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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 conception des lentilles intraoculaires

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Foreword

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This document was prepared by Technical Committee ISO/TC 172, *Optics and photonics*, SC 7 *Ophthalmic optics and instruments*.

This second edition cancels and replaces the first edition (ISO/TR 22979:2006), which has been technically revised.

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

1 Scope

This document provides guidance on the application of all parts of the ISO 11979 series of International Standards for intraocular lenses (IOLs).[1–9] It addresses factors to be considered in the risk management process of modifications to anterior and posterior chamber IOLs in accordance with ISO 14971.[11] It also suggests methods of data analysis and interpretation that can be used to determine the need for a clinical investigation and its design.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

NOTE The terms listed are related to Annex B.

3.1
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

3.2
closed-loop IOL
IOL model, which contains two loops, each loop having both ends attached to the body of the optic

3.3
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

4 Modifications to parent models

4.1 General

IOLs, that are modifications of a parent IOL, have different requirements for clinical investigations depending on the risk associated with the modifications and depending on their location in the eye.

This document provides considerations for the risk assessment to determine the clinical investigation effort that is needed based on the level of modification which is defined in 4.2.

ISO 13485[10] provides requirements for the design and development of medical devices, which are applicable to intraocular lenses including modifications of existing models. The risk assessment and design evaluation are part of the risk management in the design control process in accordance with ISO 14971, and can be used as input for the clinical evaluation. ISO 14971 describes sources for data and information for estimating risks. To determine and evaluate the hazards associated with the modification of IOL models, the manufacturer can additionally use the following sources:

a) clinical data;

b) literature study of equivalent features of similar IOL models. The literature can be general published and unpublished reports, proprietary evaluations and post-market surveillance reports;

c) physical model-eyes, laboratory bench testing or numerical/computational models, which have been verified and validated for evaluation of optical and mechanical behaviour;

d) usability and human factor engineering data resulting from the application of IEC 62366-1[12] or ANSI/AAMI HE75[13] such as the use of error risk analysis, formative and summative evaluation results, including studies to evaluate surgical manipulation and delivery of the IOL in the eye.

Modifications to the delivery system are subject to the design control process in accordance with ISO 13485 and factors that pertain to the interaction of IOL and delivery system, as described in ISO 11979-3, and user interaction during surgery are to be considered in a risk assessment.

4.2 Modification levels

4.2.1 General

Design modifications to parent model IOLs are classified as Level A, B or C. The classification depends on the safety and performance risks that are identified. Examples of risks associated with design modifications are provided in Annex A.

4.2.2 Level A modifications

Level A modifications of a parent model are those for which all safety and performance questions can be adequately addressed without clinical investigation. The modified model is essentially equivalent to the parent model(s). All risks resulting from risk assessment to the modification are adequately addressed by existing clinical evidence. The residual risk will have to be outweighed by the benefits.

4.2.3 Level B modifications

Level B modifications of a parent model are those that raise safety and/or performance risks that can be adequately addressed with a limited clinical investigation of a justified number of subjects followed up for a justified period.

NOTE Typically 100 subjects followed up for 4 months to 6 months. The statistical precision of a 100-subject investigation to detect differences from the safety and performance end points (SPE) ratings is provided in ISO 11979-7.

4.2.4 Level C modifications

Level C modifications are modifications that raise safety and/or performance risks that can only be addressed with a full clinical investigation as defined in ISO 11979-7 and ISO 11979-10.

4.2.5 Clinical investigation with multiple IOL models

More than one IOL model can be studied in the same investigation and with the same study end points if supported by a risk assessment and provided these models are Level A modifications of one another. If the intent is that data from the various models are to be pooled, a justification from the manufacturer is required per study end point to demonstrate that the design differences between models will affect neither investigation outcomes nor investigation execution nor interfere with the application of statistically sound test design techniques such as randomization and masking.

5 Considerations for the assignment of modification level

5.1 General

The process of assignment of a modification level is illustrated in Figure A.1. A risk assessment of the model modifications is performed, especially considering any safety and performance changes due to the differential design aspects compared with the parent models. Multiple parent models can be considered in the evaluation given the premise that the modifications are related to these parent model(s).

The assigned modification level depends on the additional potential hazards or hazardous situations, their probability of occurrence and the probability that they will lead to harm, as well as the severity of the harm(s) compared with that of the parent model. For additional guidance, see ISO 14971.

Overall, the risk assessment would weigh the risk/performance impact and benefit to determine modification Level A, B or C. Examples of potential Level A modifications to parent models are provided in Annex A. A plurality of modifications may change the level assignment. If there is insufficient data to assess the risk of plurality of modifications, as compared with parent IOLs, a suitable clinical investigation should be performed.

5.2 Risk assessment

In the risk assessment, the hazards and hazardous situations that are related to the modification(s) relative to the parent model will be considered. By assigning modification Level A, B or C, the clinical performance relative to the parent model is addressed. Table A.5 includes examples of potential hazards and harms that may be associated with the modification and that can be included in the risk assessment. Table A.5 also includes references to test methods described in the ISO 11979 series, which can be considered to assess the potential risks. The risk assessment addresses all changes made to the product and includes changes of labelling, packaging and package inserts.

5.3 Special considerations

5.3.1 Phakic lenses

Phakic lenses require additional considerations in the risk assessment to determine the modification level because of the proximity of other tissue compared with aphakic anterior and posterior chamber lenses. The clinical requirements are outlined in ISO 11979-10.

5.3.2 Anterior chamber lenses

Additional hazards may arise from the potential direct IOL-tissue interaction, static or dynamic, which needs to be evaluated including the risk of rotation, displacement, aqueous flow and corneal damage. The clearance analysis described in ISO 11979-3 can be used to assess the clearance to the cornea.

5.3.3 Posterior chamber lenses intended for implantation in the sulcus

Posterior chamber lenses implanted in the sulcus have more potential interaction with surrounding tissue than lenses implanted in the capsular bag. Examples of potential tissue interaction effects are pigment dispersion and changes to the ciliary body.

6 Modifications of optical design features

6.1 Optical design changes

Optical bench testing of imaging quality, as defined in ISO 11979-2, is performed and analysed to compare the modified IOL model and parent IOL model(s).

Interchanging optics or combining two or more optical design concepts (spherical, aspheric, monofocal, toric, multifocal and/or accommodative optics) may be considered Level A modifications if the optical designs have been evaluated in parent IOL models. The risk assessment is conducted to evaluate any new risk when interchanging optical designs and includes the following:

a) the potentially increased misalignment of the IOL optic (i.e. tilt, decentration and rotation) due to the parent IOL body and haptic designs. The analysis includes comparison of clinical study reports of centration and mechanical differences in IOL design;

b) evaluation of the potential for changes in the predictability and stability of post-operative refraction and, if applicable, changes in the stability and magnitude of the accommodative amplitude at the point of stabilization;

c) when combining two or more approved optical concepts, all clauses applicable to these concepts and their interaction are considered.

Examples of Level A and B modifications are listed in Annex A.

6.2 Multifocal lenses (MIOL)

When the modification of the multifocal parent design is a change of the fundamental technology creating the multiple dioptric powers, e.g. diffraction versus refraction, this modification is potentially a Level B or Level C modification depending on the risk assessment. A change to a multifocal design that can be verified and compared with a parent multifocal may be considered a Level A modification if it does not increase the risk profile. However, if the modification increases the risk profile, for example adding risks of visual disturbances, the change is potentially a Level B or Level C modification. If the material of the modified model IOL is different from the material of the multifocal parent IOL with respect to optical material characteristics, in particular refractive index and dispersion, this is potentially a Level B or Level C modification.

6.3 Toric lenses (TIOL)

Refer to ISO 11979-7 and ISO 11979-10 for evaluation of modifications of the mechanical design platform, in particular with respect to rotational stability. Changes in mechanical design affecting the axial and rotational stability are potentially Level B or Level C modifications.

6.4 Accommodating lenses (AIOL)

Any change in optic design (single and multi-optic lenses) or haptic design is reviewed for potential impact on the accommodative power of the IOL and optical performance, as defined in ISO 11979-2 and ISO 11979-7, of the IOL at far power configuration and configurations associated with the designed range of accommodation in 0,5 D increments. The risks associated with interaction with surrounding tissue due to the accommodative action need to be evaluated to classify the modification level of a model change. Any characteristic of the parent lens optics and material that may have an impact on the accommodative performance of the approved AIOL is considered in the risk assessment.

7 Modifications to the mechanical design

7.1 General

Evaluation of modifications of the mechanical design considers the impact of the modification on the mechanical interaction with ocular tissue, consequences for the surgical handling, interaction with delivery systems, refractive outcomes, visual outcomes including visual disturbances and any potential biological response. Examples of modifications to the mechanical design and the biological response are:

a) changes in the vault height, sagitta, axial displacement under compression may affect the refraction stability and axial position of the IOL;

b) changes in the compression force and contact angle may damage the capsular bag and the zonular fibres with the effect of tilt and decentration, and may change the shape of the capsular bag with the consequences of capsular striae and optical disturbances and posterior capsule opacification.

Any modification to the mechanical design of anterior chamber IOLs is considered a Level B modification.

7.2 Mechanical analysis

The data from the compression force, compression force decay and angle of contact, tested in accordance with ISO 11979-3, is used to assess the difference in mechanical behaviour between the modified IOL model and potential parent IOL model(s). The methods for assessment of the differences in compression force (decay) and angle of contact between a modified IOL model and one or more parent IOL models are described in Annex B. These methods can be used to determine whether a modified posterior chamber IOL is a Level A modification of one or more parent IOL models included in the analysis.

8 Modifications to material

8.1 Interchanging IOL materials

Interchanging IOL materials may be considered Level A modifications if the materials and designs have each been evaluated in a parent IOL. The risk assessment is conducted to evaluate any new risk when interchanging IOL materials in particular when interchanging material from one-piece, three-piece or plate lens design.

8.2 New materials

If the material of the modified IOL model is different from the material of the parent IOL model(s), a clinical investigation is considered depending on the risk assessment. If the change in material is a change in polymeric structure, and there is no experience for use of this polymer in the eye, typically a full clinical investigation is performed.

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. This annex provides typical examples of potential Level A and B modifications with additional criteria where applicable.

The examples in this annex do not apply to phakic IOLs or iris fixation lenses.

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

a) P designates non-plate posterior chamber IOLs, for in the capsular bag implantation;

b) A designates anterior chamber IOLs;

c) S designates IOLs for sulcus implantation;

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

A.2 Potential Level A modification examples

Examples of potential Level A modifications are listed in Tables A.1 and A.2. If the risk assessment brings forward new risks or results in increased risks from individual or multiple changes over the parent models(s), the classification of modification level should be reconsidered.

Table A.1 — Change in optic design

Modification	Applicability
Change in dioptric power range Whereby any power of the IOL model is in the range that the manufacturer makes available.	P/A/PL/S
Change of dioptric power increments Inclusion or deletion of power steps inside the range of the power steps of the parent model e.g. the current power steps are 5,0 D, 6,0 D, 7,0 D, etc., are modified to 5,0 D, 5,5 D, 6,0 D, 6,5 D, 7,0 D, etc.	P/A/PL/S
Change in cylinder power range (TIOL) Where any cylinder power ≥1,0 D of the IOL model is within the range of manufacturer's available cylinder power range.	P/A/PL/S
Change in addition power (MIOL) Whereby any addition power of the IOL is within the range of manufacturer's available addition powers, that the manufacturer makes available for parent models with identical optical principles to accomplish the multifocality and the same optical specifications.	P/A/PL/S

Table A.1 *(continued)*

Modification	Applicability
Change to axis indicator marks of TIOL Provided that the markings remain compatible with a vision evaluation system.	P/A/PL/S
Change in spherical aberration level Whereby the spherical aberration remains within the range of that the manufacturer makes available.	P/A/PL/S
The application of a multifocal optic design of one parent model to the optic of another parent model Whereby optical design, optical specifications, material and technology to accomplish the multifocality of the IOL are identical to the parent model(s).	P/A/PL/S

Table A.2 — Change in mechanical design

Modification	Applicability	Mechanical data analysis
Changes in haptic features Changes such as the addition of notches or the addition of eyelets or rounded ends to loops.	P/S	No
Change in overall diameter Changes within the previously clinically investigated overall diameter range.	P/S	Yes
Change in haptic thickness or width	P/S	Yes
Change in haptic configuration (shape)	P/S	Yes
Change in optic or body size 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 circular to an ovoid body) and not greater then 7,5 mm along any meridian.	P/S	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/S	No

A.3 Potential Level B modification examples

Examples of potential Level B modifications are listed in Tables A.3 and A.4. If the risk assessment brings forward new risks, the classification of modification level should be reconsidered.

Table A.3 — Change in optic design

Modification	Applicability
Change in addition power outside the range of addition power made available by the MIOL parent lenses Whereby any addition power of the IOL follows the identical optical principles as the parent model(s) to accomplish the multifocality and the same optical specifications as the parent model(s).	P/A/PL/S