changing documents
(as amended by the decision of the Council of the Eurasian Economic Commission
dated 12/24/2021 N146)

“Clinical data” - Data on safety and (or) effectiveness obtained during the clinical use of a medical device. Clinical data are also data on safety and (or) effectiveness obtained during the clinical use of medical devices, the equivalence of which to the medical device in question can be proven;

6. Clinical data obtained for another medical device can be accepted for consideration only if evidence of its equivalence to the claimed medical product is provided and the following conditions are simultaneously met:
a) the medical products in question have the same purpose;
b) the technical and biological characteristics of the medical devices in question are the same to the extent that guarantees that there are no differences in their clinical effectiveness and safety.

The term “equivalence” appears in the legal field of the EAEU!

Взаимозаменяемые медицинские изделия

Approved
By decision of the council
Eurasian Economic Commission
dated February 12, 2016 N29

Rules
conducting clinical and clinical laboratory tests
(research) of medical devices

List of changing documents
(as amended by the decision of the Council of the Eurasian Economic Commission
dated 12/24/2021 N146)

3. The investigator's brochure must contain the following information about previously conducted tests of the medical device:
a) results of preclinical studies and tests;

b) available clinical data, including:

scientific literature data regarding the design, safety, effectiveness and purpose of similar or equivalent medical devices;

scientific literature data regarding the design, safety, effectiveness and purpose of similar or equivalent medical devices from the same manufacturer, including data on their time on the market, as well as information about any safety and effectiveness problems identified and corrective actions taken;

c) results of risk analysis, information about side effects and contraindications;

d) a list of possible adverse events (incidents) and adverse effects of the medical device;

e) a list of standards applied in full or in part.

Interchangeable medical devices

The problem of the "difficulty" of the concept of interchangeability:

- A huge variety of medical devices according to purpose, principle of operation, design features, level of complexity, technical characteristics.

- Positioning of MD by manufacturers as "Unique".

Division of medical devices into types in accordance with the nomenclature classification is the first step to determining their interchangeability.

A type of MD is a set of devices that have the same or similar purpose and/or common technology.

The global nomenclature of medical devices GMDN includes **over 27 thousand medical devices.**

The European Union Directive on medical devices provides for the possibility of not conducting a clinical trial for the purpose of admission to the market (except for medical devices of class 3 PRP) if there is clinical data on the safety and effectiveness of medical devices for which there is evidence of equivalence to the product in question.

Interchangeable medical devices

Approach of the Food and Drug Administration FDA, USA:

- The main condition for admission to the market is proof of “substantial equivalence” with at least one product;

- The period for materials review by FDA experts is 90 days.

MD are interchangeable if they have:

- Equivalent purpose;
- Equivalent functional technical and technological characteristics;
- Equal operating efficiency.

Algorithm for determining the interchangeability of medical devices:

1. Purpose analysis. Differences in indications for use should not be associated with differences in therapeutic/diagnostic efficacy and clinical safety of use.

2. Analysis of technical and technological characteristics. If the MD in question have differences, but they cannot affect clinical efficacy and safety, then such MD can be considered interchangeable.

Interchangeable medical devices

Algorithm for determining the interchangeability of medical devices:

3. Analysis of the completeness and specificity of descriptive information on the functioning of the MD under consideration.

4. Analysis of test and research results.

5. Determination of the equivalence of the functioning efficiency of the considered devices.
As a result, it is probably possible to form groups of interchangeable MD within the same type of MD.

- **Conclusion:**

If differences are identified in the parameters and characteristics of a product applied for registration and a previously registered product, it is recommended to provide a reasoned justification for the interchangeability of devices.

Clinical trial form

Typical admonition when conducting a clinical trial (a form of assessment and analysis of clinical data):

- A sample of a medical device has not been submitted (Section V, paragraph 38.b Order of the Ministry of Health of Russia dated August 30, 2021 No. 885n “On approval of the Procedure for assessing the conformity of medical devices in the form of technical tests, toxicological studies, clinical trials for the purpose of state registration of medical devices”

  In relation to medical devices, the installation (commissioning) of which requires obtaining permits (for example, licenses), major repairs, construction of individual capital structures and additional training of specialists, it is allowed to travel to the organization where the medical device is located and (or) permitted for use in accordance with the legislation of the country to which travel is carried out.
- It is recommended that operational documentation be provided for review by the consumer on paper (together with the medical device or separately from it) and in the form of an electronic document by posting on the Internet (Section III, paragraph 8. Order of the Ministry of Health of Russia dated January 19, 2017 No. 11n “On approval of requirements for the content of technical and operational documentation of the manufacturer (manufacturer) of a medical device.”).
- If differences in the parameters and characteristics of a product applied for registration and a previously registered product are identified, it is recommended to provide a reasoned justification for the interchangeability of the products.
- The Protocol or CT Act contains some information about another MD.
- CT not submitted, but required (Amendments to the Registration Dossier)

Clinical trial form

Typical admonition when conducting a clinical trial:

- The operational documentation does not contain sections “Side effects” and “Risks of use”. It is recommended to provide operational documentation with sections: risks of using a medical device, contraindications, expected and predictable side effects associated with the use of a medical device for its intended purpose (section III, paragraph 6.5. Order of the Ministry of Health of Russia dated January 19, 2017 No. 11n “On approval of requirements for the contents of the technical and operational documentation of the manufacturer (manufacturer) of the medical device.”).
- In the document “Instructions for Use”, taking into account home use, it is necessary to indicate information about the circumstances under which the consumer should consult with a medical professional (Section III, paragraph 19 of the Order of the Ministry of Health of Russia dated January 19, 2017 No. 11n “On approval of content requirements technical and operational documentation of the manufacturer (manufacturer) of the medical device.").
- In the presented comparison table, the registered devices is compared with the products included in the composition as accessories, and therefore, this comparison table cannot be accepted for consideration. Registered medical devices must be compared with medical devices registered in the Russian Federation, and not with their accessories.
- The Purpose, Indications and Contraindications for use contain non-specific information, “and others, etc.” are used, non-commonly used medical terminology such as “increased blood pressure” is used, and unspecified information “diseases of the endocrine system” is used.

Clinical trial form

Comparison parameter	Registered device	Comparison device
xx	xx	xx
Comment	Reasoned justification	

- *Order of the Ministry of Health of Russia dated June 16, 2012 No. 4n "On approval of the nomenclature classification of medical devices."*
- *Order of the Ministry of Health of the Russian Federation dated January 19, 2017 No. 11n "On approval of the requirements for the content of technical and operational documentation of the manufacturer (manufacturer) of a medical device."*
- *Order of the Ministry of Health of the Russian Federation dated August 30, 2021 No. 885n "On approval of the Procedure for assessing the conformity of medical devices in the form of technical tests, toxicological studies, clinical trials for the purpose of state registration of medical devices."*
- *Methodological recommendations No. 20 "Clinical trials of artificial intelligence systems (radiation diagnostics)", prepared by the State Budgetary Institution "Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health", 2023.*
- *GOST R IEC 62304-2013 "Medical products. Software. Life cycle processes"*

Conducting clinical trials during registration of a medical product with artificial intelligence

Medical Device - Artificial Intelligence Software

- **Medical decision support system for analyzing diagnostic or screening studies:**

A) formation of a binary response;

B) formation of a quantitative answer;

- **Medical decision support system for prescribing drug therapy;**

- **Medical decision support system during a diagnostic test or surgical procedure: marking the area of interest, warning about anatomically dangerous areas;**

- ***The design of clinical trials of such medical devices cannot be the same!***

- **A binary classifier is usually called a rule that allows one to classify an observation or a group of observations into one of two known or experimentally determined classes with some accuracy.**

- **Application of binary classifiers: diagnostic models (based on a number of tests). The purpose of a diagnostic test is to determine the presence or absence of a disease, depending on the results of the tests needed to make a diagnosis.**
- **Therefore, the following important tasks for the clinician are solved: reducing test results, which are often difficult to visually interpret, to a simple and understandable division into two classes (sick/healthy).**

- **This approach allows us to determine a probabilistic assessment of the presence or absence of a disease, which makes it possible to reduce the degree of uncertainty in decision making.**

GOST R 59921.1-2022 “Artificial intelligence systems in clinical medicine. Part 1. Clinical assessment"
Introduction date: from September 1, 2022.
164 “Artificial Intelligence”

GOST R 59921.5 Artificial intelligence systems in clinical medicine. Part 5. Requirements for the structure and order of using a data set for training and testing algorithms

- General approaches to clinical assessment
“The artificial intelligence system does not have a direct impact on patients and medical personnel, but performs interpretation when processing data and presents the result to the user, including for the purpose of supporting medical decision-making.”

- All declared parameters of the effectiveness and safety of MD must be confirmed by data during clinical trials!

GOST R 59921.1-2022 "Artificial intelligence systems in clinical medicine. Part 1. Clinical assessment"

Introduction date: from September 1, 2022.

164 "Artificial Intelligence"

Artificial intelligence: A set of technological solutions that allows you to imitate human cognitive functions (including self-learning, searching for solutions without a predetermined algorithm and achieving insight) and obtaining results when performing specific practically significant data processing tasks **that are comparable, at least, with the results of intellectual human activity**

GOST R 59921.1-2022 "Artificial intelligence systems in clinical medicine. Part 1. Clinical assessment"

The methodology for conducting a clinical trial (study) *of an artificial intelligence system involves using a data set as a research subject, which was obtained with human participation through retrospective analysis.*

- It should be noted that there are systems to support medical decision-making during a diagnostic test or surgical procedure: marking the area of interest, warning about anatomically dangerous areas.
- ***Retrospective analysis?***
- ***Clinical trials involving humans?***
- ***Combined design?***

GOST R 59921.1-2022 "Artificial intelligence systems in clinical medicine. Part 1. Clinical assessment"

- **Clinical validation:** Confirmation of the ability of an artificial intelligence system to produce clinically relevant output data associated with the intended use of the artificial intelligence system within the manufacturer's specified functional purpose.

- **Clinical association:** Scientific substantiation of the compliance of the results of the artificial intelligence system with its functional purpose established by the manufacturer (manufacturer).

- **Clinical evaluation:** The result of the process of analyzing and evaluating clinical data related to a medical device to verify the manufacturer's claims of clinical effectiveness and the clinical safety of the device when used as intended and under the conditions intended by the manufacturer.

GOST R 59921.1-2022 "Artificial intelligence systems in clinical medicine. Part 1. Clinical assessment"

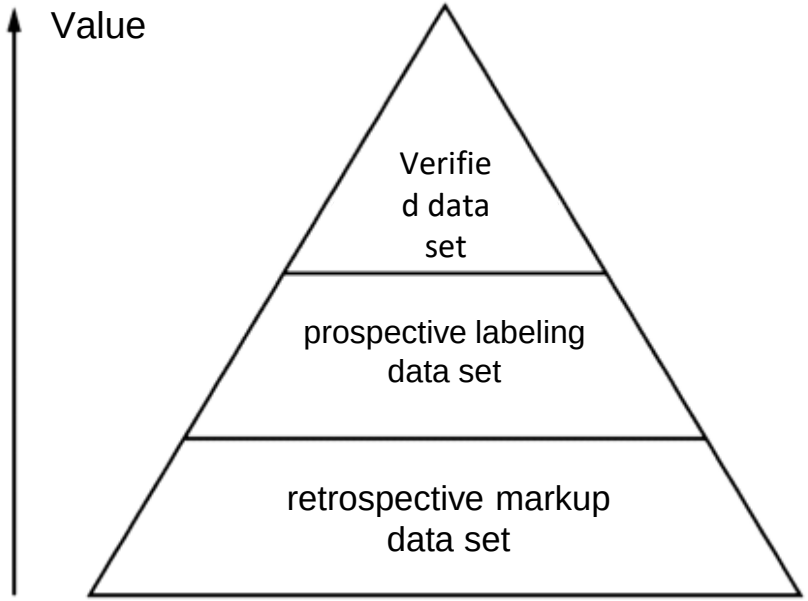
- **Data set: A** set of data that has undergone preliminary preparation (processing) in accordance with the requirements of the legislation of the Russian Federation on information, information technology and information protection and the need for the development of software based on artificial intelligence.
- **Software as a medical device:** Software intended by the manufacturer for medical use that is not a component and/or accessory of another medical device.
- **Sensitivity:** The proportion of individuals testing positive for the target population with the disease being studied (i.e., the likelihood that subjects with the disease being studied will be identified as pathological).
- **Specificity:** The proportion of individuals in the target population who test negative without the disease being studied (i.e., the probability that subjects without the disease being studied will be identified as healthy).

GOST R 59921.5-2022 "Artificial intelligence systems in clinical medicine. Part 5. Requirements for the structure and order of using a data set for training and testing algorithms"

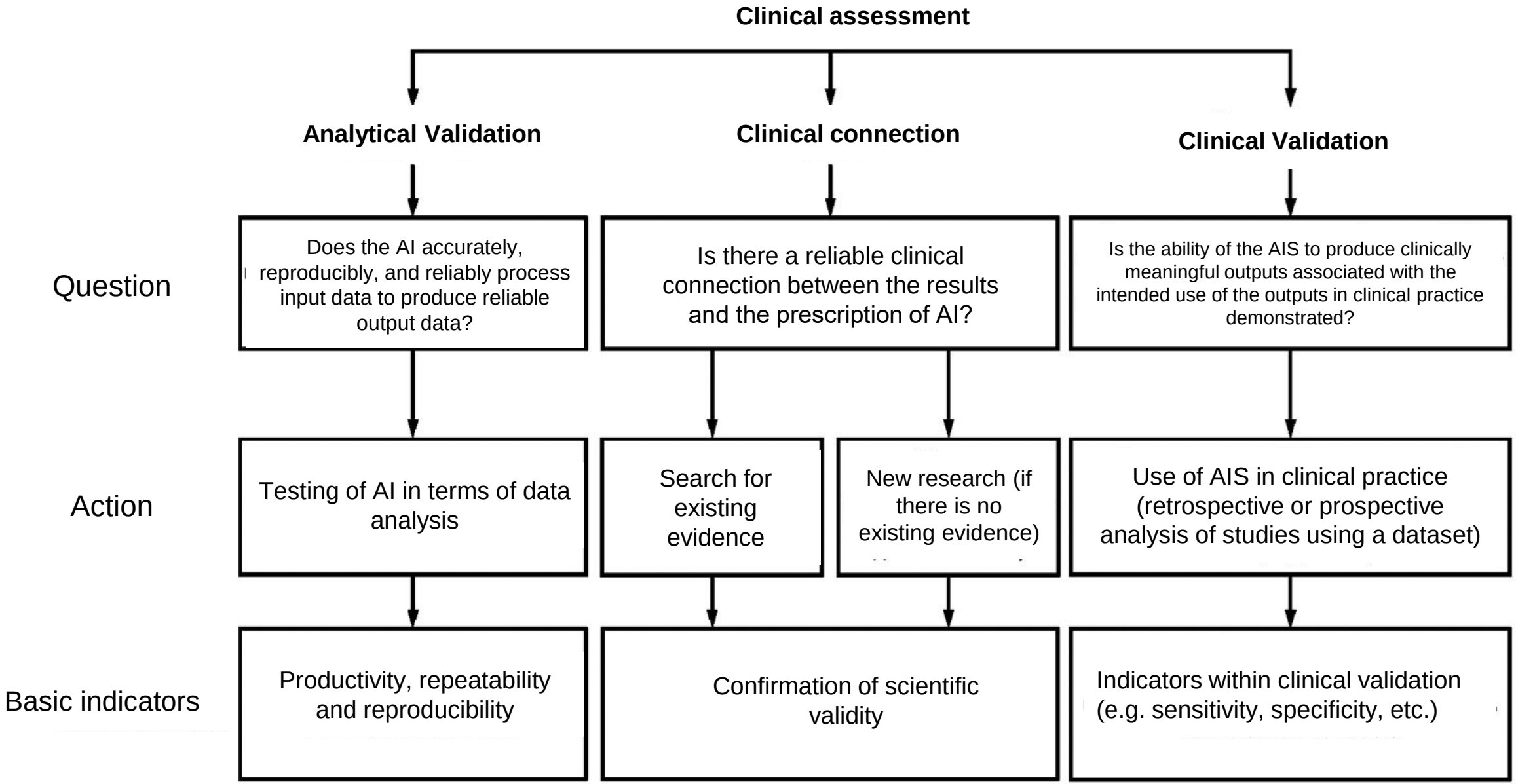
- 3 types of data set:

Retrospective markup is a collection of elements in accordance with the specified metadata, the list of which is selected in accordance with the intended purpose. This marking is carried out by downloading data from the medical information system. Retrospective markup does not involve any manipulation or processing of elements. For each element of the data set, a correspondence with medical information (diagnosis, laboratory test results, etc.) is established. Such marking requires the participation of a physician, but can be performed by a technician who has experience working with data sets.

Prospective markup is the collection of elements in accordance with the intended purpose, as well as carrying out additional manipulations with the elements (for example, suspending the start and end marks of an event, sign detection marks, pathology designations, etc.). Such marking is carried out with the participation of trained medical personnel by manually annotating the content of the data or parts thereof, which can be done in graphical or textual form, or a combination.



A verified data set is obtained by supplementing the data set prepared by prospective labeling with data from medical records, including the final and/or pathological diagnosis. As a method for verifying a data set, you can use the "gold standard" method for the target pathology, re-examination of the patient after a certain time, the results of pathological, immunological studies.


Clinical assessment
Analytical Validation
Clinical connection
Clinical Validation
Question
Does the AI accurately, reproducibly, and reliably process input data to produce reliable output data?
Is there a reliable clinical connection between the results and the prescription of AI?
Is the ability of the AIS to produce clinically meaningful outputs associated with the intended use of the outputs in clinical practice demonstrated?
Action
Testing of AI in terms of data analysis
Search for existing evidence
New research (if there is no existing evidence)
Use of AIS in clinical practice (retrospective or prospective analysis of studies using a dataset)
Basic indicators
Productivity, repeatability and reproducibility
Confirmation of scientific validity
Indicators within clinical validation (e.g. sensitivity, specificity, etc.)

Stages of clinical evaluation

- ***Analytical Validation:***
- confirming and providing objective evidence that the software has been properly designed to correctly and reliably process input data and generate output data with an appropriate level of accuracy and repeatability and reproducibility;
- confirmation that the AI meets the stated requirements of the manufacturer, and that the requirements for the AI meet the user's needs and intended use.

- ***Clinical connection:***
- As part of the assessment of clinical communication, it is necessary to justify the compliance of the output data of the AI with the functional purpose declared by the manufacturer.
- The determination of a clinical connection is carried out by analyzing existing data or obtaining new information that substantiates the existence of a connection between the output data of the SII and its functional purpose: literature data, approved clinical recommendations.

- ***Clinical Validation:***
- Clinical validation **consists of assessing effectiveness** (confirmation of achievement of the intended goal in the target sample in practical application using the output data).
- For the purpose of clinical validation of SII, a CI design is developed and, in accordance with it, researchers create a data set.

Rules for forming the Design of clinical trials of medical devices with Artificial Intelligence

- **Clinical validation of the AI is carried out on a data set that was not used for training, tuning and initial evaluation of the AI.**

- In addition to calculating clinical validation indicators (sensitivity, specificity, etc.), at this stage the model's stability to changes in input data (for example, data from another medical organization that did not participate in the training process) should be tested.

- Based on the results of the clinical connection assessment and clinical validation, reporting documents are drawn up confirming the results of clinical trials (studies) of the AI.

- Experts and researchers participating in the conduct of clinical trials and the subsequent evaluation of the results obtained must have qualifications confirmed by training, internship or experience in specialization in accordance with the purpose of the research institute, which must be confirmed by information about education, professional certification/licenses, status in professional/scientific associations/organizations.

Features of composing up a CT Program with AI

- **The CI program is developed in accordance with the description of the purpose of the AI,** the analysis of data regarding the operational **characteristics of the AI,** and the intended method of application.

- The clinical trial program should be designed so that the received trial results allow an assessment of the suitability of the study AI for the purpose(s) and patient population(s) for which it is intended, as well as its clinical efficacy.

- The CT program must clearly define the hypothesis and objectives of the CT (primary and secondary), as well as the sample size, declared characteristics and expected effectiveness of the device that should be verified.

- The CT program must indicate methods for analyzing and processing data, including statistical methods for justifying the sample size.

- Conducting clinical trials with human participants is recommended for medical software products with artificial intelligence intended to assist medical decision-making directly during a diagnostic study or medical procedure/operation, if the design of the clinical trial does not allow you to prove the declared characteristics using test databases.

Features of composing up a CT Program with AI

- **It is necessary to confirm all declared nosologies or declared characteristics** that are significant for clinical use (for each nosology of the defined cancer, for each degree of lung damage, for each quantitative parameter - for example, the size of the pathological focus in the brain).

- To confirm clinical effectiveness, i**t is recommended to indicate for each declared characteristic its own parameters of evidence of effectiveness that can be controlled** (for example, sensitivity, specificity, accuracy for each nosology separately).

- **It is recommended to conduct reproducibility tests of the results** obtained on a test base with assessment and analysis of reproducibility by a medical organization.
- **For prognostic DSS,** it is recommended to calculate and analyze the Relative Risk, absolute risk changes, Threat Ratio with the calculation of the confidence interval

Preparation of documentation for clinical trials

- Reporting documents based on the results of clinical trials must be drawn up in accordance with GOST R ISO 14155 and current regulations.

- The applicant and principal investigator must retain clinical trial reporting documents in accordance with applicable regulatory requirements, but **for a minimum of three years from the date of completion of the clinical trial.**

- Completion procedures must be conducted to confirm that all documents required by the applicant have been received, the AI has been uninstalled, previously identified issues have been resolved, and all parties have been notified.

Suspension or termination of CT (features)

- AI software failure.
- Revision of the CI program during testing.
- I**f monitoring or auditing of clinical trials reveals serious or repeated deviations** on the part of the investigator. (opportunity to participate in a clinical trial at a specific research center).

Effectiveness indicators

- **The size of the data set (sample size)** for assessing the characteristics of the AI is established using methods for determining the sample size for proportions and taking into account the rules of statistics (using a method for establishing the required accuracy for the estimated sensitivity, specificity).
- When conducting clinical validation, **it is necessary to use a verified data set.**
- For each specific case of using AII, researchers must set parameters for the effectiveness of AI, and indicators from the manufacturer for AII must be transferred for verification within the framework of a clinical trial.

Clinical efficacy assessment (binary system)

Result type			
True Positive (TP)	True Negative (TN)	False Positive (FP)	False negative (FN)
AI detected pathology if present	AI did not reveal pathology in its absence	AI revealed pathology in its absence	AI did not reveal pathology if present

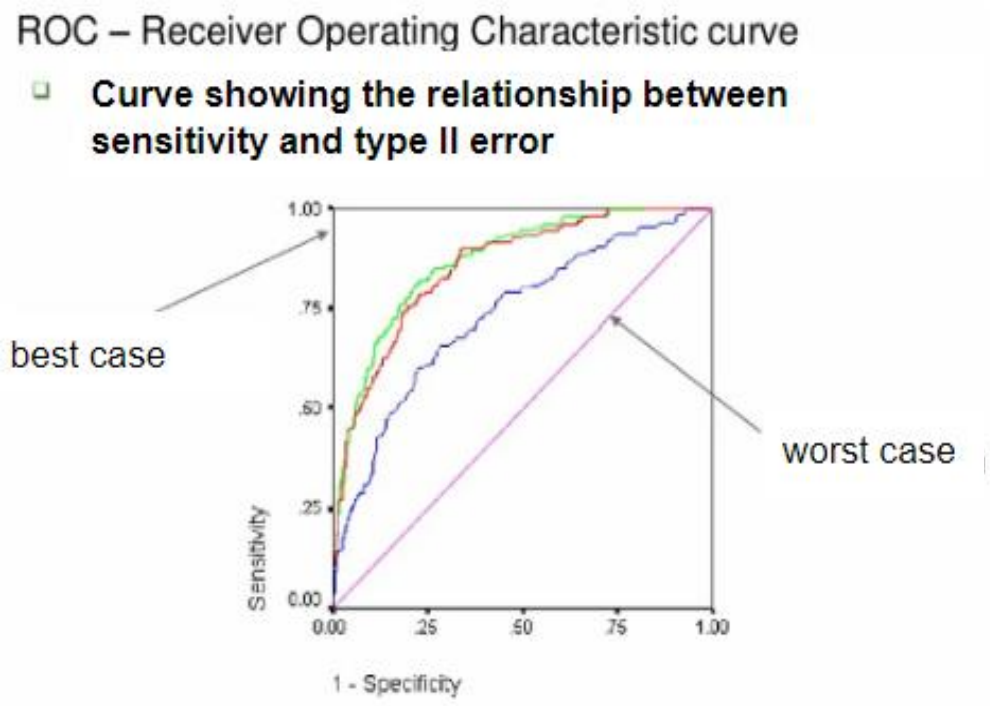
Clinical efficacy assessment (binary system)

Indicator	Meaning	Formula
Sensitiveness	Proportion of persons with a negative result of the AI in the target population without the disease being studied	TP/(TP + FN)
Specificity **Precision**	Proportion of persons with a negative result of the AI in the target population without the disease being studied Proportion of correct results among all examined people	TN/(TN + FP) TP+TN
Positive predictive value (PPV)	Probability of disease with a positive AI result	TP/(TP + FP)
Negative predictive value (NPV)	Probability of absence of disease with a negative (normal) AI result	TN/(TN + FN)
Positive Likelihood Ratio (LR+)	Mathematically displays how many times with a positive AI result the probability of the presence of the target pathology exceeds the probability of its absence	Sensitiveness/(1-специфичность)
Negative likelihood ratio (LR-)	Mathematically displays how many times with a negative AIresult the probability of the presence of the target pathology exceeds the probability of its absence	(1-чувствительность)/специфичность

- **ROC - the curve shows the dependence of the number of correctly classified positive results on the number of incorrectly classified negative results in graphical form.**

- An ideal discriminator and identifier will have an ROC curve that passes through the upper left corner. The percentage of true positive and negative cases in this situation is 100%, and the percentage of false positive and false negative results is zero.
- The approximation of the ROC curve to the diagonal line indicates the ineffectiveness of the studied AI software.

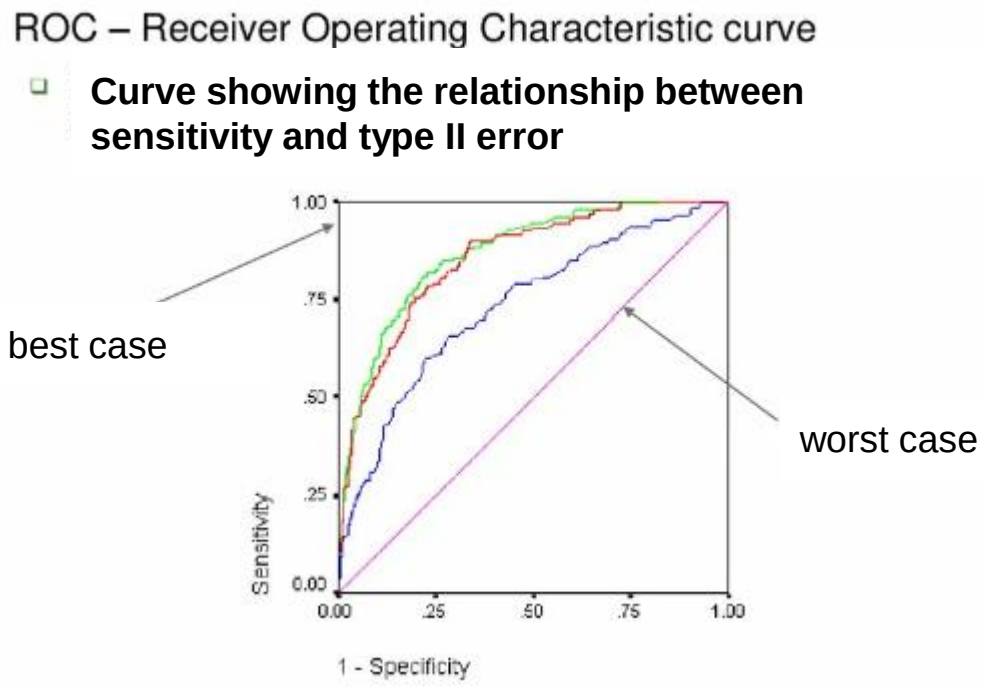
The result of the studied method / test / model	Actual state of the research object	
	Positive	Negative
Positive	TP (True Positives)	FP (False Positives)
Negative	FN (False Negatives)	TN (True Negatives)



- **ROC - the curve shows the dependence of the number of correctly classified positive results on the number of incorrectly classified negative results in graphical form.**

  - **Estimation of the area under the ROC curve is used for comparative analysis of several studied methods: the larger the area under the ROC curve, the higher the diagnostic information content of the classifier.**
  - **<u>Conventionally, there is the following relationship between the information content of the method being studied and the area under the ROC curve:</u>**

- **for high information content,** an area equal to 0,9-1,0,
- **for good** – 0,8-0,9,
- **for average** – 0,7-0,8,
- **for satisfactory** – 0,6-0,7,
- **for unsatisfactory** – менее 0,6.



Calculation of necessary sample size

All methods for determining the sample size can be divided into 2 groups:

- **First group:** methods that do not require prior knowledge of the phenomenon being studied.

- **Second group:** methods that require the researcher to have prior knowledge of what will be investigated.

Methods that do not require prior knowledge about the phenomenon being studied:

- Methodology by K.A. Otdelnova new.
- Methodology by V.I. Paniotto.
- Table N.Fox.

Methods that require prior knowledge depend on:

- Type of characteristics being studied: quantitative or qualitative
- **General summation**: known/unknown

The use of statistical calculators is recommended.

Methodology by K.A. Otdelnova [1980]:

Significance level (p)	Accuracy level		
	Indicative Introduction	Average Accuracy Study	Increased Accuracy Study
0,05	44	100	400
0,01	100	225	900

Methodology by V.I. Paniotto at significance level 0,05 [1982]:

General summation volume	500	1000	2000	3000	4000	5000	10000	100000	∞
Sample size	222	286	333	350	360	370	385	398	400

This table shows the correlation between the size of the population and the required sample size at a significance level of 0.05

Methodology N.Fox [2007]:

Provides for estimation of error to determine the required sample size

Amount of permissible error, %	Sample size
10	88
5	350
3	971
2	2188
1	8750

When using available clinical data, it is possible to reduce the sample size, which will be statistically significant, in GOST R ISO 14155-2022 consider this possibility in the case of a combined clinical trial design.

Recommended form of report on the clinical component of preliminary clinical and technical tests of software with AI (postscript A, reference GOST R 59921.1-2022)

Summary	Structured presentation of research design, materials, methods, results and conclusions
Purpose, tasks and final result of PCTT	Structured presentation of research design, materials, methods, results and conclusions
Data set	Detailed description of data sets used for PCTT
Data type	Type(s) of data (medical records, research results, etc.), research modalities, other characteristics
Number of clinical cases included	Number of clinical cases included (patients, study results, etc.)
Sample characteristics	Population characteristics (racial, gender, demographic, other characteristics)
Characteristics of data set and markup	Information about where and when the data set was generated indicating key characteristics (state registration of the database, information about depersonalization, the availability of informed voluntary consent of patients, inclusion/exclusion criteria, sources of clinical cases). Method for preparing (tagging) a data set

Recommended form of report on the clinical component of preliminary clinical and technical tests of software with AI (postscript A, reference GOST R 59921.1-2022)

Characteristics of pathology in the data set	Target pathology and diagnostic groups with their distribution. Verification method and availability of relevant information in the data set
Data set generation method	The data set is formed sequentially, randomly, or by other means. Sample size rationale
Data sources	Number and location of medical facilities that served as sources of clinical cases included in the PCTT
Independence mark PCTT	The data set used for the PCTT must not be used in whole or in part for training or calibration of the index test
Testing AI on a dataset	Information about use, installation, access organization and other characteristics of AI testing on a data set

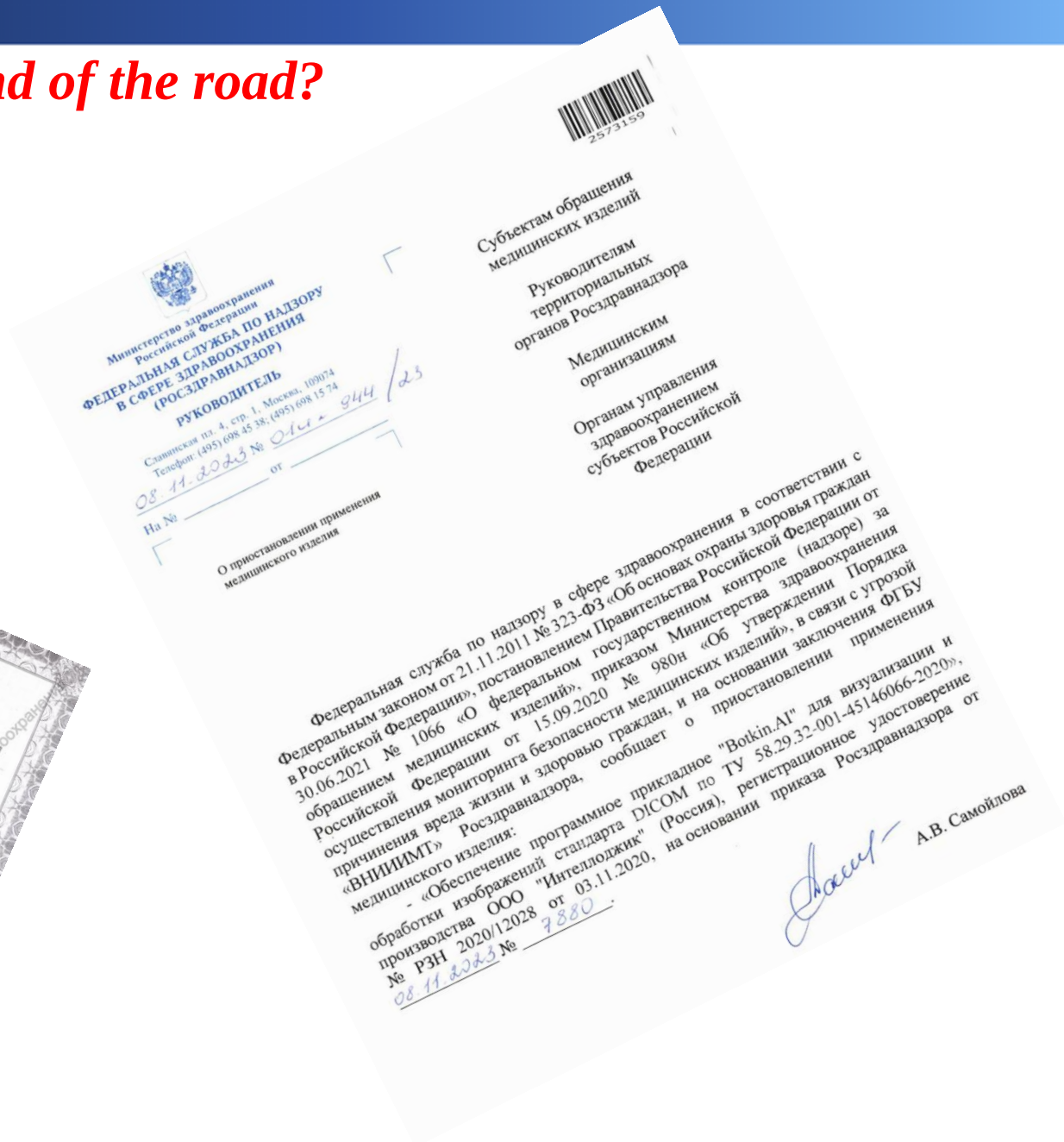
Recommended form of report on the clinical component of preliminary clinical and technical tests of software with AI (postscript A, reference GOST R 59921.1-2022)

Results table	Комбинированная таблица результатов сравнения показателя набора данных и результата тестирования СИИ на наборе данных
Activation limit	Cut-off point for testing AI on a data set, including dividing outcomes into “expected” and “unexpected”
Diagnostic accuracy indicators	Diagnostic accuracy metrics with 95% confidence interval (sensitivity, specificity, overall accuracy, area under the characteristic curve, etc.)
Restrictions	Any limitations of PCTT, including sources of systematic errors, statistical inaccuracies and generalizations. Any significant differences in the methods for generating a data set and testing the AI on a data set
Conclusions	Summary of results

The formation of CT documents is regulated by decree of the Russian Ministry of Health No. 885n.

Is receiving a registration certificate not the end of the road?

- On the official website of Roszdravnadzor on November 8, 2023, an information letter was published on the suspension of the use of the medical device "Software application "Botkin.AI" for visualization and image processing of the DICOM standard according to TU 58.29.32-001-45146066-2020", registration certificate No. RZN 2020/12028



THANK YOU FOR ATTENTION!

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