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Non-active surgical implants — General requirements

Implants chirurgicaux non actifs — Exigences générales

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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 14630 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*.

This third edition cancels and replaces the second edition (ISO 14630:2005), which has been technically revised.

Introduction

This International Standard provides a method of addressing the fundamental principles outlined in ISO/TR 14283, as they apply to non-active surgical implants. It also provides a method to demonstrate compliance with the relevant essential requirements as outlined in general terms in Annex 1 of the European Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, as they apply to non-active surgical implants, hereafter referred to as implants. It might also assist manufacturers to comply with the requirements of other regulatory bodies.

There are three levels of standards dealing with non-active surgical implants and related instrumentation. For the implants themselves these are as follows, with level 1 being the highest:

— level 1: general requirements for non-active surgical implants;

— level 2: particular requirements for families of non-active surgical implants;

— level 3: specific requirements for types of non-active surgical implants.

Level 1 standards, such as this International Standard and reference [4] in the Bibliography, contain requirements that apply to all non-active surgical implants. They also anticipate that there are additional requirements in the level 2 and level 3 standards.

Level 2 standards (e.g. references [5] – [9] in the Bibliography) apply to a more restricted set or family of non-active surgical implants, such as those designed for use in neurosurgery, cardiovascular surgery, or joint replacement.

Level 3 standards (e.g. references [10] – [13] in the Bibliography) apply to specific types of implants within a family of non-active surgical implants, such as hip joints or arterial stents.

To address all requirements for a specific implant, it is advisable that the standard of the lowest available level be consulted first.

NOTE The requirements in this International Standard correspond to international consensus. Individual or national standards or regulatory bodies can prescribe other requirements.

Non-active surgical implants — General requirements

1 Scope

This International Standard specifies general requirements for non-active surgical implants, hereafter referred to as implants. This International Standard is not applicable to dental implants, dental restorative materials, transendodontic and transradicular implants, intra-ocular lenses and implants utilizing viable animal tissue.

With regard to safety, this International Standard gives requirements for intended performance, design attributes, materials, design evaluation, manufacture, sterilization, packaging and information supplied by the manufacturer, and tests to demonstrate compliance with these requirements. Additional tests are given or referred to in level 2 and level 3 standards.

NOTE This International Standard does not require that the manufacturer have a quality management system in place. However, the application of a quality management system, such as that described in ISO 13485, could be appropriate to help ensure the implant achieves its intended performance.

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 31 (all parts), *Quantities and units*

ISO 8601, *Data elements and interchange formats — Information interchange — Representation of dates and times*

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

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

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

ISO 11137-2, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

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

ISO 13408-1, *Aseptic processing of health care products — Part 1: General requirements*

ISO 14155-1, *Clinical investigation of medical devices for human subjects — Part 1: General requirements*

ISO 14155-2, *Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans*

ISO 14160, *Sterilization of single-use medical devices incorporating materials of animal origin — Validation and routine control of sterilization by liquid chemical sterilants*

ISO 14937, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

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

ISO 17664, *Sterilization of medical devices — Information to be provided by the manufacturer for the processing of resterilizable medical devices*

ISO 17665-1, *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 22442-1, *Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management*

ISO 22442-2, *Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling*

ISO 22442-3, *Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents*

3 Terms and definitions

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

3.1
coating
layer of material covering or partially covering a surface of an implant

3.2
implantable state
condition of an implant prepared for implantation into a human subject

3.3
leakage
unintended movement of fluid, including body fluids, into or out of an implant

NOTE An unintended diffusion phenomenon is an example of leakage for the purposes of this International Standard.

3.4
magnetic resonance environment
MR environment
volume within the 0,50 mT [5 gauss (G)] line of a magnetic resonance imaging (MRI) system, which includes the entire three-dimensional volume surrounding the magnetic resonance imaging scanner

[ASTM F2503-05 [1)], definition 3.1.7]

NOTE For cases where the 0,50 mT line is contained within the Faraday shielded volume, the entire room is considered the MR environment. For cases where the 0,50 mT line is outside the Faraday shielded volume (e.g. in the adjacent room or area), it is advisable that the entire adjacent room or area be considered part of the MR environment.

1) Definitions for magnetic resonance environment and magnetic resonance imaging are reproduced from ASTM F2503-05 and ASTM F2119-01 respectively, copyright ASTM. Reproduced with permission of ASTM International, http://www.astm.org/.

3.5
magnetic resonance imaging
MRI
diagnostic imaging technique that uses static and time varying magnetic fields to provide images of tissue by the magnetic resonance of nuclei

[ASTM F2119-01 [1)], definition 2.1.4]

3.6
non-active surgical implant
surgical implant, the operation of which does not depend on a source of electrical energy or any source of power other than that directly generated by the human body or gravity

3.7
safety
freedom from unacceptable risk

[ISO/IEC Guide 51:1999, definition 3.1]

3.8
surgical implant
device that is intended to be totally introduced into the human body, or to replace an epithelial surface or the surface of the eye, by means of surgical intervention and that is intended to remain in place after the procedure, or any medical device that is intended to be partially introduced into the human body by means of surgical intervention and that is intended to remain in place after the procedure for at least 30 days

4 Intended performance

The intended performance of an implant shall be described and documented by addressing the following, with particular regard to safety:

a) intended purpose(s);

b) functional characteristics;

c) intended conditions of use;

d) intended lifetime.

NOTE For this purpose, it is advisable that particular account be taken of

— published standards,

— published clinical and scientific literature, and

— validated test results.

5 Design attributes

The design attributes to meet the intended performance shall take into account at least the following:

a) materials and their biocompatibility (see Clause 6);

b) physical, mechanical and chemical properties of materials, including endurance properties and ageing (see Clauses 6 and 7);

c) wear characteristics of materials and the effects of wear and wear products on the implant and the body (see Clauses 6 and 7);

d) degradation characteristics of materials, and the effects of degradation, degradation products and leachables on the implant and the body (see Clauses 6 and 7);

e) the extent and effect of leakage (see Clauses 6 and 7);

f) safety with respect to viruses and other transmissible agents (unclassified pathogenic entities, prions and similar entities), of animal tissues or derivatives of animal tissue utilized in the implant or during its manufacture (see Clause 6);

g) the effect of manufacturing processes (including sterilization) on material characteristics and performance (see Clauses 6, 7, 8 and 9);

h) possible effects on the implant and its function due to interactions between its constituent materials and between its constituent materials and other materials and substances (see Clauses 6 and 7);

i) interconnections and their effects on the intended performance (see Clause 7);

j) interface(s) between the implant and body tissue(s), particularly relative to fixation and connection, and surface conditions (see Clause 7);

k) shape and dimensions, including their possible effects on tissues and body fluids (see Clause 7);

l) biocompatibility of the implant in its implantable state (see Clauses 6 and 7);

m) physical and chemical effects of the body and external environment on the implant (see Clause 7);

n) effects of radiation, electromagnetic and magnetic fields on the implant and its function, and any consequential effects on the body (see Clauses 6 and 7);

NOTE Particular attention is drawn to the fields used for magnetic resonance imaging (MRI) in respect of patient safety. The test methods in ASTM F2052, ASTM F2119, ASTM F2182 and ASTM F2213 can be used to evaluate the safety of an implant in the MR environment.

o) the ability to implant and, when applicable, to remove or replace the implant (see Clause 7);

p) the ability to visualize the position and orientation of the implant by radiological or other imaging procedures;

q) microbiological and particulate contamination levels (see Clauses 8, 9 and 10);

r) the suitability and effectiveness of packaging (see Clause 10).

Implant design attributes shall be documented. Where any of the above are not considered to be relevant, the reason shall be documented and justified.

6 Materials

Implant materials shall be selected with regard to the properties required for the intended purpose, also taking into account the effects of manufacture, handling, sterilization and storage, as well as any treatment (chemical, electro-chemical, thermal, mechanical, etc.) applied to the surface or a part of the surface of the implant material in order to modify its properties. Possible reactions of implant materials with human tissues and body fluids, other materials, other implants, substances and gases shall be considered. Possible effects of radiation, magnetic and electromagnetic fields on the material shall also be considered.

When a medicinal product is an integral part of an implant, the medicinal product shall be assessed according to pharmaceutical principles. The performance of the medicinal product used in combination with the implant shall not be affected by the implant and/or vice versa.

NOTE 1 For the assessment of the safety, quality and usefulness of the medicinal product incorporated as an integral part of an implant, appropriate methods might be specified in national or regional regulations (e.g. European Directive 2001/83/EC).

Materials, including biological materials, used for implants and coatings shall be acceptably compatible with the biological tissues, cells and body fluids with which they are in contact in their implantable state. The compatibility of possible wear and degradation products shall also be acceptable. The acceptability in the particular application shall be demonstrated either

a) by documented assessment in accordance with ISO 10993-1, or

b) by selection from the materials found suitable by proven clinical use in similar applications.

NOTE 2 Some of the level 2 standards include lists of materials which have been found acceptable in certain applications.

For implants utilizing materials of animal origin that are non-viable or have been rendered non-viable either in the implant or in its manufacture, these materials shall be evaluated and their safety with respect to viruses and other transmissible agents shall be in accordance with the requirements of ISO 22442-1, ISO 22442-2 and ISO 22442-3.

NOTE 3 See ISO 22442-1 for the definition of the terms “animal” and “tissue”.

7 Design evaluation

7.1 General

Implants shall be evaluated to demonstrate that the intended performance (see Clause 4) is achieved. The extent to which the intended performance has been achieved shall be determined and documented. Safety and intended performance shall be demonstrated by pre-clinical evaluation, clinical evaluation and post-market surveillance, including appropriate risk management at all stages of the life cycle of the implant, in accordance with the requirements of ISO 14971.

7.2 Pre-clinical evaluation

Implants shall undergo pre-clinical evaluation based on

a) the relevant scientific literature relating to the safety, performance, the design characteristics, and the intended use of the implant,

b) analysis of available predictive and outcome data from sources such as national and other registries, and

c) analysis of data obtained from testing including bench-testing and, when available, data from validated techniques for evaluating implant safety and intended performance.

Pre-clinical testing of implants shall simulate conditions of intended use. Test methods and related limits for specific types of implants shall be defined and justified by the manufacturer.

NOTE Test methods and limits for particular implants can be described in other related International Standards, such as those listed in the bibliography.

7.3 Clinical evaluation

Implants shall undergo clinical evaluation based on:

a) a critical review of the relevant scientific and clinical literature relating to the safety, the performance, the design characteristics and the intended use of the implant, or demonstrably similar implants; or

b) the results of all clinical investigations made; or

c) the combination of the clinical data provided in a) and b) above.

Where a clinical investigation is carried out, it shall be performed in accordance with the requirements of ISO 14155-1 and ISO 14155-2.

NOTE 1 Requirements for clinical investigation of specific product types can be included in other related International Standards.

NOTE 2 ISO 14155-2 requires that the Clinical Investigation Plan (CIP) include the follow-up period in a particular subject within the clinical investigation and the justification for this follow-up period. It is advisable that the follow-up period permit the demonstration of performance over a period of time sufficient to represent a realistic test of the performance of the device and to allow identification and risk assessment of any associated adverse device effects over that period.

7.4 Post-market surveillance

A systematic procedure to review post-market experience gained from implants shall be in place.

When the manufacturer's risk analysis indicates that there is a significant risk for the patient in the event of failure or incompatibility between the implant and the patient during its intended lifetime, the manufacturer shall take steps to make sure that the performance and the security of the implant are maintained.

NOTE Suitable methods for monitoring performance and the security of implants include survival analysis (with revision as the end point), clinical follow-up of patients, or other methodologies based on scientifically valid rationales (see reference [3] in the Bibliography).

8 Manufacture

Implants shall be manufactured in such a way that the specified design attributes are achieved.

NOTE Manufacturing requirements for certain product types are included in other related International Standards.

9 Sterilization

9.1 General

The manufacturer shall demonstrate that the effects of the method(s) used for sterilization or, when applicable, re-sterilization of the implant do not impair its safety or performance.

9.2 Products supplied sterile

Sterilization processes shall be validated and routinely controlled.

For terminally-sterilized implants to be designated “STERILE”, the theoretical probability of there being a viable micro-organism present on or in the device shall be equal to or less than 1×10^{-6}.

NOTE Requirements for other sterility assurance levels for some specific implants are given in relevant level 2 and level 3 standards.

Manufacturers may use other sterility assurance levels, provided that this is justified by a documented risk assessment.

If implants are to be sterilized by ethylene oxide, ISO 11135-1 shall apply.

If implants are to be sterilized by irradiation, ISO 11137-1 and ISO 11137-2 shall apply.

If implants are to be sterilized by steam, ISO 17665-1 shall apply.

If implants containing materials of animal origin are to be sterilized by chemical liquid agents, ISO 14160 shall apply.

If implants are to be sterilized by any other terminal sterilization method, ISO 14937 shall apply.

If implants are to be produced by aseptic processing, ISO 13408-1 shall apply.

9.3 Sterilization by the user

9.3.1 Products supplied non-sterile

For implants that are supplied non-sterile, the manufacturer shall specify at least one appropriate method of sterilization with its appropriate cycle parameters, such that other safety and performance characteristics of the implant are not adversely affected. If multiple sterilization cycles are not allowed, this shall be stated in the information provided by the manufacturer (see Clause 11).

9.3.2 Re-sterilization

Information supplied by the manufacturer shall state whether the implant is suitable for re-sterilization and, if so, the method(s) with cycle parameters shall be specified in accordance with ISO 17664. The manufacturer shall specify the maximum number of re-sterilization cycles that may be performed without the safety and intended performance of the implant being adversely affected.

9.4 Sterilization residuals

Testing for residuals of sterilization shall be in accordance with the principles set out in ISO 10993-1. The levels of residuals shall not exceed the limits specified in ISO 10993-7.

10 Packaging

10.1 Protection from damage in storage and transport

For each implant, the packaging shall be designed so that, under conditions specified by the manufacturer for storage, transport and handling (including control of temperature, humidity and ambient pressure, if applicable), it protects against damage and deterioration and does not adversely affect the implant.

NOTE 1 Test methods given in IEC 60068-2-27, IEC 60068-2-32 and/or IEC 60068-2-47 can be used when appropriate.

NOTE 2 Before any method of packaging is adopted, it is advisable that it has been evaluated to establish its suitability for the intended purpose. This can be done by hazard journey trials designed to simulate the conditions the package might encounter.

10.2 Maintenance of sterility in transit

Implants labelled “STERILE” shall be packaged so that they maintain their initial sterility assurance level under normal storage, transport and handling conditions, unless the package that maintains sterility is damaged or opened. The packaging shall comply with ISO 11607-1.

11 Information supplied by the manufacturer

11.1 General

Information supplied by the manufacturer and intended for direct visual recognition shall be legible when viewed under illumination of 215 lx using normal vision, corrected if necessary, at a distance that takes into account the form and size of the individual implant.

NOTE 1 It is advisable that the information presented be understandable by the intended user and/or other persons, where appropriate.

If there is insufficient space on the device’s container, the relevant information may be given on an insert, accompanying document or in the next layer of packaging, as applicable.

The recognition of certain markings on small or specialized implants might require the use of methods other than visual, e.g. electronic methods.

When appropriate, symbols, abbreviations and identification colour may be used in the markings and accompanying documents of an implant. Any symbols, abbreviations and identification colours used shall conform to published International Standards (e.g. ISO 7000). Where no such standards exist, the manufacturer shall describe the symbols, abbreviations or identification colours used in the documentation supplied with the implant.

The information supplied by the manufacturer shall not be presented in such a manner that it can be confused with other essential information.

Any units of measurement shall be expressed in SI units, as specified in the ISO 31 series. Equivalent units may be stated in parentheses.

NOTE 2 Attention is drawn to ISO 1000, which gives further guidance on application of SI units.

As far as practicable and appropriate, the information needed to use the implant safely shall be set out on the implant itself and/or on the packaging for each unit or, where appropriate, on the sales packaging. If individual packaging of each unit is not practicable, the information shall be set out in the leaflet supplied with each implant or package.

When applicable, user adjustable controls shall have their function clearly specified.

Any detachable components, intended by the manufacturer to be used separately from the original implant, shall be identified by their batch code, or by other appropriate means.

Any date shall be expressed in the format YYYY-MM-DD, or YYYY-MM, or YYYY, in accordance with ISO 8601.

11.2 Labelling

The label shall bear the following information:

a) if the packaging contains any radioactive substance, it shall have markings that state the type and activity of the radioactive substance;

b) the name and address of the manufacturer, including at least the city and the country;

c) a description of the device (e.g. cardiac valve), the model designation of the device and, if applicable, the batch number or the serial number of the device preceded by an appropriate identification;

EXAMPLE 1 "LOT", "SN", or the lot or serial number symbols ISO 7000-2492 and ISO 7000-2498, respectively.

d) if the intended purpose of the implant is not obvious to the user, a clear statement of the intended purpose;

e) if applicable, an indication that the contents of the package are sterile and the method of sterilization;

EXAMPLE 2 The word "STERILE" or the sterile symbol ISO 7000-2499, or one of the "sterilized using…" symbols ISO 7000-2500, ISO 7000-2501, ISO 7000-2502 or ISO 7000-2503.

f) if identical or similar implants are sold in both sterile and non-sterile condition, a clear indication that the contents of the particular package are non-sterile, when applicable;

EXAMPLE 3 The "non-sterile" symbol ISO 7000-2609.

g) if applicable, the "use by" date, expressed as year and month;

EXAMPLE 4 The "use by date" symbol ISO 7000-2607.

h) an indication that the implant is intended for single use;

EXAMPLE 5 The "do not re-use" symbol ISO 7000-1051.

i) any special storage and/or handling conditions;

j) any special operating instructions;

k) warnings or precautions relating to use.

11.3 Instructions for use

If applicable, the instructions for use shall contain the following information:

a) if the packaging contains any radioactive substance, the type and activity of the radioactive substance;

b) the name and address of the manufacturer, including at least the city and the country, and a telephone number;

c) a description of the implant (e.g. cardiac valve) and the model designation of the implant;

d) if the intended purpose of the implant is not obvious to the user, a clear statement of the intended purpose;

e) the intended performance described in Clause 4 and any undesirable side-effects;

f) information allowing the user to select a suitable implant (including a correct size), its accessories and related devices, in order to obtain a safe combination;

g) information for proper implantation and on ways to avoid or minimize specific risks associated with implantation;

h) information needed to verify that the implant is functioning correctly and safely;

i) an indication that the contents of the package are sterile and the method of sterilization used;

EXAMPLE 1 The word “STERILE” or the sterile symbol ISO 7000-2499, or one of the “sterilized using…” symbols ISO 7000-2500, ISO 7000-2501, ISO 7000-2502 or ISO 7000-2503.

j) if identical or similar implants are sold in both sterile and non-sterile condition, an instruction, when applicable, that the contents shall be sterilized;

k) details of any treatment or handling needed before the implant can be used;

EXAMPLE 2 Final assembly, cleaning, sterilization, etc.

l) instructions on the method of sterilization with its appropriate cycle parameters for an implant that is delivered non-sterile, or for dealing with the contents of a sterile package that has been damaged or has been previously opened, and maximum number of re-sterilization cycles that may be performed;

m) an indication that the implant is intended for single use;

EXAMPLE 3 The “do not re-use” symbol ISO 7000-1051.

n) any special storage and/or handling conditions;

o) warnings or precautions relating to use, including limitations on chemicals (e.g. alcohol) to which the implant might be exposed in the clinical setting;

p) the nature of the non-viable animal tissues or their derivatives (e.g. intact tissue, highly-purified derivative), if the implant incorporates such materials;

q) a warning about the hazards caused by interference between the implant and other equipment likely to be used in the course of other clinical procedures or medical treatments;

r) a statement concerning the safety of the implant in the MR environment and, when appropriate, information about MR image artefacts to assist the physician in understanding the distortion and signal loss produced in the MR image by the implant;

EXAMPLE 4 The MR safety terms and symbols given in ASTM F2503-05.

NOTE Attention is drawn to ASTM F2119-01, which specifies a test method for evaluating MR image artefacts from passive implants.

s) instructions for the proper removal and disposal of the implant;

NOTE 2 Attention is drawn to ISO 12891-1, which gives further guidance on retrieval and analysis of implants.

t) details allowing the medical staff to brief the patient on any precautions to be taken, including:

— actions to be avoided;

— possible precautions to be taken during normal daily activities;

EXAMPLE 5 Negotiation of stairs, adopting low sitting positions.

— precautions to prevent adverse effects due to changes in implant performance;

— advice that the patient seek medical opinion before entering potentially adverse environments that could affect the performance of the implant;

EXAMPLE 6 Electromagnetic fields, extreme temperature, variations of pressure.

— information on potential interactions with other therapeutic or diagnostic procedures or devices;

EXAMPLE 7 Magnetic resonance imaging.

— information on any medicinal products incorporated in the implant (see Clause 6).

11.4 Restrictions on combinations

If the implant is intended for use in combination with other implants or devices, the whole combination including the connecting system shall be safe and shall not impair the specified performance of the implant. Any restrictions on use shall be indicated on the label or in the instructions for use.

11.5 Marking on implants

Implants shall be marked with the following:

— the manufacturer's name or trademark;

— the batch code (lot number) or serial number.

If the marking would affect the intended performance, or if the implant is too small or the physical properties of the implant prevent legible marking, the information required shall be given on the label or by other means to provide traceability.

11.6 Marking for special purposes

If the implant is intended for a special purpose, the labels and instructions for use shall bear an indication of the special purpose (e.g. "custom-made device" or "exclusively for clinical investigations").

NOTE The specific marking can be the subject of particular national or regional regulation, such as section 21 CFR 812.5 of the U.S. Code of Federal Regulations, or Essential Requirements 13.3 g) and 13.3 h) of European Council Directive 93/42/EEC.