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Ophthalmic implants — Intraocular lenses —

Part 7:
Clinical investigations

Implants ophtalmiques — Lentilles intraoculaires —

Partie 7: Investigations cliniques

[Revision of second edition (ISO 11979-7:2006)]

ICS 11.040.70

ISO/CEN PARALLEL PROCESSING

This draft has been developed within the International Organization for Standardization (ISO), and processed under the **ISO-lead** mode of collaboration as defined in the Vienna Agreement.

This draft is hereby submitted to the ISO member bodies and to the CEN member bodies for a parallel five-month enquiry.

Should this draft be accepted, a final draft, established on the basis of comments received, will be submitted to a parallel two-month approval vote in ISO and formal vote in CEN.

To expedite distribution, this document is circulated as received from the committee secretariat. ISO Central Secretariat work of editing and text composition will be undertaken at publication stage.

Pour accélérer la distribution, le présent document est distribué tel qu'il est parvenu du secrétariat du comité. Le travail de rédaction et de composition de texte sera effectué au Secrétariat central de l'ISO au stade de publication.

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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 11979-7 was prepared by Technical Committee ISO/TC 172, *Optics and photonics*, Subcommittee SC 7, and by Technical Committee CEN/TC 170, *Ophthalmic optics* in collaboration.

This second edition cancels and replaces the first edition (ISO 11979-7:2006, ISO 11979-7:2006/Amd1:2012), which has been technically revised.

ISO 11979 consists of the following 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*

— *Part 9: Multifocal lenses*

— *Part 10: Phakic intraocular lenses*

Ophthalmic implants — Intraocular lenses — Part 7: Clinical investigations

1 Scope

This part of ISO 11979 specifies particular requirements for clinical investigations for posterior and anterior chamber intraocular lenses (IOLs).

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 11979-1, *Ophthalmic implants — Intraocular lenses — Part 1: Vocabulary*

ISO 11979-10:2006, *Ophthalmic implants — Intraocular lenses — Part 10: Phakic intraocular lenses*

ISO 14155, *Clinical investigation of medical devices for human subjects — Good clinical practices*

ISO 14971, *Medical devices — Application of risk management to medical devices*

3 Terms and definitions

For the purposes of this document the terms and definitions given in ISO 11979-1 and ISO 14155 shall apply.

4 Justification for a clinical investigation

A clinical evaluation in accordance with ISO 14155 shall be performed together with risk analysis, in accordance with ISO 14971.

If the need for a clinical investigation is identified, the requirements of ISO 14155 shall apply, with additional requirements given below.

If a new IOL model is a modification of a model for which the safety and performance have been established through clinical investigation in accordance with this part of ISO 11979 no or limited clinical investigation is needed. ISO TR 22979 [1] provides guidance in determining if a modification is minor.

5 Ethical considerations

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

6 General requirements

6.1 General

The requirements for a clinical investigation given in ISO 14155 shall apply, with additional requirements given below.

6.2 Design

6.2.1 General

A clinical investigation shall be designed in one of two ways:

a) As an uncontrolled investigation, in which case the results are compared to historical data on adverse events and visual acuity rates. This design is applicable only to those IOL types for which there are historical data in Annex B.

b) As a controlled investigation, with the provision that the statistical power to detect differences in the adverse event rates and visual acuity is similar to the uncontrolled investigation. The control lens shall be an IOL previously approved under national regulations.

Annex A provides general guidance for the design of a clinical investigation.

6.2.2 Additional requirements for toric IOLs

For all toric IOLs, the rotational stability of a non-toric version that is mechanically and geometrically equivalent to the toric IOL shall be demonstrated.

The following performance criteria for rotational stability shall be fulfilled:

— The rotation of the meridian defined by the IOL axis indicator as measured and compared between the Day 1 (the day after surgery) post-operative examination and the 4 to 6 month examination shall be less than 10° in 90 % of the cases, and less than 20° in 99 % of the cases.

Then, if necessary due to national requirements, a clinical investigation shall be performed using the toric version of the model.

The following performance criterion for clinical investigation shall be fulfilled:

— The mean achieved reduction in cylinder shall be ≥ 68 % of the intended cylinder reduction.

In the event that a toric IOL clinical investigation is required due to national regulations, the subjects that undergo secondary surgery to correct IOL mark axis rotation shall have their clinical results prior to the secondary surgery carried forward as the final results for that subject. In the case of examinations that are scheduled to be performed later in the clinical investigation (e.g., questionnaire), the sponsor shall consider requiring each of these examinations to be performed prior to the secondary surgery, if possible.

Additional elements for toric IOLs are outlined in Annex C.

6.2.3 Additional requirements for accommodating IOLs

A clinical investigation of an accommodating IOL shall evaluate the additional safety and performance concerns outlined in Annex D, specifically including the evaluation of accommodative amplitude using at least one objective method. It shall consist of two phases, with phase two beginning only after the first phase has demonstrated that the accommodating IOL provides an average of at least 1 D of objective accommodation. The overall study shall demonstrate that the accommodating IOL provides statistically greater objective accommodative amplitude compared to the control IOL.

6.3 Variables

The following variables shall be considered. If additional claims are to be made, additional corresponding variables shall be studied.

The clinical investigational plan should provide instructions regarding recording observations. In the event of any lens displacement or dislocation from the intended position causing visual symptoms, the instructions should include obtaining a photographic image if possible (or a detailed sketch) and recording as much detailed information in the subject's chart as possible.

6.3.1 General variables

a) best spectacle corrected visual acuity (BSCVA);

b) subjective refraction;

c) intraocular pressure;

d) corneal status;

e) anterior chamber cells;

f) anterior chamber flare;

g) cystoid macular edema;

h) hypopyon;

i) endophthalmitis;

j) pupillary block;

k) retinal detachment;

l) status of anterior and posterior capsule;

m) IOL decentration [2];

n) IOL tilt [2];

o) IOL discoloration;

p) IOL opacity.

6.3.2 Toric IOL variables

a) uncorrected visual acuity;

b) keratometry;

c) IOL mark axis rotation;

d) subject questionnaire.

6.3.3 Accommodating IOL variables

a) uncorrected visual acuity at distance, intermediate and near;

b) visual acuity at near and intermediate with best distance correction;

c) best corrected near visual acuity;

d) add power (over best distance subjective correction) required to achieve best corrected near acuity;

e) objective accommodative amplitude;

f) contrast sensitivity;

g) subject questionnaire;

h) pupil size.

6.3.4 Additional variables

If justified by the risk analysis, these additional variables shall be considered.

a) cycloplegic refraction;

b) specular microscopy;

c) gonioscopic examination;

d) pupil size;

e) anterior chamber depth measurement.

6.4 Investigation duration

The minimum duration of the clinical investigations shall be 1 year (see Annex A for visit window tolerance) for aphakic posterior chamber IOLs which are not modifications of a model for which safety and performance data have been established through clinical investigation.

The minimum duration of the clinical investigations shall be 3 years (see Annex A for visit window tolerance) for aphakic anterior chamber IOLs which are not modifications of a model for which safety and performance data have been established through clinical investigation.

The minimum study duration for accommodating IOLs through clinical investigation shall be 1 year but may require up to 3 years based on the risk analysis.

For all toric IOLs, a 6 month study of the non-toric version of the IOL shall be performed to insure rotational stability. Then for toric IOLs that are a modification of an IOL that has met the requirements of all parts of ISO 11979, national regulations may require that this rotational stability study is followed by a clinical investigation of the actual toric IOL for 6 months. Toric IOLs that are not a modification of an IOL that has met the requirements of all parts of ISO 11979 shall require a full clinical investigation of 1 year duration.

Consult ISO/TR 22979 for guidance on investigation duration for modifications of lens models for which safety and performance has been established through clinical investigation.

All subjects in a clinical investigation that have not been discontinued shall complete all visits of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation, including subjects whose IOL was removed or replaced, have reached the final reporting period.

6.5 Enrollment

To minimize the risks associated with the clinical investigation of a new IOL, subject enrollment shall occur in stages. The subject data from each stage shall be evaluated and found acceptable by the sponsor and the coordinating investigator (and by the regulatory body, if applicable) prior to the continuation of the clinical investigation. Guidance on phased enrollment is included in Annex A (monofocal IOL), Annex C (toric IOL) and Annex D (accommodating IOL).

Risk analysis should be used to determine if an earlier phase than the phase 1 listed in the Annexes above is needed to address safety issues associated with the IOL design.

6.6 Bilateral implantation

Any plans for fellow eye implantation shall be described in the clinical investigation plan. Bilateral implantation shall not be implemented until initial safety and performance data have been collected, evaluated and confirmed by the sponsor and coordinating investigator (and by the regulatory body, if applicable). Only the first eye of each subject shall be included in the primary statistical analysis.

When implantation of fellow eye is permitted, the clinical investigation plan shall specify time period between implantation of first eye and of fellow eye, based upon risk analysis.

NOTE The review of data from at least 50 eyes with six months of follow-up is recommended prior to fellow eye implantation. Previous clinical experience, i.e., results from well-documented clinical investigations, may be adequate justification to begin bilateral implantation earlier in the investigation as determined through the risk analysis.

6.7 Surgical technique

The clinical investigation plan shall contain descriptions of the surgical technique, the intraoperative use of ophthalmic viscosurgical devices, and the use of preoperative, intraoperative and postoperative medications. Any deviation shall be recorded on the case report forms.

For toric IOLs, the clinical investigation plan shall specify the type and location of the incision. The estimated effect of the incision on the corneal astigmatism shall be used in the protocol for choosing the appropriate cylindrical power.

6.8 Examination and treatment of subjects

The reporting periods are described in Annex A.

The clinical investigation plan shall describe how subject visits and ophthalmic adverse events that occur between standard reporting periods will be handled in the data analyses.

6.9 Adverse events reports

Serious adverse events and all adverse device effects shall be reported using a special case report form and forwarded to the sponsor as required. All other ophthalmic adverse events shall be reported using either the standard visit case report form or specific adverse event forms and be collected during monitoring. Non-ophthalmic events that are non-serious are not required to be reported.

6.10 Inclusion and exclusion criteria

6.10.1 General

The following inclusion/ exclusion criteria shall be considered. Additional criteria shall be included depending on the risk analysis for the particular IOL model.

6.10.1.1 Inclusion criteria

a) adult;

b) clinically significant cataract (does not apply for phakic IOL);

c) best corrected visual acuity projected to be better than 0,2 logMAR;

d) calculated IOL power is within the range of the investigational IOL;

e) signed informed consent form.

6.10.1.2 Exclusion criteria

a) any ocular condition that could affect the possibility of a visual outcome worse than 0,2 logMAR;

b) previous intraocular and corneal surgery;

c) traumatic cataract;

d) pregnancy and lactation;

e) concurrent participation in another drug or device investigation;

6.10.2 Additional criteria for toric IOL

6.10.2.1 Inclusion criteria

a) corneal cylindrical error within the range defined in the clinical investigation plan (CIP);

b) stability of the cornea has been demonstrated by keratometry;

c) expected dilated pupil size at least large enough to visualize the axis markings.

6.10.2.1.1 Additional inclusion criteria for phakic toric IOLs

a) the inclusion criteria described in ISO 11979-10 shall be considered.

6.10.2.2 Exclusion criteria

6.10.2.2.1 Additional exclusion criteria for phakic toric IOLs

a) the exclusion criteria described in ISO 11979-10 shall be considered;