Republic of Latvia

Cabinet

Regulation No. 455

Adopted 15 August 2023

**Procedures for Conducting Clinical Investigations of Medical Devices Intended for Human Use and Performance Studies on in Vitro Diagnostic Medical Devices**

*Issued pursuant to*

*Section 34, Paragraph two, Clause 1 of the Medical Treatment Law*

**I. General Provisions**

1. The Regulation prescribes the procedures for conducting clinical investigations of medical devices intended for human use (hereinafter – the clinical investigations) and performance studies on in vitro diagnostic medical devices (hereinafter – the performance studies).

2. The provisions of this Regulation regarding clinical investigations shall be applicable together with the requirements laid down for the products listed in Annex XVI to Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (hereinafter – Regulation No 2017/745), concurrently taking into account Commission Implementing Regulation (EU) 2022/2346 of 1 December 2022 laying down common specifications for the groups of products without an intended medical purpose listed in Annex XVI to Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices.

3. The terms used in the Regulation shall correspond to the terms used in Article 2 of Regulation No 2017/745 and Article 2 of Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (hereinafter – Regulation No 2017/746).

**II. Composition, Operation, and Provision of an Opinion of the Ethics Committee**

4. Prior to initiating a clinical investigation and a performance study, the ethics committee shall express a view on any issue of public interest related to clinical research in order to ensure the rights and safety of a subject and also to reassure the public about the protection of the subject. The ethics committee shall be an independent organisation operating within or outside a medical treatment institution.

5. The ethics committee shall consist of persons with an appropriate qualification and experience who are capable of professionally assessing the ethical and scientific aspects of the relevant clinical investigation and performance study.

6. The ethics committee shall consist of at least nine members. The ethics committee shall include at least one person who has no medical education and also at least two independent persons who are not related to the investigation site. The ethics committee shall include representatives of both genders.

7. The ethics committee may invite experts without the right to vote.

8. The ethics committee shall operate in accordance with the by-laws approved by the chairperson of the ethics committee. The by-laws shall be developed in accordance with Regulation No 2017/745 and Regulation No 2017/746, this Regulation, good clinical practice recommendations, and the laws and regulations regarding protection of personal data.

9. The ethics committee shall have a quorum if at least half of members of the ethics committee participate in the meeting thereof.

10. The opinion of the ethics committee shall be adopted by simple majority of votes of the committee members in an open vote. In the case of a tied vote, the opinion shall be considered negative.

11. The opinion of the ethics committee shall be valid within the meaning of Article 62(4)(b), Article 70(7)(a) and (b), Article 75(3)(b), Article 78(10) of Regulation No 2017/745 and Article 58(5)(b), Article 66(7)(a) and (b), Article 71(3)(b), and Article 74(10) of Regulation No 2017/746 if the information on the ethics committee referred to in Paragraph 15 of this Regulation is posted on the website of the Ministry of Health.

12. Minutes are taken during the meetings of the ethics committee, and decisions of the meeting are recorded in the minutes. A member of the committee whose view differs from the final decision of the committee may express his or her view in an annex to the minutes.

13. Only members of the committee who are independent of the specific investigator and sponsor may vote and express their views on issues related to the specific clinical investigation or performance study.

14. The ethics committee shall store all documents for 15 years after completion of the relevant clinical investigation or performance study, except for the cases where the laws and regulations regarding the procedures for keeping medical records specify a longer period for the storage of documents.

15. Information on the staff of the ethics committee and the qualification of the members thereof, and also the by-laws of the ethics committee shall be available upon request to the investigator, the State Agency of Medicines (hereinafter – the Agency), and the Ministry of Health.

16. The ethics committee shall submit information on the staff thereof to the Ministry of Health, indicating contact details and also information on the area of expertise and the fee for the examination of the research submission. The Ministry of Health shall post this information on its website.

17. In order to obtain the opinion of the ethics committee, the sponsor shall submit the following documents to the ethics committee:

17.1. a clinical investigation plan or performance study plan;

17.2. a description of the measures to involve the subjects;

17.3. a document of the informed consent of the subject;

17.4. documentation indicating whether a compensation is intended for the subject in relation to his or her participation in the clinical investigation or performance study;

17.5. a confirmation that the ethical aspects of the clinical investigation plan or performance study plan have been addressed;

17.6. a power of attorney issued by the sponsor if the documents are submitted by his or her legal representative or point of contact.

18. If the sponsor of a clinical investigation or performance study is not established in the European Union, he or she shall ensure that a natural or legal person is established in a European Union Member State or state of the European Economic Area as his or her legal representative, except for the case where the clinical investigation or performance study is only conducted in the territory of the Republic of Latvia or in the territory of the Republic of Latvia and a third country and the sponsor has appointed at least one point of contact for the specific clinical investigation or performance study in the territory of the Republic of Latvia, and this point of contact will receive all notifications intended for the sponsor in accordance with Regulation No 2017/745 or Regulation No 2017/746.

19. The ethics committee shall assess the documents referred to in Paragraph 17 of this Regulation from an ethical aspect, taking into account Chapter I, Section 1 of Annex XV to Regulation No 2017/745 or Part A, point 2.2 of Annex XIII to Regulation No 2017/746, and, within 30 days from receipt of the documents, provide the sponsor with a written opinion on the clinical investigation or performance study. A copy of the opinion shall be submitted to the Agency.

20. The ethics committee shall prepare and submit to the Agency, at least on a quarterly basis, a list of all applications for clinical investigations and performance studies examined and opinions provided.

**III. Issue of Authorisations for Conducting a Clinical Investigation and Performance Study**

21. For the purpose of conducting a clinical investigation, the sponsor shall obtain an authorisation of the Agency, except for the case referred to in Article 70(7)(a) of Regulation No 2017/745.

22. For the purpose of conducting the performance study referred to Article 58(1)(b) and (c) and Article 58(2) of Regulation No 2017/746, the sponsor shall obtain an authorisation of the Agency, except for the case referred to in Article 66(7)(a) of Regulation No 2017/746.

23. In order to obtain the authorisation of the Agency to conduct a clinical investigation, the sponsor shall submit to the Agency an application for clinical investigation (the application form is available on the website of the Agency) and append the documentation referred to in Chapter II of Annex XV to Regulation No 2017/745.

24. In order to obtain the authorisation of the Agency to conduct the performance study referred to in Paragraph 22 of this Regulation, the sponsor shall submit to the Agency an application for performance study (the application form is available on the website of the Agency), appending the documents referred to in Part A, Sections 2 and 3 of Annex XIII and in Annex XIV to Regulation No 2017/746.

25. The sponsor shall cover expenditures related to the examination of the documentation of the application for clinical investigation and performance study for obtaining the authorisation in accordance with the price list of paid services of the Agency. If the Agency takes the decision to refuse to issue the authorisation, the fee specified in the price list of paid services of the Agency for the examination of the application for clinical investigation or performance study shall not be refunded to the sponsor.

26. The Agency shall issue to the sponsor the authorisation for clinical investigation and performance study for the duration of the clinical investigation and performance study specified in the clinical investigation plan and the performance study plan.

27. If the Agency has a reason to believe that the requirements laid down in Regulation No 2017/745 or Regulation No 2017/746 are not conformed to, the Agency shall take one of the decisions referred to in Article 76(1) of Regulation No 2017/745 or Article 72(1) of Regulation No 2017/746.

28. The Agency shall take the decision to renew the authorisation for clinical investigation or performance study after elimination of the non-conformities referred to in Paragraph 27 of this Regulation with the requirements laid down in Regulation No 2017/745 or Regulation No 2017/746.

29. The sponsor may contest the decision of the Agency to the Ministry of Health. The sponsor may appeal the decision of the Ministry of Health to a court in accordance with the procedures laid down in the Administrative Procedure Law.

**IV. Obligations and Responsibility of the Persons Participating in Clinical Investigations and Performance Studies**

30. The sponsor shall ensure supply of the investigational medical devices and in vitro diagnostic medical devices, and also comparative devices if such are used in the clinical investigation or performance study, to the investigation site free of charge.

31. The sponsor shall be responsible for the safety, quality, supply to the investigation site, storage conditions, duration of use, and accounting system of the medical device and in vitro diagnostic medical device.

32. The sponsor shall provide all persons participating in the clinical investigation and performance study with information on the safety, quality, storage conditions, duration of use, and accounting of use of the medical device and in vitro diagnostic medical device. The persons participating in the clinical investigation and performance study shall precisely follow all storage and operational conditions for the medical device and in vitro diagnostic medical device specified by the sponsor.

33. The investigator shall be responsible for the storage of the medical device and in vitro diagnostic medical device at the investigation site.

**V. Protection of the Subject**

34. The investigator shall be responsible for providing the subject with health care and for all activities related to the clinical investigation and performance study. If necessary, the sponsor shall provide additional training for the investigator.

35. Persons requiring active treatment of a disease shall not be included in the control group of the clinical investigation and performance study.

36. For the purpose of ensuring the protection of personal data of the subject, the investigator shall assign an identification code to each subject which replaces the given name and surname of the subject and shall provide the relevant information to the sponsor, the Agency, and the ethics committee.

37. If the investigator obtains information in the clinical investigation on the circumstances that may pose a threat to the life or health of the subject, he or she shall immediately inform the subject thereof in writing.

38. In the case referred to in Paragraph 38 of this Regulation, the investigator shall re-obtain the informed consent of the subject for further participation in the clinical investigation or performance study.

39. If the clinical investigation or performance study is suspended or completed before the date provided for in the clinical investigation plan or the performance study plan, the investigator shall inform the subject thereof and ensure continued observation, examination, and treatment of the subject within the framework of a specific treatment episode during which the medical device or in vitro diagnostic medical device was used, and also in the case where harm has been caused to the subject.

**VI. Supervision and Reporting of Research**

40. For the purpose of ensuring that the course of the clinical investigation and performance study conforms with the requirements of Regulation No 2017/745, Regulation No 2017/746, and this Regulation, the Agency shall:

40.1. register, evaluate, and, in cooperation with the sponsor, assess any serious adverse event that has a causal relationship with the investigational medical device or in vitro diagnostic medical device, the comparable device, or the study procedure, or where such a causal relationship is reasonably possible, and also any deficiency of the device which, without appropriate measures, interventions, or favourable circumstances, could have caused a serious adverse event, and any new findings related to any of the abovementioned cases;

40.2. maintain the electronic database of the research section of the LATMED Register of Medical Devices;

40.3. develop and publish guidelines, recommendations for clinical investigations and performance studies, and other documents for exchange of information.

41. For the purpose of ensuring that clinical investigations and performance studies are conducted in accordance with the requirements laid down in Regulation No 2017/745 and Regulation No 2017/746 and in accordance with the approved clinical investigation plan and the performance study plan, the Health Inspectorate (hereinafter – the Inspectorate) shall inspect the investigation site according to its competence and upon request of the Agency. The Inspectorate shall report the results of the inspection to the Agency.

42. For the purpose of ensuring supervision and appropriate quality control, the persons participating in the clinical investigation and performance study shall provide the Agency and the Inspectorate with direct access to documents at all sites related to the clinical investigation and performance study.

43. If necessary, the Agency shall involve experts with appropriate qualification and experience in the evaluation of documentation of clinical investigation and performance study.

44. If the Agency has information at its disposal on any risks not identified and analysed previously which pose a risk to the life or health of the subject or medical practitioner, or if there is reason to believe that the sponsor or investigator does not conform to the requirements laid down in Regulation No 2017/745, Regulation No 2017/746, and this Regulation, the Agency shall immediately inform the Inspectorate thereof.

45. The sponsor shall, once a year, submit to the Agency and the ethics committee a report on adverse events that have occurred during the clinical investigation and performance study.

**VII. Closing Provisions**

46. The authorisations for conducting a clinical investigation which have been issued by the Agency before 26 May 2021 in accordance with Cabinet Regulation No. 891 of 21 September 2010, Procedures for the Clinical Trial of Medical Devices Intended for Human Use, shall be valid until completion of the relevant clinical investigation.

47. The authorisations for conducting a performance study which have been issued by the Agency before 26 May 2022 in accordance with Cabinet Regulation No. 891 of 21 September 2010, Procedures for the Clinical Trial of Medical Devices Intended for Human Use, shall be valid until completion of the relevant performance study.

48. The authorisations for conducting the clinical investigation or performance study referred to in Paragraphs 46 and 47 of this Regulation in accordance with the amendments made to the investigation or study documentation which have been issued by the Agency in accordance with Cabinet Regulation No. 891 of 21 September 2010, Procedures for the Clinical Trial of Medical Devices Intended for Human Use, shall be valid until completion of the relevant clinical investigation or performance study.

49. Cabinet Regulation No. 891 of 21 September 2010, Procedures for the Clinical Trial of Medical Devices Intended for Human Use (*Latvijas Vēstnesis*, 2010, No. 155), is repealed.

Prime Minister, Acting Minister for Foreign Affairs A. K. Kariņš

Minister for Health L. Meņģelsone