Irish Standard
I.S. EN ISO 14155:2011

Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155:2011)

I.S. EN ISO 14155:2011

Incorporating amendments/corrigenda/National Annexes issued since publication:

The National Standards Authority of Ireland (NSAI) produces the following categories of formal documents:

I.S. xxx: Irish Standard – national specification based on the consensus of an expert panel and subject to public consultation.

S.R. xxx: Standard Recommendation - recommendation based on the consensus of an expert panel and subject to public consultation.

SWiFT xxx: A rapidly developed recommendatory document based on the consensus of the participants of an NSAI workshop.

This document replaces:
EN ISO 14155:2011

This document is based on:	*Published:*
EN ISO 14155:2011	31 October, 2011
EN ISO 14155:2011	9 February, 2011

This document was published under the authority of the NSAI and comes into effect on:
31 October, 2011

ICS number:
11.100.20

NSAI
1 Swift Square,
Northwood, Santry
Dublin 9

T +353 1 807 3800
F +353 1 807 3838
E standards@nsai.ie

W NSAI.ie

Sales:
T +353 1 857 6730
F +353 1 857 6729
W standards.ie

Údarás um Chaighdeáin Náisiúnta na hÉireann

I.S. EN ISO 14155:2011

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 14155

October 2011

ICS 11.100.20

Supersedes EN ISO 14155:2011

English Version

Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155:2011)

Investigation clinique des dispositifs médicaux pour sujets humains - Bonnes pratiques cliniques (ISO 14155:2011)

Klinische Prüfung von Medizinprodukten an Menschen - Gute klinische Praxis (ISO 14155:2011)

This European Standard was approved by CEN on 20 September 2011.

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

Management Centre: Avenue Marnix 17, B-1000 Brussels

Ref. No. EN ISO 14155:2011: E

Contents

Page

Foreword

This document (EN ISO 14155:2011) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 258 “Clinical investigation 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of an identical text or by endorsement, at the latest by April 2012, and conflicting national standards shall be withdrawn at the latest by April 2012.

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

This document supersedes EN ISO 14155:2011.

This new edition contains revised Annexes ZA and ZB.

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 relationship with EU Directives, see informative Annexes ZA and ZB, which are an integral part of this document.

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, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 14155:2011 has been approved by CEN as EN ISO 14155:2011 without any modification.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the 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.

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

For all requirements related to clinical investigations contained in the directive and referred to in the following chart: Obligations attributed to the "sponsor" under ISO 14155 shall be incumbent, under the MDD 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.

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
Entire standard	Annex I. 6a	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[1] and 2) parts of Annex X.2 listed below.
4.1, 5.2 and 5.3	Annex X: 2.2.	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.
5,3, 5.4, A.7	Annex X: 2.3.1	
5.3, A.3 and A.6	Annex X 2.3.2.	

[1] See MEDDEV 2.7/1, Section 6.3.

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
5.3, A.3 and A.6	Annex X: 2.3.3.	
5.3, A.5 and 8.2.5	Annex X: 2.3.4.	
6.4.1, 8.2.5 d) and 9.8	Annex X: 2.3.5.	Partial compliance: covers internal procedures of sponsor to address SAE[2]-reporting requirements of the Directive.
5.5, 5.8, 6, 9.2, 9.3 and Annex B	Annex X: 2.3.6.	
7.3	Annex X: 2.3.7.	
5.4, Annex A; 5.5, Annex B; 4.7	Annex VIII, 2.2., structure/content of the documents required in the 2nd, 3rd and 5th indent.	National/regional requirements for ethics in clinical research and for protecting the safety, wellbeing, health and rights of subjects must be observed.

WARNING — Other requirements and other EU Directives may be applicable to the product(s)/clinical investigations falling within the scope of this standard.

[2] SAE = Serious Adverse Event.

Annex ZB
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 90/385/EEC on Active Implantable Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 90/385/EEC on active implantable medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the 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.

Table ZB.1 — Correspondence between this European Standard and Directive 90/385/EEC on active implantable medical devices

For all requirements related to clinical investigations contained in the directive and referred to in the following chart: Obligations attributed to the "sponsor" under ISO 14155 shall be incumbent, under the MDD 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.

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
Entire standard	6a	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[3] and 2) parts of Annex VII.2 listed below.
4.1, 5.2 and 5.3	Annex 7: 2.2.	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.
5,3, 5.4, A.7	Annex 7: 2.3.1.	

[3] See MEDDEV 2.7/1, Section 6.3.

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
5.3, A.3 and A.6	Annex 7: 2.3.2.	
5.3, A.3 and A.6	Annex 7: 2.3.3.	
5.3, A.5 and 8.2.5	Annex 7: 2.3.4.	
6.4.1, 8.2.5 d) and 9.8	Annex 7: 2.3.5.	Partial compliance: covers internal procedures of sponsor to address SAE[4]-reporting requirements of the Directive.
5.5, 5.8, 6, 9.2, 9.3 and Annex B	Annex 7: 2.3.6.	
7.3	Annex 7: 2.3.7.	
5.4, Annex A; 5.5, Annex B; 4.7	Annex 7, 2.2., structure/content of the documents required in the 2nd, 3rd and 5th indent.	National/regional requirements for ethics in clinical research and for protecting the safety, wellbeing, health and rights of subjects must be observed.

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

4 SAE = Serious Adverse Event.

This page is intentionally left BLANK.

I.S. EN ISO 14155:2011

INTERNATIONAL STANDARD

ISO 14155

Second edition
2011-02-01

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

Investigation clinique des dispositifs médicaux pour sujets humains — Bonnes pratiques cliniques

Reference number
ISO 14155:2011(E)

PDF disclaimer

This PDF file may contain embedded typefaces. In accordance with Adobe's licensing policy, this file may be printed or viewed but shall not be edited unless the typefaces which are embedded are licensed to and installed on the computer performing the editing. In downloading this file, parties accept therein the responsibility of not infringing Adobe's licensing policy. The ISO Central Secretariat accepts no liability in this area.

Adobe is a trademark of Adobe Systems Incorporated.

Details of the software products used to create this PDF file can be found in the General Info relative to the file; the PDF-creation parameters were optimized for printing. Every care has been taken to ensure that the file is suitable for use by ISO member bodies. In the unlikely event that a problem relating to it is found, please inform the Central Secretariat at the address given below.

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Contents

Page

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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 14155 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This second edition cancels and replaces the first edition of ISO 14155-1:2003 and the first edition of ISO 14155-2:2003, which have been technically revised.

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

1 Scope

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

The principles set forth in this International Standard also apply to all other clinical investigations and should be followed as far as possible, considering the nature of the clinical investigation and the requirements of national regulations.

This International Standard 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.

It does not apply to *in vitro* diagnostic medical devices.

NOTE Standards developed by ISO/TC 194 are intended to be applied to medical devices. Users of this International Standard will need to consider whether other standards and/or requirements also apply to the investigational device(s) under consideration.

2 Normative references

The following referenced documents are indispensable for the application 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 14971:2007, *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.

3.1
adverse device effect
ADE
adverse event related to the use of an investigational medical device

NOTE 1 This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2 This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

3.2
adverse event
AE
any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device

NOTE 1 This definition includes events related to the investigational medical device or the comparator.

NOTE 2 This definition includes events related to the procedures involved.

NOTE 3 For users or other persons, this definition is restricted to events related to investigational medical devices.

3.3
audit
systematic independent examination of activities and documents related to clinical investigation to determine whether these activities were conducted, and the data recorded, analysed and accurately reported, according to the CIP, standard operating procedures, this International Standard and applicable regulatory requirements

3.4
blinding/masking
procedure in which one or more parties to the clinical investigation are kept unaware of the treatment assignment(s)

NOTE Single blinding usually refers to the subject(s) being unaware of the treatment assignment(s). Double blinding usually refers to the subject(s), investigator(s), monitor and, in some cases, centralized assessors being unaware of the treatment assignment(s).

3.5
case report forms
CRFs
set of printed, optical or electronic documents for each subject on which information to be reported to the sponsor is recorded, as required by the CIP

3.6
clinical investigation
systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a medical device

NOTE “Clinical trial” or “clinical study” are synonymous with “clinical investigation”.

3.7
clinical investigation plan
CIP
document that state(s) the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation

NOTE The term “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 International Standard.

3.8
clinical investigation report
document describing the design, execution, statistical analysis and results of a clinical investigation

3.9
clinical performance
behaviour of a medical device or response of the subject(s) to that medical device in relation to its intended use, when correctly applied to appropriate subject(s)

3.10
comparator
medical device, therapy (e.g. active control), placebo or no treatment, used in the reference group in a clinical investigation

3.11
contract research organization
CRO
person or organization contracted by the sponsor to perform one or more of the sponsor's clinical investigation-related duties and functions

3.12
coordinating investigator
investigator who is appointed by the sponsor to coordinate work in a multicentre clinical investigation

3.13
data monitoring committee
DMC
independent committee that may be established by the sponsor to assess, at intervals, the progress of the clinical investigation, the safety data or the critical performance endpoints and to recommend the sponsor whether to continue, suspend, modify, or stop the clinical investigation

NOTE Examples of DMCs are “data safety monitoring board (DSMB)” or “data safety monitoring committee (DSMC)”.

3.14
deviation
instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP

3.15
device deficiency
inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance

NOTE Device deficiencies include malfunctions, use errors, and inadequate labelling.

3.16
endpoint(s)
⟨primary⟩ principal indicator(s) used for assessing the primary hypothesis of a clinical investigation

3.17
endpoint(s)
⟨secondary⟩ indicator(s) used for assessing the secondary hypotheses of a clinical investigation