

IN VITRO DIAGNOSTIKAMEDITSIINISEADMED.
INIMPROOVIDEGA LÄBIVIIDAVAD KLIINILISED
TOIMIVUSUURINGUD. HEAD UURINGUTAVAD

In vitro diagnostic medical devices - Clinical
performance studies using specimens from human
subjects - Good study practice (ISO 20916:2019)

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 20916:2024 sisaldab Euroopa standardi EN ISO 20916:2024 ingliskeelset teksti. Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas. Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 06.03.2024. Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest.	This Estonian standard EVS-EN ISO 20916:2024 consists of the English text of the European standard EN ISO 20916:2024. This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation. Date of Availability of the European standard is 06.03.2024. The standard is available from the Estonian Centre for Standardisation and Accreditation.
---	---

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile standardiosakond@evs.ee.

ICS 11.100.10

Standardite reprodutseerimise ja levitamise õigus kuulub Eesti Standardimis- ja Akrediteerimiskeskusele

Andmete paljundamine, taastekitamine, kopeerimine, salvestamine elektroonsesse süsteemi või edastamine ükskõik millises vormis või millisel teel ilma Eesti Standardimis-ja Akrediteerimiskeskuse kirjaliku loata on keelatud.

Kui Teil on küsimusi standardite autorikaitse kohta, võtke palun ühendust Eesti Standardimis-ja Akrediteerimiskeskusega: Koduleht www.evs.ee; telefon 605 5050; e-post info@evs.ee

The right to reproduce and distribute standards belongs to the Estonian Centre for Standardisation and Accreditation

No part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, without a written permission from the Estonian Centre for Standardisation and Accreditation.

If you have any questions about copyright, please contact Estonian Centre for Standardisation and Accreditation:

Homepage www.evs.ee; phone +372 605 5050; e-mail info@evs.ee

English Version

In vitro diagnostic medical devices - Clinical performance studies using specimens from human subjects - Good study practice (ISO 20916:2019)

Dispositifs médicaux de diagnostic in vitro - Études des performances cliniques utilisant des prélèvements de sujets humains - Bonnes pratiques d'étude (ISO 20916:2019)

In-vitro-Diagnostika - Klinische Leistungsuntersuchungen an menschlichem Untersuchungsmaterial - Gute Studienpraxis (ISO 20916:2019)

This European Standard was approved by CEN on 7 August 2023.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and United Kingdom.



EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

European foreword

The text of ISO 20916:2019 has been prepared by Technical Committee ISO/TC 212 "Clinical laboratory testing and in vitro diagnostic test systems" of the International Organization for Standardization (ISO) and has been taken over as EN ISO 20916:2024 by Technical Committee CEN/TC 140 "In vitro diagnostic medical devices" the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by September 2024, and conflicting national standards shall be withdrawn at the latest by March 2027.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

This document has been prepared under a standardization request addressed to CEN by the European Commission. The Standing Committee of the EFTA States subsequently approves these requests for its Member States.

For the relationship with EU Legislation, see informative Annex ZA, which is an integral part of this document.

Any feedback and questions on this document should be directed to the users' national standards body. A complete listing of these bodies can be found on the CEN website.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and the United Kingdom.

Endorsement notice

The text of ISO 20916:2019 has been approved by CEN as EN ISO 20916:2024 without any modification.

Contents

Page

Foreword	v
Introduction	vi
1 Scope	1
2 Normative references	1
3 Terms and definitions	2
4 Ethical considerations	11
4.1 General	11
4.2 Improper influence or inducement	11
4.3 Responsibilities	11
4.4 Ethics committee involvement	11
4.5 Informed consent	12
5 Clinical performance study planning	12
5.1 General	12
5.2 Risk evaluation	13
5.3 Design of the clinical performance study	14
5.4 Investigator brochure	14
5.5 Clinical Performance Study Protocol (CPSP)	15
5.5.1 General	15
5.5.2 Principal investigator responsibilities	15
5.5.3 Contents of the CPSP	16
5.6 Case report forms	19
5.7 Recording of specimen information	20
5.8 Specimen accountability and integrity	20
5.9 Study site selection	20
5.9.1 Site qualification	20
5.9.2 Site assessment	20
5.9.3 Site selection	20
5.10 Monitoring plan	21
5.11 Agreements	21
5.12 Labelling	21
6 Study site initiation	21
6.1 General	21
6.2 Prerequisites	22
6.3 Training	22
6.4 Initiation of the study site	22
7 Clinical performance study conduct	23
7.1 General	23
7.2 Responsibilities of the sponsor	23
7.3 Study site monitoring	23
7.3.1 General	23
7.3.2 Routine monitoring	23
7.3.3 Monitoring reports	24
7.4 Security and confidentiality of data	25
8 Close-out of the clinical performance study	25
8.1 Close-out activities	25
8.2 Clinical performance study report	25
8.3 Document retention	27
8.4 Suspension or premature termination of the clinical performance study	27
9 Auditing	28
Annex A (normative) Additional general requirements for certain studies	29

Annex B (normative) Clinical performance study protocol (CPSP)	32
Annex C (normative) Investigator brochure	36
Annex D (normative) Clinical performance study report	38
Annex E (normative) Communication with the ethics committee	41
Annex F (normative) Informed consent	43
Annex G (normative) Adverse event categorization	47
Annex H (informative) Good clinical performance study documentation	51
Annex I (informative) Auditing	56
Bibliography	57

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

In vitro diagnostic (IVD) medical devices are used to conduct tests outside of the human body to provide valuable information regarding a person's health or physiological status. They include tests and related devices, such as test strips and reagents, using specimens such as blood, tissue or urine, to carry out screening, diagnosis, prognosis, predictive testing, and monitoring of conditions. IVD medical devices are fundamentally different from other medical devices because they perform their function outside of the body on specimens taken from the human body. Human subjects are typically not exposed to risks with the performance testing of IVD medical devices, except for the risk associated with specimen collection procedures or when the obtained information is used for patient management. The specimens are obtained via normal body functions (e.g. urine) or through the use of invasive medical devices to allow for the specimen to be obtained (e.g. biopsy). The specimens are never reintroduced into the human body. These differences make the performance and risk characteristics of IVD medical devices different and unique from other medical devices.

Most of the studies for IVD medical devices are performed using samples resulting from the remnants of specimens taken for purposes of standard of care (leftover or archived). In these studies, there is no risk for the subjects arising from either the information provided by the IVD medical device or from the collection procedure of the specimen. However, when leftover specimens are not used, additional requirements should be considered

- when the specimens are collected specifically for the study and the specimen collection procedures present additional risk of direct harm for the subject (e.g. lumbar puncture or tissue biopsy, blood collection from neonates or critically ill patients), and/or
- when the information obtained from the IVD medical devices during the study is used to make patient management decision (i.e. interventional studies), presenting a risk of indirect harm for the subject (e.g. false negative or false positive result leading to inappropriate patient management decisions).

For the majority of IVD clinical performance studies, issues related to the use of vulnerable subjects might not arise but should be considered on a case by case basis.

Considering the reliance on specimens taken from the body and the absence of direct contact of the IVD with the patient, issues related to procedures for obtaining informed consent for IVD clinical performance studies differ from those associated with other medical devices, especially for studies with leftover or archived specimens. This document will provide guidance on the requirements for the various situations described above for IVD medical devices.

This document is intended for clinical performance studies as these studies involve specimens taken from the human body. When specimens other than leftover or archived specimens are used, there might be additional collection risks for the subject. Also in interventional studies, there might be a risk for the subject coming from the information provided by the result of the IVD under investigation.

This document is specific for IVD medical devices and therefore uses definitions and concepts that are appropriate for IVD medical devices. It is a stand-alone standard for clinical performance studies for IVD medical devices. In the situation for which there is an IVD medical device and a medical device used in an integrated system (e.g. a lancet, an IVD test strip and a glucose meter), the respective jurisdiction's regulation will define it as either an IVD medical device or a medical device and subsequently, aspects of both this document and ISO 14155 might need to be considered.

Except for these situations, this document should not be read in conjunction with ISO 14155, which excludes IVD medical devices from its scope.

The flowchart represented in [Figure 1](#) provides guidance on how to use this document.

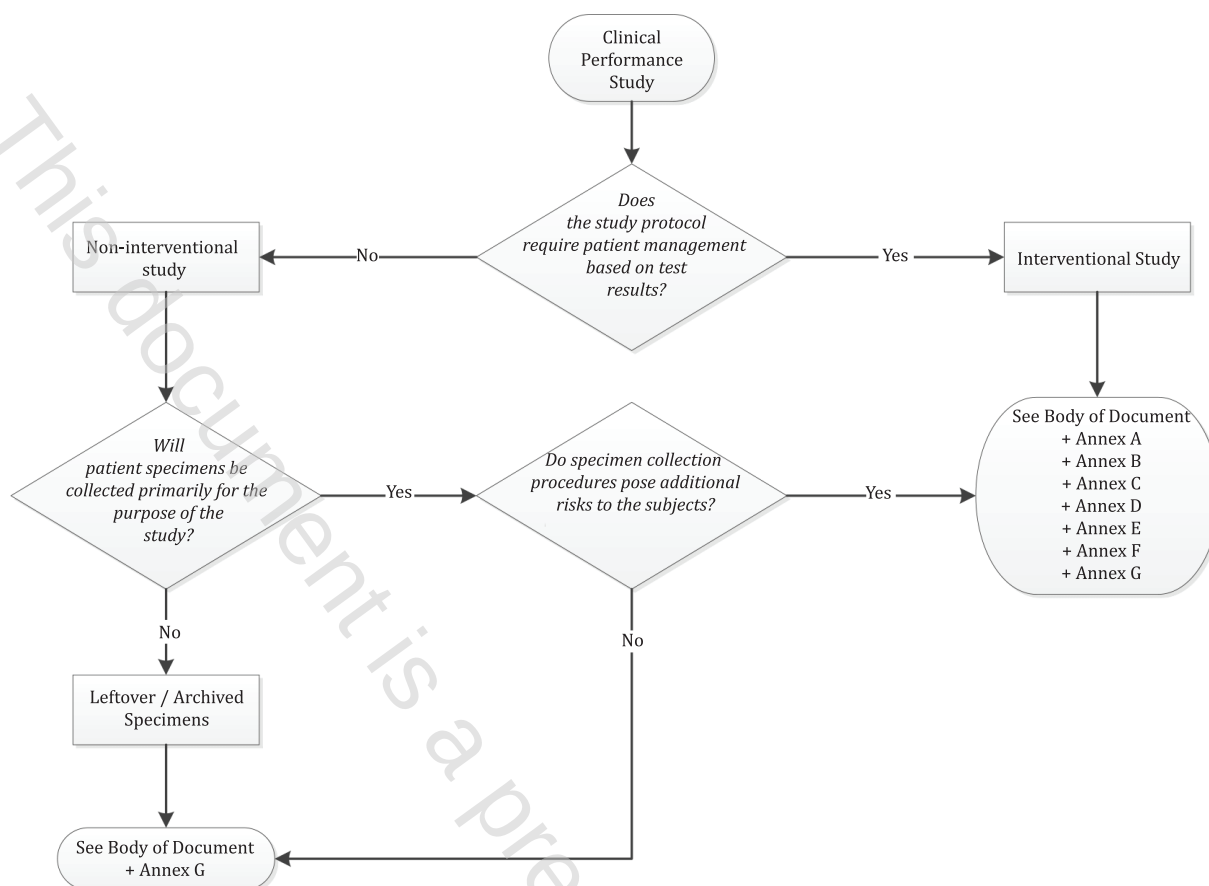


Figure 1 — Clinical performance study flow chart

The main body of the document, in addition to [Annex G](#), includes minimum requirements for all studies. No additional requirements apply for studies using leftover/archived specimens or studies with specimen collection procedures that pose no additional risks to the subject.

However, additional requirements for interventional studies, and those studies in which the specimen collection procedures pose a risk to subjects primarily recruited for the study, are found in [Annexes A](#) to [E](#). The nature of these studies warrants an increased level of stringency in the requirements for conduct of the study. The flowchart indicates the annexes which describe the additional requirements for each type of more complex studies. When necessary, the annexes describe differences in the requirements for the different types of study. Additionally, informative annexes are included to provide information on good study practice documentation (see [Annex H](#)) and auditing (see [Annex I](#)).

In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice

1 Scope

This document defines good study practice for the planning, design, conduct, recording and reporting of clinical performance studies carried out to assess the clinical performance and safety of in vitro diagnostic (IVD) medical devices for regulatory purposes.

NOTE 1 The purpose of these studies is to assess the ability of an IVD medical device in the hands of the intended user, to yield results pertaining to a particular medical condition or physiological/pathological state, in the intended population.

The document is not intended to describe whether the technical specifications of the IVD medical device in question are adequately addressed by the clinical performance study.

This document identifies the principles that underpin clinical performance studies and specifies general requirements intended to

- ensure the conduct of the clinical performance study will lead to reliable and robust study results,
- define the responsibilities of the sponsor and principal investigator,
- assist sponsors, clinical research organization, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of IVD medical devices, and
- protect the rights, safety, dignity and well-being of the subjects providing specimens for use in clinical performance studies.

Analytical performance studies are out of the scope of this document.

NOTE 2 When the collection of specimens specifically for the analytical performance study creates an additional collection risk for subjects, some of the elements of this document (particularly the annexes) can be useful for ensuring subject safety.

Clinical performance studies that are performed for reasons other than pre- and post-market regulatory purposes, such as for re-imburement purposes, are out of the scope of this document.

NOTE 3 Some of the elements of this document can be useful for the design of such studies, including subject safety and data integrity.

This document does not include safety information for laboratory workers or other personnel collecting the study specimens.

NOTE 4 Such information is included in other publications[1][12][13].

NOTE 5 Users of this document can consider whether other standards and/or requirements also apply to the IVD medical device which is the subject of the clinical performance study, for instance, in the situation for which there is an IVD medical device and a medical device used in an integrated system (e.g. a lancet, an IVD test strip, and a glucose meter), aspects of both this document and ISO 14155 can be considered.

2 Normative references

There are no normative references in this document.