INTERNATIONAL STANDARD

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Clinical investigation of medical devices for human subjects —

Part 1: General requirements

Investigation clinique des dispositifs médicaux pour sujets humains — Partie 1: Exigences générales

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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.

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 14155-1 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This first edition of ISO 14155-1, together with ISO 14155-2, cancels and replace ISO 14155:1996, which has been technically revised.

ISO 14155 consists of the following parts, under the general title *Clinical investigation of medical devices for human subjects:*

— *Part 1: General requirements*

— *Part 2: Clinical investigation plans*

Introduction

This part of ISO 14155 is intended to be applied worldwide to clinical investigations of medical devices in order to fulfil the technical aspects of the various national, regional and international regulatory requirements. As the legal regulatory requirements presently differ throughout the world, regulatory specifics have been excluded from the scope of this part of ISO 14155. They are part of national or regional legislative texts and can be referenced in the national or regional forewords, as appropriate.

Clinical investigation of medical devices for human subjects —

Part 1:
General requirements

1 Scope

This part of ISO 14155 defines procedures for the conduct and performance of clinical investigations of medical devices. It specifies general requirements intended to

— protect human subjects,

— ensure the scientific conduct of the clinical investigation,

— assist sponsors, monitors, investigators, ethics committees, regulatory authorities and bodies involved in the conformity assessment of medical devices.

This part of ISO 14155

a) specifies requirements for the conduct of a clinical investigation such that it establishes the performance of the medical device during the clinical investigation intended to mimic normal clinical use, reveals adverse events under normal conditions of use, and permits assessment of the acceptable risks having regard to the intended performance of the medical device,

b) specifies requirements for the organization, conduct, monitoring, data collection and documentation of the clinical investigation of a medical device,

c) is applicable to all clinical investigation(s) of medical devices whose clinical performance and safety is being assessed in human subjects.

This part of ISO 14155 is not applicable to *in vitro* diagnostic medical devices.

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 14155-2, *Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans*

3 Terms and definitions

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

3.1
adverse device effect
any untoward and unintended response to a medical device

NOTE 1 This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device.

NOTE 2 This definition includes any event that is a result of a user error.

3.2
adverse event
any untoward medical occurrence in a subject

NOTE This definition does not imply that there is a relationship between the adverse event and the device under investigation.

3.3
case report form
document designed to record all information to be reported to the sponsor on each subject as required by the clinical investigation plan

3.4
clinical investigation
any designed and planned systematic study in human subjects undertaken to verify the safety and/or performance of a specific device

3.5
clinical investigation plan
CIP
document that states the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation

NOTE The word “protocol” is often used synonymously with the term “clinical investigation plan”. However, it has many different meanings, some not related to clinical investigations, and these may differ from country to country. Therefore, it is not used in this part of ISO 14155.

3.6
clinical investigator
individual and/or institution responsible for the conduct of a clinical investigation who and/or which takes the clinical responsibility for the well-being of the subjects involved

NOTE Whether this is an individual or an institutional responsibility may depend on national legislation.

3.7
clinical investigator's brochure
compilation of the clinical and non-clinical information on the device(s) under investigation, that is relevant to the investigation in human subjects

3.8
clinical performance
behaviour of a specific medical device and/or its performance in relation to its intended use when correctly applied to appropriate subjects

3.9
coordinating clinical investigator
clinical investigator who is appointed by the sponsor to coordinate work in a multicentre clinical investigation

3.10
ethics committee
independent and properly constituted competent body whose responsibility is to ensure that the safety, well-being and human rights of the subjects participating in a clinical investigation are protected

NOTE For the purposes of this part of ISO 14155, "ethics committee" is synonymous with "research ethics committee" or "institutional review board". The regulatory requirements pertaining to ethics committees or similar institutions may differ from country to country.

3.11
final report
description, results and evaluation of the clinical investigation after its completion

3.12
informed consent
legally effective, documented confirmation of a subject's (or his/her legal guardian or representative) voluntary agreement to participate in a particular clinical investigation after information has been given to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate

3.13
investigation centre
investigation site
institution or site where the clinical investigation is carried out

3.14
medical device

any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used on human beings for the purpose of

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation or compensation for an injury or handicap,

— investigation, replacement or modification of the anatomy or of a physiological process,

— control of conception,

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

NOTE The term "medical device" is usually defined by national law. In order to inform the user of this part of ISO 14155, the definition from reference [1] is listed (see Bibliography). More information is given in reference [3].

3.15
monitor
individual appointed by the sponsor responsible for assessing the investigator's compliance with the clinical investigation plan and for performing source-data verification

NOTE The monitor is also responsible for reporting to the sponsor on the progress of the clinical investigation, including the compliance of the investigators.

3.16
multicentre investigation
clinical investigation which is conducted according to a single clinical investigation plan and which takes place at two or more sites

3.17
principal clinical investigator
clinical investigator responsible for the organization of the clinical investigation at one site

3.18
serious adverse device effect
adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune

3.19
serious adverse event
adverse event that

a) led to a death,

b) led to a serious deterioration in the health of the subject that

   1) resulted in a life-threatening illness or injury,

   2) resulted in a permanent impairment of a body structure or a body function,

   3) required in-patient hospitalization or prolongation of existing hospitalization,

   4) resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function.

c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

3.20
source data
all information in original and identified records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation

3.21
source documents
original documents, data and records

NOTE This may be for example, hospital records, laboratory notes, pharmacy dispensing records, copies or transcriptions certified after verification as being accurate copies, photographic negatives, radiographs, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical investigation.

3.22
sponsor
individual or organization who or which takes responsibility for the initiation and/or implementation of a clinical investigation

NOTE 1 For the purposes of this part of ISO 14155 the word “sponsor” is synonymous with the word “promoter”.

NOTE 2 When a clinical investigator independently initiates, implements and takes full responsibility for the clinical investigation, the clinical investigator also assumes the role of the sponsor.

3.23
subject
individual who participates in a clinical investigation, either as a recipient of the device under investigation or as a control

4 Justification for a clinical investigation

In order to determine the justification and optimal design for a clinical investigation, an objective review of published and available unpublished medical and scientific data and information shall be conducted and documented.

NOTE 1 Guidance for such a literature review is given in Annex A.

The decision to embark upon a clinical investigation of a medical device requires *inter alia* the residual risks to be balanced against the anticipated benefits of the clinical investigation.

NOTE 2 For further information, see ISO 14971[6].

5 Ethical considerations

5.1 Declaration of Helsinki

The rights, safety and wellbeing of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the Declaration of Helsinki. This shall be understood, observed and applied at every step in the clinical investigation.

5.2 Improper influence or inducement

The sponsor and the clinical investigator(s) shall avoid improper influence or inducement of the subject, monitor, the clinical investigator(s) or other parties participating in or contributing to the clinical investigation.

5.3 Compensation and additional health care

The sponsor shall state what provision will be made for compensation of subjects in the event of injury arising from participation in the clinical investigation and this shall be documented. Arrangements for additional health care for subjects required as a result of an adverse device effect shall be made and documented.

NOTE This may be the subject of national legislation.

5.4 Responsibilities

All parties involved in the conduct of the clinical investigation shall share the responsibility for its ethical conduct in accordance with their respective roles in the investigation.

6 General requirements

6.1 Formal agreement(s)

There shall be agreement(s) between the sponsor, the clinical investigator(s) and other relevant parties which define(s) their responsibilities. All formal agreements shall be recorded in writing and signed by all parties involved.

6.2 Qualifications

All parties participating in the conduct of the clinical investigation shall be appropriately qualified by education and/or experience to perform their tasks.