TECHNICAL REPORT

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Ophthalmic implants — Intraocular lenses — Guidance on assessment of the need for clinical investigation of intraocular lens design modifications

Implants ophtalmiques — Lentilles intraoculaires — Directives relatives à l'évaluation de la nécessité d'investigation clinique pour les modifications de dessin des lentilles intraoculaires

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Foreword

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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.

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

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.

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Ophthalmic implants — Intraocular lenses — Guidance on assessment of the need for clinical investigation of intraocular lens design modifications

1 Scope

This Technical Report provides guidance on the application of Parts 3, 7 and 9 of the ISO 11979 series of International Standards for intraocular lenses (IOLs). It addresses factors to be considered in a risk analysis of the significance of modifications to anterior and posterior chamber, monofocal and multifocal, intraocular lenses. It also suggests methods of data analysis and interpretation that can be used to determine the need for and the design of a clinical investigation.

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*

3 Terms and definitions

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

4 Monofocal lenses

4.1 General

Monofocal IOLs that are modifications of a parent IOL, have different requirements for clinical investigations depending on the magnitude of the modifications. This Technical Report provides considerations for the risk analysis to determine which of the following are needed.

a) No clinical investigation.

b) Limited clinical investigation of 100 subjects followed up to and including Form 4, see ISO 11979-7.

c) Full clinical investigation as defined in ISO 11979-7.

4.2 Modification levels (categories)

4.2.1 Level A modifications

Level A modifications are minor modifications for which all safety and performance questions can be adequately addressed by non-clinical testing. Level A modifications require no clinical investigation.

4.2.2 Level B modifications

Level B modifications are modifications that raise safety and/or performance questions that can be adequately addressed with a limited clinical investigation.

4.2.3 Level C modifications

Level C modifications are modifications that raise safety and/or performance questions that can only be addressed with a full clinical investigation.

4.3 Clinical investigation with multiple IOL models

More than one IOL model can be studied in the same clinical investigation provided that the models are Level A modifications of each other. A model qualifies as a parent only if it has been investigated in a minimum of 100 subjects as defined in ISO 11979-1.

4.4 Mechanical data analysis

4.4.1 General

The mechanical data analysis method in this clause can be used to determine whether a modified posterior chamber IOL is a Level A modification.

The testing to characterize the mechanical characteristics of an IOL is described in ISO 11979-3. The data from the compression force, compression force decay and angle of contact testing is used to determine the difference in mechanical behaviour between the parent IOL(s) and a modification of the parent IOL(s).

Two methods of mechanical data analysis that can be considered to determine the differences between a modified IOL and parent IOL(s) are outlined in 4.4.2 and 4.4.3. A detailed description of the methods with examples is given in Annex B.

4.4.2 Comparison to a single parent IOL model

For comparison between a modified model and a single parent model, the manufacturer assesses whether the mechanical properties of the modified IOL are similar to those of the parent model.

4.4.3 Comparison to multiple parent IOL models

For comparison between a modified model and multiple parent models, the manufacturer assesses whether the mechanical properties of the modified IOL fall inside the ranges of mechanical characteristics defined by the parent models.

5 Multifocal lenses

5.1 General

This clause provides guidance to the risk analysis to assess whether a clinical investigation is warranted with regard to modifications of a multifocal IOL (MIOL) model. A modified MIOL can be compared to both monofocal and multifocal parents for mechanical properties, but only to multifocal parents for optical properties.

5.2 Addition of a parent multifocal optic to a parent monofocal model

5.2.1 General

The factors below are considered when adding a parent multifocal optic to a parent monofocal model. When a significant additional risk is identified, a clinical investigation, designed to address the specific risk area, is considered.

5.2.2 Material

Determine whether any characteristic of the monofocal lens material has an impact on the performance of the multifocal optic. If the material of the monofocal parent is different from that of the approved MIOL, a clinical study is considered, particularly if the optical or mechanical testing results in clinical concerns.

5.2.3 Mechanical design

Determine whether the design or placement of the monofocal parent affects the optical performance expected with the multifocal design. The risk analysis comprises the following.

a) The potential for increased variability in IOL centration (i.e. tilt and decentration) due to the monofocal parent's IOL body and haptic design. The comparison includes analysis of clinical study reports of centration issues and mechanical differences in IOL design.

b) Optical sensitivity to IOL decentration and tilt are evaluated using methods outlined in ISO 11979-2 by comparison of the decentration and tilt characteristics of the new multifocal design to the parent multifocal design.

c) Evaluation of the potential for changes in the predictability and stability of post-operative refraction.

5.3 Modification of the optical design geometry of a parent multifocal optic

The following factors are considered when modifying the geometry of a multifocal optic of a parent MIOL model.

a) A change in the fundamental technology creating the multiple powers (e.g. diffraction versus refraction) is a change to the multifocal parent design and a clinical investigation is performed as specified in ISO 11979-9.

b) Minor modifications to a parent multifocal design can be made to enhance or optimize performance. Optical bench testing as defined in ISO 11979-9, including measurement of the modulation transfer function (MTF) as function of spatial frequency (through-frequency MTF) and as function of defocus (through-focus MTF), is performed and analysed to assess the potential for significant changes in clinical function. Additional analysis is performed to assess specific concerns raised with the design modification. When an additional risk is identified, a clinical investigation is considered that is designed to address the specific risk area.

Annex A
(informative)

Examples of modifications to a parent IOL model

A.1 General

Modifications to an IOL that has undergone a clinical investigation can be classified in one of three categories depending on the level of modification: Level A, Level B or Level C. The applicable criteria to determine what level of modification has occurred to the parent model are described below.

The applicability column indicates the type of IOL that the modification is applicable to:

— P designates posterior chamber IOLs, excluding one-piece plate designs;

— A designates anterior chamber IOLs;

— PL designates posterior chamber IOLs made from flexible materials that are of a one-piece plate design.

A modified model may have various combinations of the modifications listed below, as long as all the applicable criteria are met.

A.2 Level A modifications

The Level A modifications are listed in Tables A.1 to A.3. Modifications in Table A.3 differ from the other modifications in that they involve material/design substitutions of parent models only.

Table A.1 — Change in loop configuration

Modification	Applicability	Mechanical data analysis
Mirror-image version of a model	P/A/PL	No
Change in overall diameter Addition of a size specific to patients with a certain anterior chamber width.	A	No
Changes in loop features Changes such as the addition of notches or the addition of eyelets or rounded ends to loops.	P/A	No
Change in loop angulation Changes to a design with the body angulated posterior to the loops resulting in a change in sagitta value up to a maximum of 1,6 mm for the 20 D version of the model.	P	No
Change in overall diameter	P	Yes
Change in loop thickness or width	P	Yes
Change in loop configuration (shape)	P	Yes

Table A.2 — Change in optic configuration

Modification	Applicability	Mechanical data analysis
Change in dioptric power range Whereby the IOL of any power in the range that the manufacturer makes available meets ISO 11979. The clearance between the surface of the anterior chamber IOL and the ocular tissue is a subject for consideration for each new power range, see ISO 11979-3.	P/A/PL	No
Change in optic or body size and addition of tabs to the periphery of the optic Changes in body circumference design or optic size if the length is not less than 5,0 mm along any meridian (e.g. going from a circular to an ovoid body) and not greater than 7,5 mm along any meridian.	P/PL	No
Change of clear optic Any obstruction that interferes with the performance of the optic, provided that the clear optic diameter is greater than 4,25 mm.	P/A/PL	No

Table A.3 — Interchanging IOL materials and designs

Modification	Applicability	Mechanical data analysis
Interchanging materials and design from parent IOLs Assuming that the interchange is within the limits of a Level A modification mechanically.	P	Yes

A.3 Level B modifications

The Level B modifications are listed in Tables A.4 and A.5.

Table A.4 — Change in loop configuration or material

Modification	Applicability	Mechanical data analysis
Change in loop configuration Including change in overall diameter, loop thickness or width, when not meeting the Level A criteria mechanically. If the change in loop configuration of the modified lens appears to have the potential to cause different or greatly increased safety concerns as compared to the parent model(s), it is considered to be a Level C modification.	P	Yes
Change to new loop material This is a change in loop material to a material that is new to the manufacturer, but is a material the long-term safety of which as a loop material can be supported by the ophthalmic literature, provided that the articles disclose the identity of the material used and the manufacturer uses the identical material.	P	Yes

Table A.5 — Change in optic material or configuration

Modification	Applicability	Mechanical data analysis
Change in body material This is a change in body material to a material that is new to the manufacturer, but is a material the long-term safety of which as a body material can be supported by the ophthalmic literature, provided that the articles disclose the identity of the material used and the manufacturer uses the identical material.	P	Not applicable
Change in body or optic diameter This is a change in body or optic diameter outside the range from 5,0 mm to 7,5 mm. Evaluations of models that incorporate optics less than 5,0 mm in diameter should include clinical testing to evaluate the effects of glare on the subject's visual acuity that may result from the small optic.	P	Not applicable

A.4 Level C modifications

Modifications not described in A.2 or A.3 are Level C modifications.

Annex B
(informative)

Mechanical data analysis

B.1 Principle

The methods in this annex apply to two-looped lens models only. Mechanical data, i.e. compression force, compression force after decay and angle of contact, can be used to assess whether a modified IOL is a Level A modification of a parent IOL, as described in Annex A.

B.2 Terms and definitions

The following terms and definitions in this paragraph apply for this Annex only.

B.2.1
open-loop IOL
IOL model which contains two loops, each loop having one end attached to the body of the IOL and the other end free

B.2.2
closed-loop IOL
IOL model, which contains two loops, each loop having both ends attached to the body of the optic

B.2.3
hybrid open-loop/closed-loop IOL
IOL model which contains two loops, with one loop having one end attached to the body of the IOL and the other end free, and the other loop having both ends attached to the body of the IOL

B.3 Mechanical comparison methods

B.3.1 General

For comparisons between a modified model and a single parent model, which is either currently undergoing a clinical investigation or has completed a clinical investigation, the manufacturer demonstrates that the mechanical properties of the modified lens are not significantly different from those of the parent model.

For comparisons between a modified model and multiple parent models, the manufacturer demonstrates that the mechanical properties of the modified lens are not significantly different from the range of properties associated with the parent models.

The analysis between the modified model and the manufacturer's parent model(s) includes the following comparisons:

— compression force divided by angle of contact per loop;

— compression force after decay divided by angle of contact per loop.

For each test needed for the analysis, the lens is evaluated at 10,0 mm compressed diameter if the modified lens is only for capsular bag fixation, at 11,0 mm if it is only for ciliary sulcus fixation, or at both diameters if intended for both capsular bag and ciliary sulcus fixation.