INTERNATIONAL STANDARD

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Clinical investigation of medical devices for human subjects —

Part 2: Clinical investigation plans

Investigation clinique des dispositifs médicaux pour sujets humains — Partie 2: Plans d'investigation 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.

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 14155-2 was prepared by the European Committee for Standardization (CEN) in collaboration with Technical Committee ISO/TC 194, *Biological evaluation of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

Throughout the text of this document, read "...this European Standard..." to mean "...this International Standard...".

This first edition, together with the first edition of ISO 14155-1, cancels and replaces 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*

For the purposes of this part of ISO 14155, the CEN annex regarding fulfilment of European Council Directives has been removed.

Contents

Foreword

This document (EN ISO 14155-2:2003) has been prepared by Technical Committee CEN /TC 258 "Clinical investigation of medical devices", the secretariat of which is held by AFNOR, in collaboration with Technical Committee ISO/TC 194 "Biological evaluation of medical devices".

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 November 2003, and conflicting national standards shall be withdrawn at the latest by November 2003.

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).

Annex A is informative.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Slovakia, Spain, Sweden, Switzerland and the United Kingdom.

Introduction

This standard is the second part of EN ISO 14155 "Clinical investigation of medical devices for human subjects", and should be read in conjunction with that standard.

The standard is intended to assist manufacturers, sponsors, monitors and clinical investigators in the design and conduct of clinical investigations. It is also intended to assist regulatory bodies and ethics committees in their roles of reviewing Clinical Investigation Plans (CIP). The CIP is a framework within which appropriate experience, insight, judgement, qualification and education need to be applied. The scientific rigour of a CIP can be verified and possibly improved by an independent review of the CIP.

1 Scope

This part of EN ISO 14155 provides requirements for the preparation of a Clinical Investigation Plan (CIP) for the clinical investigation of medical devices. The compilation of a CIP in accordance with the requirements of this standard and adherence to it will help in optimising the scientific validity and reproducibility of the results of a clinical investigation.

This Standard does not apply to in vitro diagnostic medical devices.

2 Normative references

This European Standard incorporates by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text, and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies (including amendments).

EN ISO 14155-1:2003, *Clinical investigation of medical devices for human subjects — Part 1: General requirements. (ISO 14155-1:2001)*

3 Terms and definitions

For the purposes of this European Standard, the terms and definitions given in EN ISO 14155-1:2003 and the following apply.

3.1
end point - primary
principal indicator measured or determined to assess the primary objective of a clinical investigation

3.2
end point - secondary
indicator measured or determined in addition to the primary end-point to assess some other objective of a clinical investigation

3.3
point of enrolment
time at which, following recruitment, a subject has signed the informed consent form and is regarded as part of the study population

3.4
follow-up period
period of the clinical investigation after the application of the device under investigation in each subject during which the effects of the device are observed

3.5
recruitment
process of identifying subjects who may be suitable for enrolment into the clinical investigation

4 Requirements

4.1 General

All requirements of EN ISO 14155-1 apply.

4.2 Clinical Investigation Plan (CIP)

The CIP shall be a document developed by the sponsor and the clinical investigator(s). The CIP shall be designed in such a way as to optimise the scientific validity and reproducibility of the results of the study in accordance with current clinical knowledge and practice so as to fulfil the objectives of the investigation.

The CIP shall include the information specified in the subsequent clauses. Alternatively, if the required information is written in other documentation, for example the clinical investigator's brochure or the sponsor's standard operating procedures, such documentation shall be referenced in the CIP and shall be made available on request.

In the event of the sponsor deciding that any requirement given in 4.3 to 4.10 is not applicable, relevant or appropriate, a clear statement justifying the omission of the information specified shall be provided on each occasion.

4.3 General information

4.3.1 Identification of the clinical investigation plan

The CIP and any amended version shall state the title of the clinical investigation and its reference number. The CIP shall also include a version/issue number and date to ensure that it may be traced to the signatories (see 4.3.7). Each page of the CIP shall be referenced with the version number.

4.3.2 Clinical investigators, principal clinical investigator, co-ordinating clinical investigator, investigation centres/site(s)

The CIP shall state or refer to a list of the name(s), address(es), and professional position(s) of the clinical investigator(s), of the principal clinical investigator(s) and co-ordinating clinical investigator if appointed. The CIP shall document the name(s) and address(es) of the Institution(s) in which the clinical investigation will be conducted. Where it may affect the validity of the clinical investigation, the name(s) and address(es) of other establishments or persons involved in patient management, and associated testing and analysis shall be given.

4.3.3 Sponsor

The CIP shall state the name and address of the sponsor of the clinical investigation.

NOTE If the sponsor is not resident in the country (countries) in which the clinical investigation is to be carried out, the name and address of a representative in that country (those countries) may be required according to national or regional regulations.

4.3.4 Monitoring arrangements

The CIP shall state the monitoring arrangements to be followed during the investigation and the planned extent of source data verification.

4.3.5 Data and quality management

The CIP shall describe or refer to the procedures for database management, treatment of data, source data verification, data archiving, retention period and other aspects of quality assurance as appropriate.

4.3.6 An overall synopsis of the clinical investigation

The CIP shall provide a summary or overview of the clinical investigation.

NOTE It may be useful to include a flow chart showing the key stages of the clinical investigation or any other information that may be of value for the conduct of the investigation.

4.3.7 Approval and agreement to the clinical investigation plan

The sponsor, the co-ordinating investigator (if appointed) and the principal clinical investigator(s) in each centre shall agree to the CIP and any amendments and indicate their approval and agreement by signing and dating an appropriate document.

4.4 Identification and description of the medical device to be investigated

The CIP shall include or refer to a summary description of the device to be investigated and its intended purpose. The following information shall be given:

a) the manufacturer of the device, its model or type number including software version and accessories, if any, to permit full identification and traceability. If this information is not known at the time the CIP is written, a description shall be given as to how traceability shall be achieved during and after the study;

b) the intended purpose of the device as stated by the manufacturer including the clinical indications and contra-indications for use in the proposed study and the populations for which it is intended;

c) a description of the device including any materials that will be in contact with tissues or body fluids. This shall include details of any medicinal products, human and/or animal tissues or their derivatives, or other biologically active substances;

d) instructions for installation and use of the device including any necessary storage and handling requirements, preparation for use and any intended re-use (e.g. sterilization), any pre-use checks of safety and performance and any precautions to be taken after use, e.g. disposal;

e) a summary of necessary training and experience needed for the use of the device under investigation;

f) a description of the necessary medical or surgical procedures involved in the use of the device.

4.5 Preliminary investigations and justification of the study

4.5.1 Literature review

The CIP shall contain a critical review of the relevant scientific literature and/or unpublished data and reports together with a list of the literature reviewed. The conclusions from this review shall justify the design of the proposed investigation. The review shall be relevant to the intended purpose of the device to be investigated and the proposed method of use. It should also help in the identification of relevant end-points and confounding factors that should be considered, and the choice and justification of control methods.

NOTE Guidance on literature review and appraisal is provided in EN ISO 14155 – 1:2003, annex A.

4.5.2 Preclinical testing

The CIP shall summarise the preclinical testing that has been performed on the device to be investigated to justify its use in human subjects, together with an evaluation of the results of such testing. The summary shall include or refer to pre-clinical experimental data including, where applicable, the results of design calculations, in vitro tests, mechanical and electrical tests, reliability checks and the validation of software relating to the function of the device. Also to be included are the results of any performance tests, ex vivo testing, biological testing and/or safety tests in animals, including the relevance of tests and the timescale of such tests.

NOTE Guidance on the biological evaluation of medical devices is given in EN ISO 10993 [6].