INTERNATIONAL STANDARD

ISO 16672

Second edition
2015-08-01

Ophthalmic implants — Ocular endotamponades

Implants ophtalmiques — Produits de tamponnement endoculaires

Reference number
ISO 16672:2015(E)

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

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 second edition cancels and replaces the first edition (ISO 16672:2003), which has been technically revised.

Ophthalmic implants — Ocular endotamponades

1 Scope

This International Standard applies to ocular endotamponades (OE), a group of non-solid implants used in ophthalmology to flatten and position a detached retina onto the choroid, or to tamponade the retina.

With regard to the safety and efficacy of OE, this International Standard specifies requirements for their intended performance, design attributes, pre-clinical and clinical evaluation, sterilization, product packaging, product labelling and the information supplied by the manufacturer.

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 10993-1:2009, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-2:2006, *Biological evaluation of medical devices — Part 2: Animal welfare requirements*

ISO 10993-6:2007, *Biological evaluation of medical devices — Part 6: Tests for local effects after implantation*

ISO 11135-1:2007, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11137-1:2006 + Amd.1:2013, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11607-1:2006, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 13408-1:2008 + Amd.1:2013, *Aseptic processing of health care products — Part 1: General requirements*

ISO 14155:2011, *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 14630:2012, *Non-active surgical implants — General requirements*

ISO 14971:2007, *Medical devices — Application of risk management to medical devices*

ISO 15223-1:2012, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

ISO 17665-1:2006, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 20857:2010, *Sterilization of health care products — Dry heat — Requirements for the development, validation and routine control of a sterilization process for medical devices*

EN 1041:2008 + A1:2013, *Information supplied by the manufacturer of medical devices*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
delivery system
sealed container in which the product is supplied and any additional component provided to introduce the product into the eye

3.2
dynamic viscosity
quotient of the part of the stress in phase with the rate of strain divided by the rate of strain under sinusoidal conditions

Note 1 to entry: The dynamic viscosity is expressed in pascal seconds (Pa·s).

3.3
interfacial tension
tension against liquids

Note 1 to entry: The interfacial tension is expressed in newton per metre (N/m).

3.4
kinematic viscosity
quotient of the dynamic viscosity with the gravity

Note 1 to entry: The kinematic viscosity is expressed in square metres per second (m^2/s).

3.5
non-solid implants
tamponade media such as gases, liquids, or gels

3.6
ocular endotamponade
OE
non-solid implant used in ophthalmology to flatten and position a detached retina onto the choroid, or to tamponade the retina

3.7
primary container
container providing mechanical and microbiological protection of the content

3.8
sterile barrier system
minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use

[SOURCE: ISO/TS 11139:2006, 2.44]

3.9
storage container
part of the packaging intended to protect the device during transport and storage, containing the sterile barrier

3.10
surface tension
tension against air

Note 1 to entry: Surface tension is expressed in newton per metre (N/m).

3.11
vapour pressure
vapour pressure of a liquid OE that defines its volatility

Note 1 to entry: Vapour pressure is expressed in Pascal (Pa) at (35 ± 2) °C.

4 Intended performance

The general requirements for the intended performance of non-active surgical implants specified in ISO 14630 shall apply.

This International Standard describes non-solid medical devices which are compatible with the ocular environment, used to reposition and/or tamponade a detached retina, and which function primarily mechanically. They are used either intra-operatively and removed at the end of surgery, as in the case of heavy liquids such as perfluorocarbons, or are designed to remain in the vitreous cavity until a reattachment of the retina is achieved.

The manufacturer shall describe and document the functional characteristics of the OE in terms of its chemical composition and physical properties, the intended surgical applications, the conditions of use and the maximum duration of contact with, and effects upon, ocular tissues, with particular regard to safety.

The intended performance shall be determined, taking into account published standards, published clinical and scientific literature, validated test results, pre-clinical and clinical evaluation, and clinical investigations.

5 Design attributes

5.1 General

The general requirements for non-active surgical implants specified in ISO 14630 shall apply.

All testing requirements specified below shall be performed with finished, sterilized product, ready for release. Any analytical methods utilized shall be validated.

NOTE Tests described herein are intended to apply when qualifying materials and not necessarily as a routine quality assurance/control programme.

5.2 Chemical and biological contaminants

The identification of potentially hazardous chemical or biological contaminants shall be determined by a risk analysis. For raw materials of biological origin, these impurities can include proteins, nucleic acids, or other biological materials. Contaminants of the finished product derived from the source materials or from the manufacturing process, such as cross-linking agents and antioxidants, that are potentially hazardous to the tissues of the eye, or systemically, shall be identified and quantified, whenever possible, and their concentration in the finished products reported.

Contaminants shall be determined using standard analytical methods when available, and all methods shall be described. Limits for identified contaminants shall be set and documented. Testing for the biological effects of these contaminants during evaluation of biological safety may be required if the risk analysis determines it necessary.

5.3 Chemical description

The manufacturer shall provide a description of each chemical component in the finished product and its quality specifications. If the component material is derived from biological sources, the organism from which it is obtained shall be stated along with its source. For synthetic polymers, the backbone and end-groups shall be identified. Residual monomers and reaction by-products shall be quantified and identified, if possible.

5.4 Concentration of the components

The concentration of each component material in the finished product shall be stated. Since the testing methodology can affect the actual concentration reported, the physical or chemical techniques utilized shall be described and validated.

5.5 Density

The density of liquid forms of OE shall be specified in kilograms per cubic metre (kg/m^3).

5.6 Gaseous expansion

For gaseous forms of OE the intraocular gaseous expansion at (35 ± 2) °C and its dependence on atmospheric pressure shall be expressed.

5.7 Interfacial tension

Where applicable, the interfacial tension against water shall be expressed in newton per metre (N/m) at (35 ± 2) °C.

5.8 Kinematic viscosity

Where applicable, the kinematic viscosity at (35 ± 2) °C shall be expressed in millimetres squared per second (mm^2/s).

5.9 Dynamic viscosity

For viscous or viscoelastic OE, the dynamic viscosity shall be determined at (35 ± 2) °C in the range between 0,01 and 100 s^{-1} and expressed in mPa·s.

5.10 Molecular mass distribution

If the OE is a polymer, the average molecular mass, the range of molecular mass distribution and the polydispersity shall be reported.

The manufacturer shall conduct and report such additional tests as necessary to provide an adequate description of the molecular mass distribution of the components in the finished product. Whenever possible, standard methods shall be used and specified.

5.11 Particulates

An assessment of risk shall evaluate the potential for contamination by, or formation of, particulates in the product during manufacture, the conditions expected during transport and storage, and during use of the product and the associated hazards.

The manufacturer shall characterize and set limits for the types, range of sizes and levels of particles present in the finished product used in the clinical study. For each type of particle present, a limit which has been validated in a clinical study shall be set and an adequate justification for the limit shall be documented.

5.12 Refractive index

Where applicable, the refractive index between OE and air shall be measured with a refractometer at (35 ± 2) °C and (546 ± 10) nm wavelength.

5.13 Spectral transmittance

The spectral transmittance of the OE shall be measured by transmission spectrophotometry over the range 300 nm to 1 100 nm. Results shall be presented graphically, plotting percentage transmission against wavelength.

5.14 Surface tension

Where applicable, the surface tension shall be expressed in newton per metre (N/m) at (35 ± 2) °C.

5.15 Vapour pressure

Where applicable, the vapour pressure shall be expressed in Pascal (Pa) at (35 ± 2) °C.

6 Design evaluation

6.1 General

The OE shall be evaluated for safety by performing a risk assessment in accordance with ISO 14971. The results of the risk assessment shall determine the tests required to evaluate the safety of the OE.

The risk assessment shall take into consideration the following:

a) the type of product and the duration of intraocular contact;

b) potential interactions of the OE with other materials likely to be used in ophthalmic surgery;

c) for intraocular gases, any impurity profile changes as the gas is depleted from the tank.

NOTE Impurity profile changes can occur as the concentration of the chemical species changes due to the differences in vapour pressure as the tank is depleted.

The OE shall be evaluated to demonstrate that the intended performance is achieved. The requirements for evaluation of non-active implants specified in ISO 14630 shall apply.

6.2 Evaluation of biological safety

6.2.1 General

The relevant biocompatibility end points specified in ISO 10993-1 and identified by the risk analysis shall be taken into account when selecting the tests to evaluate the biological safety of an OE.

NOTE Based upon the typical clinical applications in the posterior segment, OE are categorized as “Implant devices, tissue/bone”. The tests for this and other categories of devices identified in Table 1 of ISO 10993-1:2009 are for guidance only; they do not represent maximum or minimum test requirements.

6.2.2 Bacterial endotoxins test

Where applicable, the OE shall be evaluated for the presence of bacterial endotoxins using the Limulus Amoebocyte Lysate (LAL) test, in accordance applicable pharmacopoeias or an equivalent validated test procedure. Any product that exceeds a bacterial endotoxin limit of 0,5 Endotoxin Units (EU) per ml fails the test.

6.2.3 Intraocular implantation test

Tests for intraocular irritation, inflammation, intraocular pressure (IOP) and other local effects of the OE shall be conducted in a suitable animal model, in accordance with animal welfare requirements specified in ISO 10993-2 or following any local legislation.