INTERNATIONAL STANDARD

ISO 11979-6

Third edition
2014-10-01

Ophthalmic implants — Intraocular lenses —

Part 6: Shelf-life and transport stability testing

Implants ophtalmiques — Lentilles intraoculaires —

Partie 6: Durée de conservation et stabilité pendant le transport

Reference number
ISO 11979-6:2014(E)

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Contents

Page

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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 172, *Optics and photonics*, Subcommittee SC 7, *Ophthalmic optics and instruments*.

This third edition cancels and replaces the second edition (ISO 11979-6:2007), 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 testing*

— *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.

Ophthalmic implants — Intraocular lenses —

Part 6:
Shelf-life and transport stability testing

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 documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. 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 evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 10993-12, *Biological evaluation of medical devices — Part 12: 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 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

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 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 results shall demonstrate that the parameters measured with regard to performance, safety, and product acceptability are within the finished product specifications, when available. In cases where there are no finished product specifications, then the parameters measured shall remain within the limits of the applicable parts of ISO 11979. If there exists neither finished product specifications nor applicable limits specified within ISO 11979, then a comparison to time zero product shall be performed.

In view of the fact that an intraocular lens may not have sufficient storage assessments 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 indicated on the product labelling. 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. However, an accelerated study shall always be verified by a real-time study, and the real-time study results shall always take precedence over the accelerated study results. The same product or a Level A modification of it (see ISO/TR 22979) shall be used in the real-time study, and the real-time study shall be started before the release of the new intraocular lens into the market.

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. 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. The methods selected, other than those specified in Annex B, 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, thereby reducing the total number of IOLs 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.

For both real-time and accelerated testing, finished IOLs (or finished injector systems with IOLs) shall be used. For test parameters that can be affected by optical power, at least three groups, comprising lenses from one or more finished intraocular lens lots, shall be tested, one each from low, medium, and high dioptric power ranges, each group comprising one or more dioptric powers. For test parameters not affected by optical power, at least one group of lenses shall be used. See Annex A for guidance.

4.3.2 Real-time shelf-life study

4.3.2.1 Test parameters

The following parameters shall be considered:

a) dimensions;

b) dioptric power;

c) imaging quality;

d) surgical manipulation;

e) recovery of properties following simulated surgical manipulation (for IOLs intended to be folded or otherwise deformed as part of the surgical procedure);

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 group. For this testing, an extraction of the IOL using culture medium with serum needs to be performed in accordance with ISO 10993-5. The ratio of surface area to volume of extraction medium is specified in ISO 10993-12 and the extraction conditions are defined in ISO 10993-5;

l) specific surface tests (if warranted).

References to suggested test methods are 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 Combination lens-injector systems

In cases of preloaded or combined IOL delivery systems, the following additional parameters shall be considered for inclusion:

a) stability of injector system materials;

b) chemical interactions between delivery system and IOL;

c) mechanical interactions between delivery system and IOL;

d) cytotoxicity testing of any potential degraded materials;

e) lens delivery system performance.

Additional samples beyond those listed in Table A.1 might need to be required for shelf-life testing based on the results of the considerations.

4.3.2.3 Study procedure

The following is the procedure for real-time stability studies. Intraocular lens groups 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 the measurement conditions.

c) Transfer the remaining packages to storage under controlled conditions at the maximum recommended storage condition. Record actual temperature, relative humidity, and date.