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

Táto norma obsahuje anglickú verziu európskej normy.
This standard includes the English version of the European Standard.

Táto norma bola oznámená vo Vestníku ÚNMS SR č. 10/20

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

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EN ISO 14155:2020 (E)

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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of an identical text or by endorsement, at the latest by February 2021, and conflicting national standards shall be withdrawn at the latest by February 2021.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
ISO 14971	EN ISO 14971:2020	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.

Annex ZA
(informative)

Relationship between this European Standard and the essential requirements of Directive 93/42/EEC [OJ L 169] 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 93/42/EEC of 14 June 1993 concerning medical devices [OJ L 169].

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 ZA.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 93/42/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, 2, 5, 6, 7, 8, 9, 11 and 12 of the Directive.

NOTE 3 This Annex ZA 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 ZA.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 93/42/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 ZA.1 — Correspondence between this European Standard and Annex I of Directive 93/42/EEC [OJ L 169]

Essential Requirements of Directive 93/42/EEC	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
Annex I, 6a	Entire standard	Partial fulfilment of the ER, as regards 1) the documentation of clinical investigations of medical devices used in the clinical evaluation process as referred to in Annex X.1.1[a] and parts of Annex X.2 listed below.

Annex X, 2.2	4, 5, 6.2, 6.3 and 8.4	ISO 14155 does not refer to a particular version of the declaration of Helsinki. The latest available version of the declaration of Helsinki must be taken into account. National/regional requirements for ethics in clinical research and for protecting the safety, wellbeing, health and rights of subjects must be observed.
Annex X, 2.3.1	6.2, 6,3, 6.4, A.4, A.5, A.6 and A.7	
Annex X, 2.3.2	6.3, 6.4, A.2 i), A.3, A.4, A.5 and A.6	
Annex X, 2.3.3	6.3, 6.8, 7.3, 10.2, 10.3and A.6	Covered provided that the investigation site's facilities are similar to the facilities required for the intended use of the investigational device.
Annex X, 2.3.4	6.2, 6.3, 7.4, 9.2.5, 10.8, A.3, A.4, A.5, A.6 and A.7	
Annex X, 2.3.5	7.4, 9.2.5 and 10.8	
Annex X, 2.3.6	6.5, 6.8, 9.2.1, 10.2, 10.3 and Annex B	
Annex X, 2.3.7	8.4, 9.2.6, 10.6 r) and Annex D	
[a] See MEDDEV 2.7/1, Section 6.3.		

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 products 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	Partial fulfilment of the ER, as regards 1) the documentation of clinical investigations of medical devices used in the clinical evaluation process as referred to in Annex VII.1.1[a] and parts of Annex VII.2 listed below.

Annex 7, 2.2	4, 5, 6.2, 6.3 and 8.4	ISO 14155 does not refer to a particular version of the declaration of Helsinki. The latest available version of the declaration of Helsinki must be taken into account. National/regional requirements for ethics in clinical research and for protecting the safety, wellbeing, health and rights of subjects must 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 the investigation site's facilities are similar to the facilities required for the intended use of the investigational device.
Annex 7, 2.3.4	6.2, 6.3, 7.4, 9.2.5, 10.8 and A.3 to 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, 10.3 and Annex B	
Annex 7, 2.3.7	8.4, 9.2.6, 10.6 r) and Annex D	
[a] See MEDDEV 2.7/1, Section 6.3.		

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 products falling within the scope of this standard.

INTERNATIONAL STANDARD

ISO 14155

Third edition
2020-07

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

Investigation clinique des dispositifs médicaux pour sujets humains — Bonne pratique clinique

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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.

INTERNATIONAL STANDARD **ISO 14155:2020(E)**

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*

