



BSI Standards Publication

Clinical investigation of medical devices for human subjects — Good clinical practice

National foreword

This British Standard is the UK implementation of EN ISO 14155:2020+A11:2024. It is derived from ISO 14155:2020. It supersedes BS EN ISO 14155:2020, which is withdrawn.

The start and finish of text introduced or altered by amendment A11 is indicated in the text by tags. Tags indicating changes to CEN text carry the number of the CEN amendment. For example, text altered by CEN amendment A11 is indicated by A11 A11.

The UK participation in its preparation was entrusted to Technical Committee CH/194, Biological evaluation of medical devices.

A list of organizations represented on this committee can be obtained on request to its committee manager.

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UK Government is responsible for legislation. For information on legislation and policies relating to that legislation, consult the relevant pages of www.gov.uk.

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30 November 2020	Implementation of CEN correction notice 19 August 2020: correction of year to 2019 in table in European foreword
31 January 2025	Implementation of CEN amendment A11:2024

English Version

Clinical investigation of medical devices for human
subjects - Good clinical practice (ISO 14155:2020)

Investigation clinique des dispositifs médicaux pour
sujets humains - Bonne pratique clinique (ISO
14155:2020)

Klinische Prüfung von Medizinprodukten an Menschen
- Gute klinische Praxis (ISO 14155:2020)

This European Standard was approved by CEN on 2 May 2020.

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EUROPÄISCHES KOMITEE FÜR NORMUNG

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

European foreword

This document (EN ISO 14155:2020) has been prepared by Technical Committee ISO/TC 194 "Biological and clinical evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 "Biological and clinical evaluation of 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of an identical text or by endorsement, at the latest by February 2021, and conflicting national standards shall be withdrawn at the latest by February 2021.

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 supersedes EN ISO 14155:2011.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For the relationship with EU Directive(s) see informative Annex ZA and ZB, which is an integral part of this document.

The following referenced documents are indispensable for the application of this document. For undated references, the latest edition of the referenced document (including any amendments) applies. For dated references, only the edition cited applies. However, for any use of this document ‘within the meaning of Annex ZA’, the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this shall be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard, as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table — Correlations between undated normative references and dated EN and ISO standards

Normative references as listed in Clause 2 of the ISO standard	Equivalent dated standard	
	EN	ISO or IEC
1971	EN ISO 14971:2019	ISO 14971:2019

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, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 14155:2020 has been approved by CEN as EN ISO 14155:2020 without any modification.

European foreword to amendment A11

This document (EN ISO 14155:2020/A11:2024) has been prepared by Technical Committee CEN/TC 206 “Biological and clinical evaluation of medical devices”, the secretariat of which is held by DIN.

This Amendment to the European Standard EN ISO 14155:2020 shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by June 2025, and conflicting national standards shall be withdrawn at the latest by June 2025.

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 amends EN ISO 14155:2020 with a revised European Foreword and the European Annex ZA.

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/national committee. A complete listing of these bodies can be found on the CEN website.

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Annex ZA (informative)

A11 Relationship between this European standard and the requirements of Regulation (EU) 2017/745 aimed to be covered

This European standard has been prepared under M/575 to provide one voluntary means of conforming to Annex XV of Regulation (EU) 2017/745 of 5 April 2017 concerning clinical investigations of medical devices [O] L 117].

Once this standard is cited in the Official Journal of the European Union under that Regulation, compliance with the normative clauses of this standard given in Table ZA.1 and application of the edition of the normatively referenced standards as given in Table ZA.2 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding requirements of that Regulation, and associated EFTA Regulations.

This Annex ZA covers the relationship of this European standard with Annex XV of Regulation (EU) 2017/747 (Table ZA.1). Where requirements laid down in that Annex XV refer to Article 62 of this Regulation, the related requirements laid down in the section of Article 62 cited have also been considered when establishing the relationship of the clauses of this European standard with Annex XV in Table ZA.1.

Where a definition in this harmonised standard differs from a definition of the same term set out in Regulation (EU) 2017/745, the difference is indicated in Table ZA.3. For the purpose of using this standard in support of the requirements set out in Regulation (EU) 2017/745, the definitions set out in this Regulation prevail.

Where the European standard is an adoption of an International Standard, the scope of this document can differ from the scope of the European Regulation that it supports. As the scope of the applicable regulatory requirements differ from nation to nation and region to region the standard can only support European regulatory requirements to the extent of the scope of the European Regulation for medical devices ((EU) 2017/745).

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Regulation (EU) 2017/745. This means that risks have to be 'reduced as far as possible', 'reduced to the lowest possible level', 'reduced as far as possible and appropriate', 'removed or reduced as far as possible', 'eliminated or reduced as far as possible', 'removed or minimized as far as possible', or 'minimized', according to the wording of the corresponding General Safety and Performance Requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with General Safety and Performance Requirements 1, 2, 3, 4, 5, 8, 9, 10, 11, 14, 16, 17, 18, 19, 20, 21 and 22 of the Regulation.

For all requirements related to clinical investigations contained in Regulation (EU) 2017/47 and referred to in the following table, obligations attributed to the "sponsor" under ISO 14155 shall be incumbent under the Regulation to the Sponsor if located in the Union; When established, the Legal Representative is responsible for ensuring compliance with the sponsor's obligations pursuant to Regulation (EU) 2017/745.

Table ZA.1 — Correspondence between this European Standard and Annex XV of Regulation (EU) 2017/745 [O] L 117]

Clinical Investigation Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
Annex XV, Chapter I, 1	4 a)	Covered by a general reference to the Declaration of Helsinki; however, the latest edition of the Declaration should be used. National/regional requirements for ethics in clinical research and for protecting the safety, wellbeing, health and rights of subjects must be observed.
Annex XV, Chapter I, 2.1	6.2, 6.3, 6.4, 7.4.4, and Annex A	6.2 of this document covers risk management considerations of both the investigational device as well as the procedures required by the clinical investigation plan that are outside standard of care. 6.3 of this document refers to the literature review of the standard of care as a basis to define the appropriate study design as well as the requirement to take into consideration and relevant pre-clinical data. 6.4 of this document combined with Annex A provides a detailed outline on the study design and statistical considerations required to obtain scientific valid data on safety, performance and clinical benefits. 7.4.4 of this document covers the risk assessment process for potentially unacceptable risks.
Annex XV, Chapter I, 2.2	6.3, 6.4, A.2 i), A.3, A.4, A.5, A.6 and A.7	
Annex XV, Chapter I, 2.3	6.3, 6.4, A.3, A.4, A.5, A.6 and A.7	
Annex XV, Chapter I, 2.4	6.3, 6.4, 6.8, 9.2.1 b) to e), 10.2, 10.3, A.2 h), A.3, A.6, and A.7	Partially covered - this document does not cover the requirements of the clinical evaluation plan as this is not part of the clinical investigation. However, 6.3 does refer to the appropriate literature review required prior to designing a clinical investigation.

Clinical Investigation Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
Annex XV, Chapter I, 2.5	6.2, 6.3, A.2 e), f) and g), A.3, A.4, A.6, A.7 and B.2	
Annex XV, Chapter I, 2.6	6.3, A.6 and A.7	
Annex XV, Chapter I, 2.7	6.5, 9.2.1 g), 9.2.2, 10.2, A.2 h) and Annex B	
Annex XV, Chapter I, 2.8	8.4, 9.2.6, 10.6 r) and Annex D	
Annex XV, Chapter II, 2.1	B.2, B.4 a)	
Annex XV, Chapter II, 2.2	B.2 f) and g)	
Annex XV, Chapter II, 2.3	B.3	
Annex XV, Chapter II, 2.4	B.4	
Annex XV, Chapter II, 2.4, first indent	6.3, B.2 a), B.4	Partially covered – this document requires a prior assessment of relevant scientific literature but does not specifically require its incorporation into the Investigator's Brochure except for what is mentioned in B.2 a). Also, this document requires a prior assessment of relevant scientific literature and available data on the same or similar devices but is not specific on safety, performance and clinical benefits.
Annex XV, Chapter II, 2.4, second indent	6.3, B.2 a), B.4 a) and b)	Partially covered – this document requires a prior assessment of relevant scientific literature and available data on the same or similar devices but is not specific on safety, performance and clinical benefits.
Annex XV, Chapter II, 2.5	B.5	
Annex XV, Chapter II, 2.6	B.2 c)	Partially covered – this document does not specifically refer to a particular regulatory system. The document does not include the added value of incorporation of such constituents in relation to the clinical benefit and/or safety of the device.
Annex XV, Chapter II, 2.7	B.6	
Annex XV, Chapter II, 3.1.1	A.1.2 b)	

Clinical Investigation Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
Annex XV, Chapter II, 3.1.2	A.1.3	Partially covered - the document outlines that, when a local representative is established, the local representative acts as the sponsor fulfilling responsibilities of the sponsor, which differs from the responsibility of the legal representative outlined in Article 62(2) of Regulation (EU) 2017/745.
Annex XV, Chapter II, 3.1.3	A.1.4	
Annex XV, Chapter II, 3.1.4	A.12 f)	
Annex XV, Chapter II, 3.1.5	A.1.5	Partially covered - in the document the language used for the synopsis is not specified as this is considered as a country specific regulatory requirement.
Annex XV, Chapter II, 3.2	6.3, A.2, A.3 a) and b), A.4 a)	Background literature review and current state of the art are not covered as part of the identification of the device but as part of the justification of the design which is derived from literature review as outlined in 6.3 of the document.
Annex XV, Chapter II, 3.3	A.4	
Annex XV, Chapter II, 3.5	A.5	
Annex XV, Chapter II, 3.6	6.3, A.6.1 a) to d), A.7	
Annex XV, Chapter II, 3.6.1	A.6.1 a), A.6.1 c)	
Annex XV, Chapter II, 3.6.2	A.2 a), A.6.1 a)	
Annex XV, Chapter II, 3.6.3	A.5, A.6.3 j), A.15	To fully cover requirement 3.6.3, the information provided should also include immuno-compromised and elderly subjects, if applicable. However, clause A.5 of this document does require the study design to be relevant for the target population as well as A.6.3 j) requiring clarification of the relationship of the investigation population to the target population.
Annex XV, Chapter II, 3.6.4	A.6.1 b), A.7 i), j) and k)	
Annex XV, Chapter II, 3.6.5	A.6.4	

Clinical Investigation Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
Annex XV, Chapter II, 3.6.6	A.6.5	
Annex XV, Chapter II, 3.7	A.7	
Annex XV, Chapter II, 3.8	A.8	
Annex XV, Chapter II, 3.9	A.9	
Annex XV, Chapter II, 3.10	A.10	
Annex XV, Chapter II, 3.11	A.11	
Annex XV, Chapter II, 3.12	A.12	
Annex XV, Chapter II, 3.13	A.13	
Annex XV, Chapter II, 3.14	A.14	
Annex XV, Chapter II, 3.15	A.16, A.7 e) 6), A.7 m)	Traceability for implantable devices is not covered.
Annex XV, Chapter II, 3.16	A.6.4 f) to h), A.16 c)	To fully cover requirement 3.16, information should be provided on the additional care required that differs from that normally expected for the medical condition in question.
Annex XV, Chapter II, 3.17	A.17	
Annex XV, Chapter II, 3.18	A.2, A.5	
Annex XV, Chapter II, 3.19	A.18	
Annex XV, Chapter II, 4.2	7.1, 9.2.2 h) and i), A.12 c)	
Annex XV, Chapter II, 4.3	5.3, 9.2.2 e) and g), A.12 e)	
Annex XV, Chapter II, 4.4	5.8,	
Annex XV, Chapter II, 4.5	5.8.4 e), 7.7	
Annex XV, Chapter II, 4.5, first indent	5.8.4 e), 5.8.5 f) and g), 7.7	
Annex XV, Chapter II, 4.5, second indent	5.8.4 e), 5.8.5 f) and g), 7.7, 7.8.2 c), 7.8.3 g)	
Annex XV, Chapter III, 2	6.9, 9.2.1 a), 10.8	
Annex XV, Chapter III, 4	9.2.1 g), 9.2.3, 9.2.4	
Annex XV, Chapter III, 5	8.1, 9.2.3 f), 9.2.4.5	
Annex XV, Chapter III, 6	7.11, 9.1 c)	

Clinical Investigation Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
Annex XV, Chapter III, 7, first indent	8.4, D.2, D.4, D.12	To fully conform with this requirement, the signature page must be part of the clinical investigation report. Note 1 of 8.4 does refer to national requirements regarding the clinical report which may be different worldwide.
Annex XV, Chapter III, 7, second indent	8.4, D.2 i) and j)	
Annex XV, Chapter III, 7, third indent	8.4, D.4	
Annex XV, Chapter III, 7, fourth indent	D.6.1	
Annex XV, Chapter III, 7, fifth indent	D.6.2, D.13	This document in addition to the clinical investigation plan summary of D.6.2 does also require the full plan to be in the Annex of the report.
Annex XV, Chapter III, 7, sixth indent	D.7 g)	Justification and rationale for the analysis is required in Clause D.7 g) of the document.
Annex XV, Chapter III, 7, seventh indent	D.7 f) 2) and 3)	
Annex XV, Chapter III, 7, eighth indent	D.8	The discussion includes the clinical relevance and importance of the results in light of other existing data which should be understood including standard of care.

Table ZA.2 — Applicable Standards to confer presumption of conformity as described in this Annex ZA

Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
ISO 14971	ISO 14971:2019	Medical devices — Application of risk management to medical devices	EN ISO 14971:2019 EN ISO 14971:2019/A11:2021

The documents listed in the Column 1 of Table ZA.2, in whole or in part, are normatively referenced in this document, i.e. are indispensable for its application. The achievement of the presumption of conformity is subject to the application of the edition of Standards as listed in Column 4 or, if no European Standard Edition exists, the International Standard Edition given in Column 2 of Table ZA.2.

Table ZA.3 — Prevailing terms of Regulation (EU) 2017/754 for the use of this European standard under that Regulation

Term used in this EN	Clause(s)/sub-clause(s) of this EN	Article in (EU) 2017/745 that defines or uses this term	Differences/Consequences
adverse event AE	3.2	Article 2(57)	Both definitions are substantially equivalent. The definition in this document specifies that an adverse event may be whether anticipated or unanticipated. A note specifies that the definition includes events related to the investigational medical device or the comparator and events related to the procedure involved.
clinical investigation plan CIP	3.9	Article 2(47)	Both definitions are substantially equivalent. In the MDR, the definition includes statistical considerations. However, per clause A.7 of Annex A of this document, a statistical design and analysis is expected in the content of the CIP. In this document, the definition includes “record-keeping”.
clinical performance	3.11	Article 2(52)	Both definitions slightly differ. In this document, the definition does not specify that the ability of the device to achieve its intended purpose leads to a clinical benefit for

			patients when used as intended by the manufacturer.
device deficiency	3.19	Article 2(59)	Both definitions are substantially equivalent. The definition in this document includes the inadequacy of a medical device with respect to its usability. A note also specifies that the definition includes device deficiencies related to the investigational medical device or the comparator.
ethics committee EC	3.24	Article 2(56)	Both definitions are substantially equivalent. In the Regulation, the definition specifies that the EC is empowered to give opinions taking into account the views of laypersons.
informed consent	3.27	Article 2(55)	Both definitions are substantially equivalent. Per section 5.8.1 of this document informed consent is obtained in writing from the subject or where applicable, the subject's legally designated representative. In the Regulation, the definition specifies an authorization or agreement from the legally designated representative in the case of minors and of incapacitated subjects.
investigational medical device	3.29	Article 2(46)	Both definitions are substantially equivalent. The definition in this document specifies that the device is assessed in a clinical investigation for safety, clinical performance or effectiveness. It also includes notes specifying that this includes medical devices already on the market.
investigator	3.30	Article 2(54)	The definition in this document distinguishes between the terms <i>principal investigator</i> and <i>investigator</i> , whereas the Regulation only

			defines the role of the investigator which corresponds to the definition of <i>principal investigator</i> in this document.
medical device	3.34	Article 2(1)	Both definitions are substantially equivalent. In the Regulation, the definition also specifies: a medical device can be used for one or more medical purposes where the standard does not specify medical; under medical purposes, the Regulation adds in the first bullet point prediction and prognosis; the Regulation second bullet point also adds disability in addition to injury; the third bullet point adds pathological process or state; the fourth bullet has additional specification including organ, blood and tissue donations. The Regulation however does not include devices supporting or sustaining life as medical purpose.
serious adverse event SAE	3.45	Article 2(58)	Both definitions are substantially equivalent. The criterion v) chronic disease in the definition of the Regulation is part of the permanent impairment criterion in the definition of this document.
serious health threat	3.46	Article 2(66)	Both definitions are similar but used in a different target population. The definition in the Regulation includes the full target population of a market released product 'public' health threat, where the definition in this document has been adapted to target the clinical investigation population and is considered

			as a signal amongst reported serious adverse events rather than a different definition of adverse event.
sponsor	3.49	Article 2(49)	Both definitions are substantially equivalent. The definition in this document specifies that the sponsor assumes liability. A note indicates that when an investigator initiates, implements and takes full responsibility for the clinical investigation, the investigator also assumes the role of the sponsor and is identified as the sponsor-investigator.
subject	3.50	Article 2(50)	Both definitions are substantially equivalent. In this document, the definition specifies that a subject is a participant in a clinical investigation either as a recipient of the investigational medical device or a comparator. A note indicates that the definition includes healthy volunteers.

WARNING 1 — Presumption of conformity stays valid only as long as a reference to this European standard is maintained in the list published in the Official Journal of the European Union. Users of this standard should consult frequently the latest list published in the Official Journal of the European Union.

WARNING 2 — Other Union legislation may be applicable to the product(s) falling within the scope of this standard. 

Annex ZB
(informative)

Relationship between this European Standard and the essential requirements of Directive 90/385/EEC [OJ L 189] aimed to be covered

This European Standard has been prepared under a Commission’s standardization request [M/295 concerning the development of European Standards related to medical devices] to provide one voluntary means of conforming to essential requirements of Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices [OJ L 189].

Once this standard is cited in the Official Journal of the European Union under that Directive, compliance with the normative clauses of this standard given in Table ZB.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding essential requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Directive 90/385/EEC as amended by 2007/47/EC. This means that risks have to be reduced ‘as far as possible’, ‘to a minimum’, ‘to the lowest possible level’, ‘minimized’ or ‘removed’, according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer’s policy for determining acceptable risk must be in compliance with Essential Requirements 1, 4, 5, 8, 9 and 10 of the Directive.

NOTE 3 This Annex ZB is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZB.1, it means that it is not addressed by this European Standard.

For all requirements related to clinical investigations contained in the regulation and referred to in the following table: obligations attributed to the "sponsor" under ISO 14155 shall be incumbent under the Directive 90/385/EEC to the manufacturer if located in the EU/EEA/Turkey/Switzerland, and incumbent to the Authorized Representative otherwise. Both may refer to external service providers in order to fulfil their obligations.

Table ZB.1 — Correspondence between this European Standard and Annex I of Directive 90/385/EEC [OJ L 189]

Essential Requirements of Directive 90/385/EEC	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
5 a	Entire standard	fulfilment of the ER, as 1) e documentation of clinical investigations of medical devices used in the clinical evaluation process as referred in Annex VII.1.1 ^a and f Annex VII.2 listed below.

Annex 7, 2.2	4, 5, 6.2, 6.3 and 8.4	ISO 14155 does not refer particular version of the decl of Helsinki. The latest av version of the declarati Helsinki must be taken into account. National/regional requireme ethics in clinical research e protecting the safety, we health and rights of subject be observed.
Annex 7, 2.3.1	6.2, 6.3, 6.4 and Annex A	
Annex 7, 2.3.2	6.3, 6.4, A.2 i) and A.3 to A.6	
Annex 7, 2.3.3	6.3, 6.8, 7.3, 10.2, 10.3 and A.6	Covered provided that investigation site's faciliti similar to the facilities requi the intended use of investigational device.
Annex 7, 2.3.4	6.2, 6.3, 7.4, 9.2.5, 10.8 and A.7	
Annex 7, 2.3.5	7.4, 9.2.5 and 10.8	
Annex 7, 2.3.6	6.5, 6.8, 9.2.1, 10.2, 10. Annex B	
Annex 7, 2.3.7	8.4, 9.2.6, 10.6 r) and Annex E	
^a See MEDDEV 2.7/1, Section 6.3.		

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WARNING 2 — Other Union legislation may be applicable to the products falling within the scope of this standard.

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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 the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 206, *Biological and clinical evaluation of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 14155:2011), which has been technically revised. The main changes to the previous edition are as follows:

- inclusion of a summary section of GCP principles (see [Clause 4](#));
- reference to registration of the clinical investigation in a publicly accessible database (see [5.4](#));
- inclusion of clinical quality management (see [9.1](#));
- inclusion of risk-based monitoring (see [6.7](#));
- inclusion of statistical considerations in [Annex A](#);
- inclusion of guidance for ethics committees in [Annex G](#);
- reinforcement of risk management throughout the process of a clinical investigation (planning to consideration of results) including [Annex H](#);
- clarification of applicability of the requirements of this document to the different clinical development stages (see [Annex I](#));
- inclusion of guidance on clinical investigation audits (see [Annex J](#)).

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.

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Clinical investigation of medical devices for human subjects — Good clinical practice

1 Scope

This document addresses good clinical practice for the design, conduct, recording and reporting of clinical investigations carried out in human subjects to assess the clinical performance or effectiveness and safety of medical devices.

For post-market clinical investigations, the principles set forth in this document are intended to be followed as far as relevant, considering the nature of the clinical investigation (see [Annex I](#)).

This document specifies general requirements intended to

- protect the rights, safety and well-being of human subjects,
- ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- define the responsibilities of the sponsor and principal investigator, and
- assist sponsors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

NOTE 1 Users of this document need to consider whether other standards and/or national requirements also apply to the investigational device(s) under consideration or the clinical investigation. If differences in requirements exist, the most stringent apply.

NOTE 2 For Software as a Medical Device (SaMD) demonstration of the analytical validity (the SaMD's output is accurate for a given input), and where appropriate, the scientific validity (the SaMD's output is associated to the intended clinical condition/physiological state), and clinical performance (the SaMD's output yields a clinically meaningful association to the target use) of the SaMD, the requirements of this document apply as far as relevant (see Reference [4]). Justifications for exemptions from this document can consider the uniqueness of indirect contact between subjects and the SaMD.

This document does not apply to *in vitro* diagnostic medical devices. However, there can be situations, dependent on the device and national or regional requirements, where users of this document might consider whether specific sections and/or requirements of this document could be applicable.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14971, *Medical devices — Application of risk management to medical devices*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <http://www.iso.org/obp>
- IEC Electropedia: available at <http://www.electropedia.org/>

3.1
adverse device effect
ADE

adverse event (3.2) related to the use of an investigational *medical device* (3.34)

Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any *malfunction* (3.33) of the investigational medical device.

Note 2 to entry: This definition includes any event resulting from *use error* (3.53) or from intentional misuse of the investigational medical device.

Note 3 to entry: This includes '*comparator*' (3.12) if the comparator is a medical device.

3.2
adverse event
AE

untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in *subjects* (3.50), users or other persons, whether or not related to the *investigational medical device* (3.29) and whether anticipated or unanticipated

Note 1 to entry: This definition includes events related to the investigational medical device or the *comparator* (3.12).

Note 2 to entry: This definition includes events related to the procedures involved.

Note 3 to entry: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

3.3
audit

systematic examination of activities and documents related to a *clinical investigation* (3.8) performed by (an) *independent* (3.26) person(s), to determine whether these activities were conducted, and the data recorded, analysed and accurately reported, according to the CIP, standard operating procedures, this document and applicable regulatory requirements

3.4
audit trail

documentation that allows reconstruction of the course of events

3.5
blinding
masking

procedure in which one or more parties to the *clinical investigation* (3.8) are kept unaware of the treatment assignment(s)

Note 1 to entry: Single blinding usually refers to the *subject(s)* (3.50) being unaware of the treatment assignment(s). Double blinding usually refers to the *subject(s)*, *investigator(s)* (3.30), monitor and, in some cases, centralized assessors being unaware of the treatment assignment(s).

Note 2 to entry: A clinical investigation is termed 'observer blind', if at least the *primary endpoint(s)* (3.22) is/are assessed without knowledge of whether an investigational medical device (3.29) or *comparator* (3.12) has been used to treat a subject.

3.6
case report form
CRF

set of printed, optical or electronic documents for each *subject* (3.50) on which information to be reported to the *sponsor* (3.49) is recorded, as required by the CIP

3.7**certified copy**

copy (irrespective of the type of media used) of the original record that has been verified (i.e. by a dated signature or by generation through a validated process) to have the same information including data that describe the context, content, and structure, as the original

3.8**clinical investigation**

systematic investigation in one or more human *subjects* (3.50), undertaken to assess the *clinical performance* (3.11), *effectiveness* (3.20) or safety of a *medical device* (3.34)

Note 1 to entry: For the purpose of this document, “clinical trial” or “clinical study” are synonymous with “clinical investigation”.

3.9**clinical investigation plan****CIP**

document that states the rationale, *objectives* (3.37), design and pre-specified analysis, methodology, organization, *monitoring* (3.35), conduct and record-keeping of the *clinical investigation* (3.8)

Note 1 to entry: For the purpose of this document “protocol” is synonymous with “CIP”. However, protocol has many different meanings, some not related to clinical investigation, and these can differ from country to country. Therefore, the term CIP is used in this document.

3.10**clinical investigation report**

document describing the design, execution, statistical analysis and results of a *clinical investigation* (3.8)

3.11**clinical performance**

behaviour of a *medical device* (3.34) and response of the *subject(s)* (3.50) to that medical device in relation to its intended use, when correctly applied to appropriate subject(s)

Note 1 to entry: Clinical performance can be defined under national regulations.

3.12**comparator**

medical device (3.34), therapy (e.g. active treatment, normal clinical practice), placebo or no treatment, used in the *control group* (3.15) in a *clinical investigation* (3.8)

3.13**computer system**

hardware and software (including associated documents, e.g. user manual) that creates, modifies, maintains, archives, retrieves, or transmits in digital form information related to the conduct of a *clinical investigation* (3.8)

3.14**contract research organization****CRO**

person or organization contracted by the *sponsor* (3.49) to perform one or more of the sponsor's clinical investigation-related duties and functions

3.15**control group**

group of *subjects* (3.50) that receives the *comparator* (3.12)

Note 1 to entry: A control group may be concurrent or historical, or subjects may serve as their own control.

3.16

coordinating investigator

investigator (3.30) who is appointed by the *sponsor* (3.49) to assist in coordinating the work in a multicentre *clinical investigation* (3.8)

Note 1 to entry: For the purpose of this document, “national investigator” or “global investigator” are synonymous with “coordinating investigator”.

3.17

data monitoring committee

DMC

independent (3.26) committee that can be established by the *sponsor* (3.49) to assess, at intervals, the progress of the *clinical investigation* (3.8), the safety data or the critical *clinical performance* (3.11) or *effectiveness* (3.20) *endpoints* (3.22) and to recommend to the sponsor whether to continue, suspend, modify, or stop the clinical investigation

Note 1 to entry: For the purpose of this document, “data and safety monitoring board (DSMB)”, “data and safety monitoring committee (DSMC)” or “independent data monitoring committee (IDMC)” are synonymous with DMC.

3.18

deviation

instance of failure to follow, intentionally or unintentionally, the requirements of the *CIP* (3.9)

3.19

device deficiency

inadequacy of a *medical device* (3.34) with respect to its identity, quality, durability, reliability, usability, safety or performance

Note 1 to entry: Device deficiencies include *malfunctions* (3.33), *use errors* (3.53), and inadequacy in the information supplied by the manufacturer including labelling.

Note 2 to entry: This definition includes device deficiencies related to the *investigational medical device* (3.29) or the *comparator* (3.12).

3.20

effectiveness

achievement of a clinically significant intended result in a defined portion of the target population when the *investigational medical device* (3.29) is used within its intended uses and according to its instructions for use, the *investigator’s brochure* (3.31) and the *CIP* (3.9), as determined by documented scientific evidence

3.21

electronic record

combination of text, graphics, data, audio, imaging, or other information in digital form that is created, modified, maintained, archived, retrieved, or distributed by a *computer system* (3.13)

EXAMPLE An electronic CRF.

3.22

endpoint

<primary> principal indicator(s) used for providing the evidence for *clinical performance* (3.11), *effectiveness* (3.20) or safety in a *clinical investigation* (3.8)

3.23

endpoint

<secondary> indicator(s) used for assessing the secondary *objectives* (3.37) of a *clinical investigation* (3.8)

3.24**ethics committee****EC**

independent (3.26) body whose responsibility it is to review *clinical investigations* (3.8) in order to protect the rights, safety, and well-being of human *subjects* (3.50) participating in a clinical investigation

Note 1 to entry: For the purposes of this document, “ethics committee” is synonymous with “research ethics committee”, “independent ethics committee” or “institutional review board”. The regulatory requirements pertaining to ethics committees or similar institutions vary by country or region.

3.25**hypothesis**

testable statement, derived from the *objective* (3.37) of the *clinical investigation* (3.8) to draw a conclusion about this objective, based on a pre-specified statistical test

Note 1 to entry: The primary hypothesis is formulated based on the pre-defined *primary endpoint* (3.22) and is usually used to calculate the sample size.

3.26**independent**

not involved in the development of the investigational device or the conduct of a *clinical investigation* (3.8), except for their specifically assigned responsibilities, in order to avoid bias or a conflict of interest

3.27**informed consent**

process by which an individual voluntarily confirms willingness to participate in a particular *clinical investigation* (3.8), after having been informed of all aspects of the investigation that are relevant to the decision to participate

3.28**investigation site**

institution or site where the *clinical investigation* (3.8) is carried out

Note 1 to entry: For the purpose of this document, “investigation site” is synonymous with “investigation centre”.

3.29**investigational medical device**

medical device (3.34) being assessed for *clinical performance* (3.11), *effectiveness* (3.20), or safety in a *clinical investigation* (3.8)

Note 1 to entry: This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.

Note 2 to entry: This includes medical devices already on the market that are being evaluated within their intended use in a post-market clinical investigation (interventional or non-interventional).

Note 3 to entry: For the purpose of this document, the terms “investigational medical device” and “investigational device” are used interchangeably.

3.30**investigator**

individual member of the *investigation site* (3.28) team designated and supervised by the *principal investigator* (3.39) at an investigation site to perform clinical investigation-related procedures or to make important clinical investigation-related and medical treatment decisions

Note 1 to entry: An individual member of the investigation site team can also be called “sub-investigator” or “co-investigator”.

3.31
investigator's brochure
IB

compilation of the current clinical and non-clinical information on the *investigational medical device(s)* (3.29), relevant to the *clinical investigation* (3.8)

3.32
legally designated representative

individual, judicial, or other body authorized under applicable law to consent, on behalf of a prospective *subject* (3.50), to the subject's participation in the *clinical investigation* (3.8)

Note 1 to entry: "legally authorized representative" or "legally acceptable representative" are other terminologies used under national regulations for "legally designated representative".

3.33
malfunction

failure of an *investigational medical device* (3.29) to perform in accordance with its intended purpose when used in accordance with the instructions for use or CIP, or IB

3.34
medical device

instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific purpose(s) of:

- diagnosis, prevention, *monitoring* (3.35), treatment or alleviation of disease;
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
- investigation, replacement, modification, or support of the anatomy or of a physiological process;
- supporting or sustaining life;
- control of conception;
- disinfection of medical devices;
- providing information by means of *in vitro* examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means

Note 1 to entry: Products which may be considered to be medical devices in some jurisdictions but not in others include:

- disinfection substances;
- aids for persons with disabilities;
- devices incorporating animal and/or human tissues;
- devices for *in vitro* fertilization or assisted reproduction technologies.

[SOURCE: ISO 13485:2016, 3.11]

3.35
monitoring

act of overseeing the progress of a *clinical investigation* (3.8) to ensure that it is conducted, recorded, and reported in accordance with the CIP, written procedures, this document, and the applicable regulatory requirements

Note 1 to entry: Centralized monitoring is a remote evaluation of accumulated data and compliance to provide additional monitoring capabilities that can complement or reduce the extent and frequency of on-site monitoring.

3.36**multicentre investigation**

clinical investigation (3.8) that is conducted according to a single CIP and takes place at two or more *investigation sites* (3.28)

3.37**objective**

main purpose for conducting the *clinical investigation* (3.8)

3.38**point of enrolment**

time at which, following *recruitment* (3.43) and before any clinical investigation-related procedures are undertaken, a *subject* (3.50) signs and dates the *informed consent* (3.27) form

3.39**principal investigator**

qualified person responsible for conducting the *clinical investigation* (3.8) at an *investigation site* (3.28)

Note 1 to entry: If a clinical investigation is conducted by a team of individuals at an investigation site, the principal investigator is responsible for leading the team.

Note 2 to entry: Whether this is the responsibility of an individual or an institution can depend on national regulations.

3.40**quality assurance**

planned and systematic actions that are established to ensure that the *clinical investigation* (3.8) is performed, and the data are generated, documented (recorded), and reported in compliance with this document and the applicable regulatory requirement(s)

3.41**quality control**

operational techniques and activities undertaken within the *quality assurance* (3.40) system to verify that the requirements for quality of the clinical investigation-related activities have been fulfilled

3.42**randomization**

process of assigning *subjects* (3.50) to the *investigational medical device* (3.29) or *control groups* (3.15) using an established recognized statistical method using an element of chance to determine the unforeseeable assignment in order to reduce bias

3.43**recruitment**

active efforts to identify *subjects* (3.50) who can be suitable for enrolment into the *clinical investigation* (3.8)

3.44**serious adverse device effect****SADE**

adverse device effect (3.1) that has resulted in any of the consequences characteristic of a *serious adverse event* (3.45)

3.45**serious adverse event****SAE**

adverse event (3.2) that led to any of the following

- a) death,

- b) serious deterioration in the health of the *subject* (3.50), users, or other persons as defined by one or more of the following:
- 1) a life-threatening illness or injury, or
 - 2) a permanent impairment of a body structure or a body function including chronic diseases, or
 - 3) in-patient or prolonged hospitalization, or
 - 4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,
- c) foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment

Note 1 to entry: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP (3.9), without serious deterioration in health, is not considered a serious adverse event.

3.46

serious health threat

signal from any adverse event or *device deficiency* (3.19) that indicates an imminent risk of death or a serious deterioration in the health in *subjects* (3.50), users or other persons, and that requires prompt remedial action for other subjects, users or other persons

Note 1 to entry: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

3.47

source data

all information in original records, certified copies of original records of clinical findings, observations, or other activities in a *clinical investigation* (3.8), necessary for the reconstruction and evaluation of the clinical investigation

Note 1 to entry: This includes source data initially recorded in an electronic format.

3.48

source document

original or *certified copy* (3.7) of printed, optical or electronic document containing *source data* (3.47)

EXAMPLE Hospital records, laboratory notes, device accountability records, photographic negatives, radiographs, records kept at the *investigation site* (3.28), at the laboratories and at the medico-technical departments involved in the *clinical investigation* (3.8).

3.49

sponsor

individual, company, institution or organization taking responsibility and liability for the initiation and management of a *clinical investigation* (3.8), and arranging the financial setup

Note 1 to entry: When an *investigator* (3.30) initiates, implements and takes full responsibility for the clinical investigation, the investigator also assumes the role of the sponsor and is identified as the sponsor-investigator.

3.50

subject

individual who is or becomes a participant in a *clinical investigation* (3.8), either as a recipient of the investigational device or a *comparator* (3.12)

Note 1 to entry: This includes healthy volunteers.

3.51**unanticipated serious adverse device effect****USADE**

serious adverse device effect (3.44) which by its nature, incidence, severity or outcome has not been identified in the current risk assessment

Note 1 to entry: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

3.52**use error**

user action or lack of user action while using the *medical device* (3.34) that leads to a different result than that intended by the manufacturer or expected by the user

Note 1 to entry: Use error includes the inability of the user to complete a task.

Note 2 to entry: Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment.

Note 3 to entry: Users might be aware or unaware that a use error has occurred.

Note 4 to entry: An unexpected physiological response of the patient is not by itself considered a use error.

Note 5 to entry: A malfunction of a medical device that causes an unexpected result is not considered a use error.

[SOURCE: ISO 14971:2019, 3.30]

3.53**validation**

confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled

3.54**verification**

confirmation by examination and provision of objective evidence that specified requirements have been fulfilled

3.55**vulnerable subject**

individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response

4 Summary of good clinical practice (GCP) principles

- a) Clinical investigations shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (see Reference [7]), and that are consistent with this document.
- b) Before a clinical investigation is initiated, foreseeable risks and inconveniences shall be weighed against the anticipated benefit for the individual subject and society. A clinical investigation shall be initiated and continued only if the anticipated benefits justify the risk.
- c) The rights, safety, and well-being of human subjects are the most important considerations and prevail over interests of science and society.
- d) The available non-clinical and clinical information on the investigational device shall be adequate to support the proposed clinical investigation.
- e) Clinical investigations shall be scientifically sound and described in a clearly detailed CIP.