

Ophthalmic implants — Intraocular lenses —

Part 7: Clinical investigations

The European Standard EN 13503-7:2001 has the status of a British Standard

ICS 11.040.70

National foreword

This British Standard is the official English language version of EN 13503-7:2001.

The UK participation in its preparation was entrusted by Technical Committee CH/78, Ophthalmic optics, to Subcommittee CH/78/7, Eye implants, which has the responsibility to:

- aid enquirers to understand the text;
- present to the responsible European committee any enquiries on the interpretation, or proposals for change, and keep the UK interests informed;
- monitor related international and European developments and promulgate them in the UK.

A list of organizations represented on this subcommittee can be obtained on request to its secretary.

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This European Standard was approved by CEN on 11 November 2001.

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This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and United Kingdom.



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Foreword

This European Standard has been prepared by Technical Committee CEN/TC 170, "Ophthalmic optics", 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of an identical text or by endorsement, at the latest by June 2002, and conflicting national standards shall be withdrawn at the latest by June 2002.

European Standard EN 13503-7 was developed by CEN/TC 170, *Ophthalmic optics*, in cooperation with ISO/TC 172/SC 7, *Ophthalmic optics and instruments*, and is published in several parts under the general title *Ophthalmic implants - Intraocular lenses*:

- *Part 1: Vocabulary*
- *Part 2: Optical properties and test methods*
- *Part 3: Mechanical properties and test methods*
- *Part 4: Labelling and information*
- *Part 5: Biocompatibility*
- *Part 6: Shelf-life and transport stability*
- *Part 7: Clinical investigations*
- *Part 8: Fundamental requirements*

It always was and still is the intention of the Technical Committees CEN/TC 170 and ISO/TC 172/SC 7 to prepare identical ISO and CEN Standards on intraocular lenses. However, during the preparation of part 7 of the above intraocular lenses standards series, problems were encountered with normative references to the existing ISO 14155 and EN 540 horizontal standards on clinical investigation of medical devices, those being similar but not identical.

ISO and CEN principles concerning normative references made it impossible to continue the preparation of identical European and International Standards on the clinical investigation of intraocular lenses. As a result, two different standards series, ISO 11979 and EN 13503 had to be prepared.

It is the intention of CEN/TC 170 and ISO/TC 172/SC 7 to revise these standards with the goal to end up with identical ones as soon as identical ISO and CEN horizontal standards become available.

EN 13503 is the modified ISO 11979. The main difference between both series of standards is that ISO 11979 is based on the reference to ISO 14155 *Clinical investigation of medical devices* while EN 13503 is based on the reference to EN 540 *Clinical investigation of medical devices for human subjects*.

Compared with ISO 11979-7 the present EN 13503-7 does not contain an informative annex detailing modifications of IOL parent models.

Modifications of ISO 11979 are indicated as follows:

- text which has been deleted is striked out;
- text which has been changed or added is underlined.

Cross references to ISO 11979-7 are given where possible.

This Part 7 of EN 13503 contains one normative annex A and three informative annexes C, D and ZA.

EN 13503-7:2001 (E)

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, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of the International Standard ISO 11979-7:2001 was approved by CEN as a European Standard with agreed common modifications as given in the foreword and indicated in the text by strike-out and underlining.

NOTE A-deviations are given in annex ZA (informative).

Introduction

This part of ~~EN 13503 ISO 11979~~ provides fundamental requirements of a general nature for intraocular lenses. It refers to other standards applicable to intraocular lenses for specific methods and requirements.

It always was and still is the intention of the Technical Committees ISO/TC 172/SC 7 and CEN/TC 170 to prepare identical ISO and CEN (European Committee for Standardization) standards on intraocular lenses. However, during the preparation of this part of ~~EN 13503 ISO 11979~~, problems were encountered with normative references to the existing ISO 14155 and EN 540 horizontal standards on clinical investigation of medical devices, which are similar but not identical.

ISO and CEN principles concerning normative references made it impossible to continue the preparation of identical International and European Standards on the clinical investigation of intraocular lenses. As a result, two different standards series have had to be prepared. It is the intention of ISO/TC 172/SC 7 and CEN/TC 170 to revise these standards with the goal to end up with identical ones as soon as identical ISO and CEN horizontal standards on clinical investigations become available.

1 Scope

This part of ~~EN 13503 ISO 11979~~ specifies particular requirements for clinical investigation protocols for posterior and anterior chamber monofocal intraocular lenses (IOLs) for the correction of aphakia.

NOTE Any other type of IOL not directly covered by ~~EN 13503 ISO 11979~~ and any IOL for which the sponsor wishes to investigate claims in addition to those defined in ~~EN 13503 ISO 11979~~ may be clinically evaluated by reference to ~~EN 540 ISO 14155~~.

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).

~~The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 11979. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 11979 are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.~~

~~EN 540:1993, Clinical investigation of medical devices for human subjects. ISO 14155:1996, Clinical investigation of medical devices.~~

~~EN ISO 11979-1:1999, Ophthalmic implants - Intraocular lenses - Part 1: Vocabulary (ISO 11979-1:1999).~~

~~EN 13503-3:2000, Ophthalmic implants – Intraocular lenses – Part 3: Mechanical properties and test methods (ISO 11979-3:1999, modified). ISO 11979-3, Ophthalmic implants – Intraocular lenses – Part 3: Mechanical properties and test methods~~

3 Terms and definitions

For the purposes of this part of EN 13503 ~~ISO 11979~~, the terms and definitions given in EN 540 ~~ISO 14155~~ and EN ISO 11979-1 apply, together with the following.

For the convenience of users of this part of EN 13503 ~~ISO 11979~~, some definitions from EN ISO 11979-1 are reproduced in annex A. Terms relating to the design of IOLs are given in EN 13503-3 ~~ISO 11979-3~~.

3.1

serious adverse event

in addition to the definition in EN 540, an event which is potentially sight threatening is also considered a serious adverse event

NOTE 1 — ~~The definition for serious adverse event given in the ICH Harmonized Tripartite Guideline for Good Clinical Practices also applies (see reference [1] in the bibliography).~~

NOTE 2 — Examples of potentially sight-threatening adverse events are included in Tables D.1 and D.2.

4 General requirements

~~4 Ethical considerations~~

~~For clinical investigations of medical devices for human subjects, the requirements of ISO 14155 apply.~~

~~5 Requirements~~

~~5.1 General requirements~~

~~The requirements given in 5.1 to 5.7 of ISO 14155:1996 shall apply.~~

~~5.2 Additional requirements~~

Clause 4 of EN 540:1993 shall apply, together with the following additional requirements.

4.5 Addition (see 5.2.1 of ISO 11979-7:2001):

Addition:

Clinical investigators shall file adverse event reports of all serious adverse events with the sponsor immediately after learning of their occurrence. Other adverse events shall be reported on the case report forms.

The sponsor and the sponsor's investigators shall evaluate the rates of adverse events and visual acuity (VA) for the IOLs under clinical investigation on a continuing basis. If poor results at any investigational site are determined by clinical judgement to be potentially device related, consideration shall be given to termination of further enrolment in the clinical investigation.

~~5.2.1 — In addition to the requirements given in 5.5 of ISO 14155:1996, the sponsor and the sponsor's investigators shall evaluate the rates of adverse events and visual acuity (VA) for the IOLs under clinical investigation on a continuing basis.~~

NOTE — The published national study of cataract surgery in the United Kingdom may provide useful guidance on clinical performance of IOLs at periods corresponding with the early post-operative case report forms (see references [2] and [3]).

4.6 Addition (see 5.2.2 of ISO 11979-7:2001):

Addition:

The safety and effectiveness of an IOL model shall be established through either:

~~5.2.2 — In addition to the requirements given in 5.6 of ISO 14155:1996, the safety and effectiveness of an IOL model shall be established through either:~~

- a clinical investigation conducted in accordance with this part of EN 13503 ISO 11979; or
- a comparison of the model characteristics that establish the model as a minor modification of a parent model for which the safety and effectiveness has been established through clinical investigation in accordance with this part of EN 13503 ISO 11979.

~~NOTE — Annex B provides guidance in determining if a modification is minor by providing examples of modifications that have historically been considered minor.~~

For the IOL intended for correction of aphakia in a general adult population, a clinical investigation shall either be developed using the protocol elements provided in annex C or a sponsor shall develop an equivalent protocol that shall have a similar statistical power to detect differences in adverse event and visual acuity rates between the test population and a concurrent control population. Subjects implanted with a parent IOL that has met the requirements of all ~~parts of~~ EN 13503 and EN ISO 11979 may be used as a control population.

In the case of IOLs designed for either chamber, a separate clinical investigation shall be performed to assess the clinical performance of the IOL in each chamber.

~~5.2.3 — In addition to the requirements given in 5.7 of ISO 14155:1996, all subjects in a clinical investigation shall be monitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation, including those whose IOL was removed or replaced, have reached the final reporting period.~~

5 6 Methodology

5.1 General

The requirements given in 5.1 of EN 540:1993 shall apply.

6.1 Documentation

~~The requirements given in 6.1 of ISO 14155: 1996 shall apply.~~

5.2 Requirements before commencement of the clinical investigation

The requirements given in 5.2 of EN 540:1993 shall apply.

6.2 Access to information

~~The requirements given in 6.2 of ISO 14155:1996 shall apply.~~

6.3 Additional health care

~~The requirements given in 6.3 of ISO 14155: 1996 shall apply.~~

5.3 6.4 Clinical investigation plan

5.3.1 6.4.1 General requirements

The requirements given in 5.3 of EN 540:1993 ~~6.4 of ISO 14155:1996~~ shall apply.

5.3.2 6.4.2 Additional requirements

The following additional requirements shall apply.

~~The investigational lens shall only be implanted in a single eye of each subject.~~

5.3.5 Addition (see 5.2.3 of ISO 11979-7:2000):

All subjects in a clinical investigation shall be monitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation have completed the final reporting period of the investigation.

5.3.6 Addition:

The data from all subjects shall be reported including the data from subjects whose IOL was removed or replaced. The investigational lens shall only be implanted in a single eye of each subject.

5.3.7 Addition:

The clinical performance of the IOL in terms of visual acuity and adverse event rates shall be evaluated.

5.3.11 Addition:

At least the minimum sample size required by the study shall be included in the clinical investigation for each reporting period. The sponsor shall ensure a sufficient number of subjects in the clinical investigation so that the minimum number required by the investigation at each reporting period is reached. Each subject has to be monitored for the duration of the investigation. The investigation is not completed until the last subject has reached the final reporting period.

NOTE Examples of pre-operative, operative and post-operative case report forms are included in annex C.

5.4 6.5 Role of sponsor

The requirements given in 5.4 of EN 540:1993 ~~6.5 of ISO 14155:1996~~ shall apply.

5.5 6.6 Role of monitor

The requirements given in 5.5 of EN 540:1993 ~~6.6 of ISO 14155:1996~~ shall apply.

5.6 6.7 Role of clinical investigator

6.7.1 General requirements

The requirements given in 5.6 of EN 540:1993 ~~6.7 of ISO 14155:1996~~ shall apply.

6.7.2 Additional requirements

~~The following additional requirements shall apply.~~

~~Clinical investigators shall file adverse event reports of serious adverse events with the sponsor immediately after learning of their occurrence. Other adverse events shall be reported on the case report forms.~~

6 7 Presentation of results

The results shall be presented as specified in clause 6 of EN 540:1993 ~~clause 7 of ISO 14155:1996~~.