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Ophthalmic implants — Intraocular lenses —

Part 6: Shelf-life and transport stability

Implants ophtalmiques — Lentilles intraoculaires —

Partie 6: Durée de conservation et stabilité pendant le transport

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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 11979-6 was prepared by Technical Committee ISO/TC 172, *Optics and photonics*, Subcommittee SC 7, *Ophthalmic optics and instruments*.

This second edition cancels and replaces the first edition (ISO 11979-6:2002) 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 intraocular lenses*

— *Part 10: Phakic intraocular lenses*

Introduction

The purpose of a stability study is to ascertain that the properties of a product, in this case an intraocular lens (IOL), remain within specified limits for a sufficiently long period of time under the influence of a variety of environmental conditions.

The storage stability of the intraocular lens material is an important factor in the overall investigation of a new lens material, a new combination of given lens materials, a new packaging material or a new manufacturing process. To assess this, a study of the ageing of the lenses in their containers is performed.

Changes in the composition and material, material suppliers, manufacturing conditions (including the sterilization process), or the package design or material could affect the shelf-life and could therefore necessitate renewed investigations. The need for studies of product stability, package integrity and transport stability can be assessed using ISO 14971.

The design of the stability tests should be based on the known properties of the material from which the intraocular lens is made, and the recommendations for use of the intraocular lens. Knowledge of the quantity and identity of extractable substances found after storage or accelerated ageing studies are of importance in evaluating new intraocular lens materials.

On the basis of the information obtained, transport and storage conditions can be recommended that will maintain the quality of the intraocular lens in relation to its safety, efficacy and acceptability, throughout the proposed shelf-life, i.e. during storage and distribution up until the moment of dispensing. The results obtained are also used to determine the expiration date.

In practical terms it is the stability of the material from which the intraocular lens is made that is being tested, along with the integrity of the packaging that maintains the necessary environment of the intraocular lens. Stability studies for intraocular lenses are thus material specific, i.e. this type of study need not be performed for more than one intraocular lens model for a given combination of IOL material(s), packaging materials and manufacturing processes.

Stability studies of intraocular lenses allow the determination of the shelf-life and package suitability as well as recommendations for transport and storage conditions.

Ophthalmic implants — Intraocular lenses —

Part 6:
Shelf-life and transport stability

1 Scope

This part of ISO 11979 specifies tests by which the shelf-life of sterile intraocular lenses (IOLs) in their final packaging can be determined. These tests include procedures to establish the stability of IOLs in distribution and storage.

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 10993-5, *Biological testing of medical devices — Tests for in vitro cytotoxicity*

ISO 10993-12, *Biological testing of medical devices — Sample preparation and reference materials*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

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

ISO/TR 22979, *Ophthalmic implants — Intraocular lenses — Guidance on assessment of the need for clinical investigation of intraocular lens design modifications*

3 Terms and definitions

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

4 Requirements

4.1 General

If, following a risk analysis in accordance with ISO 14971, it is found that a product stability study, a package integrity study and/or a transport stability study are needed, this part of ISO 11979 shall apply to the planning and conduct of these studies.

A study protocol shall be developed prior to initiation of the study.

The study shall demonstrate that the parameters assessed with regard to performance, safety and product acceptability are within the original manufacturing specifications at the conclusion of the study.

In view of the fact that sufficiently long experience of storage of a new intraocular lens may not have been accumulated by the time it is brought to the market, the results of accelerated tests (see 4.3.2) are acceptable for initial labelling purposes, i.e. to establish a shelf-life to be used in the information on the product. A maximum of five years of shelf-life can be claimed by a real-time study or an accelerated study regardless of material used in the intraocular lens. An accelerated study shall however always be verified by a real-time study. The same product or a Level A modification of it (see ISO/TR 22979) shall be used in the real-time study. The real-time study shall be started before the release of the new intraocular lens to the market. The real-time study results always take precedence over the accelerated study results.

In case a manufacturer wishes to maintain the possibility of resterilizing finished intraocular lens lots, the finished intraocular lens lot(s) used in the stability study shall have undergone the maximum number of sterilization cycles allowed under the manufacturer's procedures.

4.2 Materials and methods

4.2.1 Test samples

The studies shall be performed using IOLs from finished intraocular lens lots (see ISO 11979-1). The proposed sample sizes are described in Annex A.

4.2.2 Methods

Suitable methods shall be chosen for any tests contained in the study protocol. The methods selected shall be recorded. Annex B contains suggested tests. Due to the variation in product and package materials and design, other tests could be more appropriate, e.g. for possible changes to the storage solution for IOLs stored in a solution. The methods selected shall be recorded and the details of validation for each test method, demonstrating the capability of the method, shall also be documented.

In certain cases more than one of the tests listed in Annex B can be performed on a single IOL (e.g. dioptric power, imaging quality and spectral transmission can all be measured on the same IOL), thereby reducing the total number of intraocular lenses required.

4.3 Product stability

4.3.1 General

If the risk analysis in accordance with ISO 14971 shows a need for a shelf-life study, the following shall apply. The rationale for choice of tests shall be documented in the risk management plan.

The shelf-life of an IOL shall be established based on data from at least three lots of finished IOLs (low, medium and high dioptric power ranges, each range comprising one or more dioptric powers), both for real-time studies and accelerated studies.

Based on a manufacturer's experience with the IOL material(s), packaging material(s), sterilization process and packaging process, a manufacturer's risk analysis can support the adequacy to perform a study on only one lot of product.

4.3.2 Real-time shelf-life study

4.3.2.1 Test parameters

The following parameters shall be considered for inclusion when a real-time shelf-life study is planned:

a) dimensions;

b) dioptric power;

c) imaging quality;

d) surgical manipulation;

e) recovery of properties following simulated surgical manipulation (for foldable IOLs);

f) surface and bulk homogeneity;

g) compression force (samples from one or more dioptric power lots);

h) dynamic fatigue (samples from one or more dioptric power lots);

i) spectral transmission;

j) exhaustive extraction (samples from one or more dioptric power lots);

k) cytotoxicity (if an increase is seen in the content of extractables and/or if a new substance is present); it is sufficient to perform cytotoxicity testing on IOL samples from one dioptric power lot. In addition to testing of the IOL itself, an aqueous extract of the IOL also needs to be tested; both tests shall be performed in accordance with ISO 10993-5; for the aqueous extraction, the ratio of surface area to volume of extraction medium specified in ISO 10993-12 can be proportionally adjusted to accommodate the small size of the IOL;

l) specific surface tests (if warranted).

References to suggested test methods are to be found in Annex B.

Testing for changes due to interaction with the packaging material shall also be considered, as shall testing for changes in surface treatments as well as the concentration of additives in the IOL or additives in a solution in which the IOL is stored.

An example of a calculation of the number of IOLs to be used in a shelf-life and transport stability study for an IOL made from a new material can be found in Annex A.

4.3.2.2 Study procedure

The following is the procedure for real-time stability studies. Intraocular lenses to be tested shall, if applicable, at each instance be evenly distributed among the different power groups.

a) Assign a unique identification to each individual intraocular lens in the total sample and put that identification on the intraocular lens packaging.

b) Collect the intraocular lenses to be tested initially and carry out the tests of the protocol. Record the unique identifications, the results and measurement conditions.

c) Transfer the remaining packages to storage under controlled conditions at the recommended storage condition (e.g. temperature 25 °C ± 2 °C and relative humidity 60 % ± 20 %). Record actual temperature, relative humidity and date.

d) Monitor temperature and relative humidity, regularly during the course of the study in a manner such that fluctuations in temperature and relative humidity are also recorded.

e) In accordance with the protocol, periodically remove a sufficient number of intraocular lenses for testing. Carry out the tests of the protocol. Record the unique identifications, the results and measurement conditions.