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Fifth edition
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# Non-active surgical implants — General requirements

*Implants chirurgicaux non actifs — Exigences générales*



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# Foreword

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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 document 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).

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This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 285, *Non-active surgical implants,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This fifth edition cancels and replaces the fourth edition (ISO 14630:2012), which has been technically revised.

The main changes are as follows:

— the scope has been revised to clarify that this document does not apply to implants utilizing viable animal or human tissue;

— definitions have been added for clinical evaluation and clinical investigation based on the International Medical Device Regulators Forum (IMDRF) guidance on clinical evaluation;

— definitions have been added for demonstrably similar implant and reference implant to clarify when data for other implants can be used during pre-clinical and clinical evaluation of the implant under investigation;

— indications, contraindications and target patient population have been added in Clause 4 to the list of factors to consider when establishing the intended performance of an implant;

— reorganized list of design attributes in Clause 5 to put then in a more logical sequence;

— revised Clause 6 on selection of material to use a risk analysis as the basis for selection of implant materials and to list factors to be taken into account when performing the risk analysis;

— Clause 7 has been significantly expanded on design evaluation to address pre-clinical evaluation, clinical evaluation and investigation, and post-market surveillance in more detail;

— Clause 8 has been expanded on manufacturing to address cleanliness of the implant;

— subclause 9.1 has been revised to list the methods of sterilizing the implant in a tabular form rather than as running text;

— a new subclause 10.3 has been added to address the determination of the use by date;

— Clause 11 has been revised on information supplied by the manufacturer to include new subclauses addressing patient record labels (11.5) and implant card (11.6);

— the subclause on restrictions on combinations (formerly 11.4) has been deleted because the safety of combinations is addressed in Clause 5 l).

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

# Introduction

There are three levels of standards dealing with non-active surgical implants and related instrumentation. For the implants themselves, they 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 include this document which contains requirements that apply to all non-active surgical implants, and ISO 16061, which contains requirement for instruments associated with non-active surgical implants. They also anticipate that there are additional requirements in the Level 2 and Level 3 standards.

Level 2 standards (see References [2], [12], [23], [27] and [42]) 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 (see References [3], [13], [24] and [25]) apply to specific types of implants within a family of non-active surgical implants, such as hip joints or arterial stents.

To address the requirements for a specific implant, all related Level 1, 2 and 3 standards should be applied.

# Non-active surgical implants — General requirements

## 1 Scope

This document specifies general requirements for non-active surgical implants, hereafter referred to as implants.

This document is not applicable to dental implants, dental restorative materials, transendodontic and transradicular implants, intra-ocular lenses and implants utilizing viable animal or human tissue.

With regard to safety, this document specifies 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 requirements applicable to specific implants or implant families are given or referred to in Level 2 and Level 3 standards.

NOTE 1 This document does not require that the manufacturer have a quality management system in place. However, many regulatory authorities require the application of a quality management system, such as that described in ISO 13485, to ensure that the implant achieves its intended performance and safety.

NOTE 2 In this document, when not otherwise specified, the term "implant" refers to each individual component of a system or a modular implant, provided separately or as a set of components, as well as to all ancillary implants or associated implants designed for improving the intended performance.

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

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

ISO 10993-17, *Biological evaluation of medical devices — Part 17: Toxicological risk assessment of medical device constituents*

ISO 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the 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 11137-3, *Sterilization of health care products — Radiation — Part 3: Guidance on dosimetric aspects of development, validation and routine control*

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

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

ISO 14160, *Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices*

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 17664-1, *Processing of health care products — Information to be provided by the medical device manufacturer for the processing of medical devices — Part 1: Critical and semi-critical medical devices*

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

ISO 20857, *Sterilization of health care products — Dry heat — 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*

ISO 25424, *Sterilization of health care products — Low temperature steam and formaldehyde — Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 80000-1, *Quantities and units — Part 1: General*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14971 and the following apply.

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

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

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

**3.1**
**ancillary implant**
implant, not included as a component of an implant system, but without which the system cannot be surgically inserted

EXAMPLE Cement for cemented stem of a hip joint replacement or screws for orthopaedic plates.

[SOURCE: ISO 16054:2019, 3.4, modified — “implantable device” has been replaced by “implant”.]

**3.2**
**associated implant**
implant, included as a component of a *modular implant* (3.13) or supplied separately, that is surgically inserted for the specific clinical condition to facilitate the use of the primary implant

EXAMPLE An augmentation device used to stabilise the tibial tray of a knee joint replacement or the acetabular cup of a hip joint replacement; sleeves applied to the stem of a hip or knee joint prosthesis to fill canal defects and prevent rotation; a cement restrictor used in hip joint replacement to occlude the intramedullary canal.

[SOURCE: ISO 16054:2019, 3.5, modified — “implantable device” has been replaced by “implant”.]

**3.3**
**$B_0$ hazard area**
space around the magnetic resonance equipment where the static magnetic field can cause harm

Note 1 to entry: The $B_0$ hazard area is not identical to the special environment as defined in IEC 60601-1-2.

Note 2 to entry: The $B_0$ hazard area is not identical to the *magnetic resonance environment* (3.10) as defined in IEC 62570.

[SOURCE: IEC 60601-2-33:2022, 201.3.202, modified — the abbreviation "MR" in the definition and Note 2 to entry has been replaced by "magnetic resonance".]

**3.4**
**clinical evaluation**
set of ongoing activities that use scientifically sound methods for the assessment and analysis of clinical data to verify the safety, clinical performance and/or effectiveness of the device when used as intended by the manufacturer

[SOURCE: IMDRF MDCE WG/N56FINAL:2019, 4.0]

**3.5**
**clinical investigation**
systematic investigation or study in or on one or more human subjects, undertaken to assess the safety, clinical performance and/or effectiveness of a medical device

[SOURCE: IMDRF MDCE WG/N56FINAL:2019, 4.0]

**3.6**
**coating**
layer of material covering or partially covering a surface of an implant

**3.7**
**final implant**
implant that has been subjected to all manufacturing processes including packaging, and if applicable, sterilization, and that is ready to be marketed

Note 1 to entry: The final implant (i.e. implant to be evaluated) is the final product referred to in ISO 10993-1:2018, 3.8.

**3.8**
**demonstrably similar implant**
legally-marketed implant with the same intended use to the *implant* under evaluation for which similarity can be demonstrated in technical, biological and clinical characteristics based on proper scientific justification and to the extent that there is no clinically significant difference in the safety and clinical performance of the implants under evaluation

Note 1 to entry: Manufacturers shall have sufficient levels of access to the data relating to implants with which they are claiming similarity in order to justify their claims of similarity.

Note 2 to entry: In a demonstrably similar implant, most of the performance parameters (technical, biological and clinical) under consideration are similar to the implant under evaluation whereas in a *reference implant* (3.15) as few as one performance parameter may be considered.

Note 3 to entry: A demonstrably similar implant is one which can be used to avoid some technical or biological tests or a clinical investigation of the implant under evaluation.

Note 4 to entry: Some regulatory authorities can require that a demonstrably similar implant is one that is legally marketed in their own country or jurisdiction.

Note 5 to entry: For a demonstrably similar implant, there shall be evidence of successful clinical use in sufficient numbers, for a sufficient period of time, and, at a minimum, without known or reasonably known evidence of design or performance-related recalls.

Note 6 to entry: The manufacturer is responsible for identifying the demonstrably similar implant according to the regulatory requirements in the jurisdictions where the implant under evaluation will be marketed.

**3.9**
**leakage**
unintended movement of fluid, including body fluids, into or out of an implant

Note 1 to entry: An unintended diffusion phenomenon is an example of leakage for the purposes of this document.

**3.10**
**magnetic resonance environment**
**MR environment**
three-dimensional volume surrounding the magnetic resonance magnet that contains both the special environment (Faraday shielded volume) and the $B_0$ *hazard area* (3.3)

Note 1 to entry: This volume is the region in which an item can pose a hazard from exposure to the electromagnetic fields produced by the magnetic resonance equipment and accessories, and for which access control is part of the risk mitigation.

Note 2 to entry: The entrance to the magnetic resonance environment is controlled by the responsible organization. The area to which entry is controlled is sometimes referred to as the magnetic resonance controlled access area.

[SOURCE: IEC 60601-2-33:2022, 201.3.224]

**3.11**
**magnetic resonance imaging**
**MRI**
imaging technique that uses a static magnetic field, time-varying gradient magnetic fields and radio frequency fields to provide images of tissue by the magnetic resonance of nuclei

[SOURCE: ASTM F2182-19e2, 3.1.6]

**3.12**
**manufacturer**
natural or legal person with responsibility for design and/or manufacture of an implant with the intention of making the implant available for use, under their name, whether or not such an implant is designed and/or manufactured by that person or on their behalf by another person(s)

Note 1 to entry: This natural or legal person has the ultimate legal responsibility for ensuring compliance with all applicable regulatory requirements for the implant in the countries or jurisdictions where it is intended to be made available or sold, unless this responsibility is specifically imposed on another person by the regulatory authority (RA) within that jurisdiction.

Note 2 to entry: The manufacturer's responsibilities are described in other Global Harmonization Task Force (GHTF) guidance documents. These responsibilities include meeting both pre-market requirements and post-market requirements, such as adverse event reporting and notification of corrective actions.

Note 3 to entry: "Design and/or manufacture" can include specification development, production, fabrication, assembly, processing, packaging, repackaging, labelling, relabelling, sterilization, installation or remanufacturing of an implant; or putting a collection of devices, and possibly other products, together for a medical purpose.

Note 4 to entry: Any person who assembles or adapts an implant that has already been supplied by another person for an individual patient, according to the instructions for use, is not the manufacturer, provided the assembly or adaptation does not change the intended use of the implant.

Note 5 to entry: Any person who changes the intended use of or modifies an *implant* without acting on behalf of the original manufacturer and who makes it available for use under their own name, should be considered the manufacturer of the modified implant.

Note 6 to entry: An authorised representative, distributor or importer who only adds its own address and contact details to the implant or the packaging, without covering or changing the existing labelling, is not considered a manufacturer.

Note 7 to entry: To the extent that an accessory is subject to the regulatory requirements of an implant, the person responsible for the design and/or manufacture of that accessory is considered to be a manufacturer.

[SOURCE: ISO 14971:2019, 3.9, modified — "medical device" has been replaced by "implant".]

**3.13**
**modular implant**
implant system which is supplied, provided separately or as a procedure pack/convenience kit, as a number of components and which is intended to be assembled by the intended user

EXAMPLE Femoral stem, modular femoral head, acetabular cup and liner are each separate components of a modular hip prosthesis.

**3.14**
**non-active surgical implant**
*surgical implant* (3.16), 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

Note 1 to entry: For the purpose of this document, the term "non-active surgical implant" is hereafter referred to as "implant".

**3.15**
**reference implant**
legally-marketed implant which, when compared to the implant under evaluation, satisfies both of the following conditions:

a) it has the same intended use, similar materials and a similar design with regard to the specific dimensional or performance criteria under evaluation to address the same clinical and technical requirements;

b) there is evidence of successful clinical use in sufficient numbers: for a sufficient period of time, and, at a minimum, without known or reasonably known evidence of design or performance-related recalls with regard to the specific dimensional or performance criteria under evaluation

Note 1 to entry: The term “reference” is not intended to imply that the implant under evaluation and the reference implant are “equivalent” or that the reference implant is a “predicate” implant. This is because for some regulatory authorities, the terms “equivalent” and “predicate” have a meaning which is beyond that intended by the term “reference” as used in this document.

Note 2 to entry: A reference implant is the comparison implant for dimensional or performance parameter(s) under evaluation. Other characteristics of the reference implant shall be considered in order for the comparison to be suitable, as in some situations there can be cross-effects. Ideally, for the majority of dimensional and performance parameters, a single reference implant should be used for comparison to the implant under evaluation. However, more than one reference implant may be used for comparison purposes, with adequate scientific and clinical justification.

Note 3 to entry: Some regulatory authorities require that a reference implant is one that is legally marketed in their own country or jurisdiction. This fact can be taken into account when selecting a reference implant for the purposes of this document.

Note 4 to entry: There is no agreed upon interpretation for what constitutes “sufficient numbers” or a “sufficient period of time” in the above definition. Typically, a determination of what constitutes “sufficient numbers” and a “sufficient period of time” is demonstrated by using statistical methods and clinical judgement in the evaluation of implant performance.

Note 5 to entry: A justification for a “similar material” may include information that although the materials are not the same, the material(s) used for the implant under evaluation can be shown to perform similarly with regard to the test or its underlying clinical concern.

Note 6 to entry: Examples of design features that can be taken into consideration when evaluating whether an implant has a ‘similar design’ to the implant under evaluation include means of fixation, modularity, constraint, key dimensions and shape, processing, surface topography, surface treatment, etc. A justification for a “similar design” therefore may include information that although the designs are not the same, the design of the implant under evaluation can be shown to perform similarly with regard to the test or its underlying clinical concern.

Note 7 to entry: The manufacturer is responsible for identifying the reference implant(s) according to the regulatory requirements in the jurisdictions where the implant under evaluation is to be marketed.

**3.16**
**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 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 d

## 4 Intended performance

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

a) intended purpose(s);

b) indications, contraindications and target patient population;

c) functional characteristics;

d) intended conditions of use, including details of required ancillary implants and associated implants designed to achieve the intended performance;

e) intended lifetime.

NOTE Information to support the description of the intended performance can be found in sources such as:

— published standards such as the Level 2 and Level 3 standards listed in the Introduction, and

— published clinical and scientific literature.

Implants shall be evaluated to demonstrate that the intended performance is achieved (see Clause 7).

## 5 Design attributes

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

a) biocompatibility of materials for their intended use, including the influence of material by-products from manufacturing and chemical residuals;

b) physical, mechanical, biological and chemical properties of materials, including endurance properties and ageing;

c) wear characteristics of materials and the effects of wear and wear products on the implant and the body;

d) degradation characteristics of materials and the effects of degradation, and degradation products and leachables on the implant and the body;

e) extent and effect of leakage of substances from the implant (e.g. fillers used in a cosmetic prosthesis);

f) compatibility with any drug or biological product incorporated into the implant including non-viable tissues or cells of human or animal origin, or their derivatives;

g) shape, dimensions and surface characteristics of the implant, including their possible effects on tissues and body fluids;

h) biocompatibility of all components of the implant including non-implantable components that can have direct or indirect tissue contact in their clinical use conditions;

i) 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;

j) the effect of manufacturing processes (including sterilization) on material characteristics and intended performance;

k) 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;

l) interconnections and their effects on the intended performance, including connections with ancillary or associated implants, and with any necessary instrumentation for use in association with the implant;

NOTE 1 The shape, dimensions and tolerances of the interconnections, as well as potential wear, degradation, corrosion and electrolytic effects can affect the intended performance of interconnections.

NOTE 2 Interconnections can include the connections with ancillary implants as well as the associated implants required for achieving the intended performance and safety.

m) interface(s) between the implant and body tissue(s), particularly relative to fixation, connection, surface characteristics and the potential for the implant to move from its intended position or orientation;

n) physical and chemical effects of the body and external environment on the implant;

o) effects of ionizing radiation, electromagnetic and magnetic fields on the implant and its function, and any consequential effects on the body;

p) the feasibility for an implant to be implanted and, where applicable, to be removed or replaced;

q) the feasibility for an implant's position and orientation to be visualized through radiological or other imaging procedures;

r) the ability to remove microbiological and particulate contamination from manufacturing;

s) the effect of a nanomaterial;

t) the suitability and effectiveness of packaging;

u) where appropriate, the anthropometric and anatomical features of the population for whom the implant is intended;

v) the condition and pathology of the host tissue;

w) required operative techniques and the appropriate care and handling of the implant to reduce the risk of use error while not impairing the intended use and performance of the implant;

x) where applicable, the nature and type of any radioactive substances incorporated in or used with the implant to achieve the intended performance while reducing or eliminating the risk of exposure of patients, intended users and other persons to unintended radiation.

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

## 6 Selection of materials

The selection of materials to be used for the manufacture of implants shall be based on a risk analysis, which shall take into account at least the following:

a) the properties required for the intended purpose considering factors such as anatomical location, dimensions, geometry, conditions for use and the intended lifetime of the implant;

b) any intended treatment to the material or to the surface of the implant (chemical, electro-chemical, thermal, mechanical, etc.) or coating applied to the surface or a part of the surface of the implant material;

c) the effects of implant manufacturing, handling, cleaning, disinfection, packaging, sterilization and storage;

d) possible adverse reactions of implant materials with:

— human tissues and body fluids;

— medicinal products incorporated into the implant;

— non-viable tissues or cells of human or animal origin, or their derivatives incorporated into the implant;

— other implants, substances and gases.

In addition, the selection of materials shall be based on their demonstrated biocompatibility.

NOTE 1 The demonstrated biocompatibility of the materials does not assure the biocompatibility of the final implant (see 7.2).

Possible effects of ionizing radiation and of magnetic and electromagnetic fields on the material, as well as the effect of the material on image quality in magnetic resonance imaging (MRI) and computed tomography (CT), shall also be considered.

The performance of the medicinal product used in combination with the implant shall not be affected by the material and the medicinal product shall not affect the performance of the material.

For implants utilizing materials of animal origin or their derivatives 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 2 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 their safety and intended performance is achieved (see Clause 4). Safety and intended performance shall be demonstrated by pre-clinical evaluation (see 7.2) followed by clinical evaluation including any clinical investigations (see 7.3) and post-market surveillance (see 7.4).

When the manufacturer’s risk analysis indicates that there is a significant risk to the patient as the result of failure or incompatibility between the implant and the patient during its intended lifetime, the manufacturer shall take steps to make sure that the safety and intended performance of the implant are maintained.

An appropriate risk management process in accordance with ISO 14971 shall be established for all stages in the life cycle of the implant.

## 7.2 Pre-clinical evaluation

Implants shall undergo pre-clinical evaluation to demonstrate the safety and intended performance of the implant under the intended use conditions. This can include evaluation of dimensional, mechanical, biological and chemical properties, cleanability, sterilizability, packaging, the effect of storage conditions,

shelf-life, or other characteristics as applicable. Unless an adequate justification is provided, the pre-clinical evaluation shall be based on all of the following:

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

b) applicable standards;

c) all available field data, safety reports, relevant complaint information and adverse event data for the implant or a demonstrably similar implant(s);

d) data obtained from:

   1) testing of the implant against established performance requirements, and/or

   2) testing of the implant as compared to an existing reference implant, and/or

   3) a demonstrably similar implant(s).

Data shall be obtained using test methods that are demonstrated to be fit for their intended purpose.

If comparing data obtained from testing of the implant and either a reference implant or a demonstrably similar implant, testing shall be performed using the same methods and test conditions unless any differences can be justified.

Pre-clinical testing of implants should simulate conditions of intended use. Test methods and related limits for specific types of implants shall be defined and justified by the manufacturer and shall include, as appropriate, in vitro handling tests to verify the intended interaction between the implant and any instruments to be used in association with the implant and, if applicable, between interconnecting implants.

Tests should take into account anticipated loading, and the impact of shelf-life and/or the in situ environment. Where appropriate, test specimens should represent as closely as possible the final implant. If static and/or dynamic loading tests are relevant for the evaluation of the implant, either accepted test standards when available or customized test models taking into account the characteristics of the implant shall be applied. Testing should also evaluate any deterioration of the implant in its packaging under the storage conditions specified by the manufacturer, and the effect of this deterioration on the intended performance of the implant. Because of the wide variation in implants and their features, testing standards can be non-existent or may be modified as needed.

In instances when implantation and, where appropriate, removal cannot be evaluated by direct comparison with existing implants, cadaveric evaluation or simulated cadaveric evaluation should be performed where possible.

Some pre-clinical tests, such as some dimensional and mechanical tests, can be comparison tests where the implant under evaluation and an existing reference implant are tested in order to evaluate the performance of the implant under evaluation for the parameter(s) under investigation.

Test methods and limits for particular implants can be described in related standards, such as those listed in the Bibliography.

Testing to demonstrate the implant usability is required unless the implant usability can be evaluated by direct comparison with the usability engineering file of existing implants.

NOTE 1 Further information on a process for demonstrating the usability of an implant can be found in IEC 62366-1.

Assessment of the possible effects of ionizing radiation, electromagnetic and magnetic fields on the final implant and its function and any consequential effects on the body shall be conducted.

NOTE 2 The test methods in ASTM F2052 (induced displacement force), ASTM F2213 (induced torque), ASTM F2182 (radio frequency induced heating) and ISO/TS 10974 (gradient heating and gradient vibration) can be used to evaluate the safety of an implant in the magnetic resonance environment. According to IEC 60601-2-33, B1+rms is used on MR equipment to provide control of radio frequency exposure and can be used for the most accurate evaluation of and labelling for radio frequency induced heating.

The biocompatibility of the final implant shall be established as part of the pre-clinical evaluation. The biological evaluation of the final implant shall be performed in accordance with ISO 10993-1, within a risk management process, as well as with other parts of the ISO 10993 series as applicable. When determining the biocompatibility of the final implant, residuals from the manufacturing processes (e.g. lubricants, cleaning agents, mould release agents) shall also be considered at a minimum.

When determining the biocompatibility of the final implant, degradation products from the implant over the product life, such as particulates and/or substances released from the device shall be considered.

If the manufacturer specifies that the implant can be processed by the intended user, the effects of the specified processing on degradation or other chemical changes that can impact biocompatibility or limit the lifetime of the implant shall be taken into account.

NOTE 3 For information on the limitations and restriction on processing, see ISO 17664-1:2021, 6.3.

Pre-clinical evaluation of implants that incorporate medicinal products into the implant shall include an assessment of the quality, safety and usefulness of the substance according to pharmaceutical principles.

NOTE 4 National or regional regulations can detail appropriate methods for the assessment of the safety, quality and usefulness of the medicinal products incorporated as an integral part of an implant.

## 7.3 Clinical evaluation and clinical investigation

**7.3.1** Implants shall undergo a clinical evaluation to demonstrate their safety and intended performance when used in accordance with their intended use and in their intended patient populations. It shall include the evaluation of undesirable side-effects and shall be connected to the risk management process including the benefit-risk analysis.

The clinical evaluation shall be planned and documented.

The clinical evaluation shall be continuously updated using data as gathered from the post-market surveillance (see 7.4).

The clinical evaluation shall be based on a critical review of:

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

b) the results of all available clinical investigations made on the implant under evaluation or the demonstrably similar implant(s).

**7.3.2** A pre-market clinical investigation shall be performed, except if:

a) the implant under evaluation is an exempted implant, or

NOTE 1 Regulatory authorities can exempt certain implants from the need for a pre-market clinical investigation such as implants with well-established technologies such as sutures, staples, screws, wedges, plates, wires, clips and connectors.

b) the implant under evaluation has been designed by modifications of an implant already marketed by the same manufacturer or by a different manufacturer, provided there is the sharing of information between these manufacturers, and

1) the modified implant is demonstrably similar to the already marketed implant, and

2) the clinical evaluation of the already marketed implant is sufficient to demonstrate the safety and intended performance of the implant under evaluation in its intended use conditions and in its intended patient populations.

NOTE 2 Some regulatory authorities can have different requirements concerning clinical investigations. In these regulatory jurisdictions, the above requirements concerning clinical investigation might not apply.

If a pre-market clinical investigation is required, it shall be performed in accordance with ISO 14155.

### 7.4 Post-market surveillance

The manufacturer shall establish a systematic procedure to collect and review the post-market experience with the use of the implant.

The design of the procedure to collect and review post-market data shall be based on the intended performance and the risk that the implant failure presents to the patient. A post-market surveillance plan shall be established for collecting and analysing data gained from the use of the implant or the implant system.

In addition to the periodical analysis and review of the post-market surveillance data, the manufacturer shall identify and fulfil requirements for the timely handling of complaints and reporting of adverse events.

NOTE 1 Regulatory authorities can have different requirements concerning the timely handling of complaints and reporting of adverse events.

NOTE 2 For guidance on post-market surveillance, see ISO 14971 and ISO/TR 24971.

NOTE 3 Useful information and guidance on the post-market surveillance process is provided in ISO/TR 20416.

NOTE 4 Useful information and guidance on adverse event reporting is provided in Reference [49].

NOTE 5 Suitable methods for collecting data include implant registries or post-market clinical follow-up studies.

NOTE 6 Suitable methods for monitoring the data related to the safety and performance of implants include survival analysis (with revision or removal of the implant or the patient death as the end point) and clinical follow-up of patients.

## 8 Manufacture

Implants shall be manufactured in such a way that the specified design attributes are achieved (see Clause 5).

Implants shall be supplied at a level of cleanliness as determined by the risk management process taking into account manufacturing and environmental contaminants. It shall be verified that the intended level of cleanliness has been achieved.

The cleaning process shall be validated. Implants for which no validated cleaning process can be applied shall be fully manufactured by aseptic processes.

NOTE 1 For information on orthopaedic implants cleaning as well as for test methods on the cleaning process validation and controls, see ISO 19227.

Implants can be delivered sterile or non-sterile.

NOTE 2 Manufacturing requirements for specific product types can be found in relevant Level 2 and Level 3 standards.

## 9 Sterilization

### 9.1 Implants supplied sterile

For terminally sterilized implants to be designated “STERILE”, the theoretical probability of there being a viable microorganism present on or in the implant shall be equal to or less than $1 \times 10^{-6}$.

Other sterility assurance levels may be used if justified by a documented risk assessment.

NOTE Sterility assurance levels for specific implants can be found in the relevant Level 2 and Level 3 standards.

If the implant to be supplied sterile is processed using one of the methods listed in Table 1, the requirements for the method that are described in the applicable standards shall be applied.

**Table 1 — Methods for processing implants supplied sterile**

| Method | Applicable standards |
|---|---|
| Ethylene oxide | ISO 11135 |
| Irradiation [a] | ISO 11137-1, ISO 11137-2 and ISO 11137-3 |
| Moist heat | ISO 17665 |
| Dry heat | ISO 20857 |
| Low temperature steam and formaldehyde [b] | ISO 25424 |
| Chemical liquid agents [c] | ISO 14160 |
| Other terminal sterilization process | ISO 14937 |
| Aseptic processing | ISO 13408-1 |

[a] If applicable, ISO 13004 may be used to meet the requirements of ISO 11137-2.

[b] In some regulatory jurisdictions, low-temperature steam and formaldehyde sterilization is not an accepted sterilization method.

[c] It is applicable for sterilization of implants containing materials of animal origin.

### 9.2 Implants supplied non-sterile

For implants that are supplied non-sterile, the manufacturer shall provide information on the processing of these implants in accordance with ISO 17664-1. If multiple sterilization cycles are not allowed, this shall be stated in the information provided by the manufacturer (see Clause 11).

### 9.3 Re-sterilizable implants

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 17664-1.

The manufacturer shall specify the maximum number of re-sterilization cycles that can be performed without the safety and intended performance of the implant being adversely affected. Alternatively, the manufacturer may specify one or more other end-of-life indicators that demonstrate that the safety and intended performance of the implant have been adversely affected such that the implant shall no longer be used.

### 9.4 Sterilization residuals

Testing for residuals of sterilization shall be in accordance with the principles set out in ISO 10993-1 and in ISO 10993-17. The levels of residuals of ethylene oxide shall not exceed the limits specified in ISO 10993-7.

NOTE For requirements for formaldehyde residuals, see EN 14180.

## 10 Packaging

### 10.1 Protection from damage in transport, storage and handling

For each implant, the packaging shall be designed so that, under conditions specified by the manufacturer for transport, storage and handling (e.g. temperature, humidity, and, if applicable, UV environment, pressure), the implant is protected against damage and deterioration and the packaging does not adversely affect the intended performance of the implant.

NOTE 1 Possible test methods are specified in IEC 60068-2-27, IEC 60068-2-31 and/or IEC 60068-2-47. Possible methods for performance testing of packaging and shipping containers can be found in ASTM D4169, ASTM D7386 and ISTA 3A.

Before any packaging is adopted, the packaging should be evaluated to establish its suitability for the intended purpose.

NOTE 2 This can be done by testing designed to simulate the conditions the package can encounter.

### 10.2 Maintenance of sterility in transport, storage and handling

Implants labelled “STERILE” shall be packaged so that they maintain their initial sterility assurance level under specified transport, storage and handling conditions, unless the package that maintains sterility is damaged or opened.

The packaging and packaging processes shall comply with ISO 11607-1 and ISO 11607-2.

NOTE See ISO 11607-1:2019, Table B.1 for a list of performance testing standards and test methods for sterile barrier systems.

### 10.3 Use by date

The "use by date" shall be determined to ensure that:

a) if applicable, the final implant’s sterility is maintained (see 10.2); and

b) any deterioration of the final implant under the storage conditions that are specified by the manufacturer does not affect its intended performance.

Material testing and/or functionality testing can be needed to evaluate the final implant’s stability in storage and the effect of any deterioration on its intended performance. If material testing and/or functionality testing is not conducted, a justification shall be provided.

If materials testing and/or functionality testing is based on accelerated aging, testing on real-time aged samples shall also be performed, unless otherwise justified.

## 11 Information supplied by the manufacturer

### 11.1 General

The medium, format, content, legibility and location of the label and instructions for use shall be appropriate for the particular implant, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.

Each implant shall be accompanied by the information needed to identify the implant and its manufacturer, and by any safety and performance information relevant to the intended user, patient or any other person, as appropriate.

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 implant.

If several devices are packaged together, the use by date given on the outer package shall be the shortest use by date of any device. Once the package is opened, any use by date given on any of the individual devices shall apply.

If packaging of each implant is not practicable or if there is insufficient space on the implant’s packaging, the relevant information may be given in an insert, in an accompanying document or on the next layer of packaging, as applicable.

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 15223-1). Where no such standards exist, the manufacturer shall describe the symbols, abbreviations or identification colours used in the documentation supplied with the implant.

Any units of measurement shall be expressed in SI units, as specified in ISO 80000-1. Equivalent units may be stated in parentheses.

NOTE 1 ISO 80000-1 gives further guidance on the application of SI units.

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

Any date shall be expressed in the format YYYY-MM-DD, YYYY-MM, or YYYY.

The information supplied by the manufacturer in accordance with Clause 11 shall be presented in such a manner that it cannot be confused with other information.

The usability of the information supplied by the manufacturer shall be evaluated. The usability of the information may be evaluated by direct comparison with the information of existing implants for which usability has been demonstrated.

NOTE 2 Further information on a process for demonstrating the usability of the information can be found in IEC 62366-1.

NOTE 3 Additional guidance on the information to be supplied by the manufacturer can be found in ISO 20417.

## 11.2 Marking on implants

Implants shall be marked in human-readable form with:

a) manufacturer's name or trademark;

b) batch code (lot number) or serial number.

If the marking can 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.

The recognition of certain markings (e.g. 2D barcodes) on implants can require the use of methods other than visual, for example, automatic identification and data capture (AIDC). Some methods can require specific lighting conditions for verification (see ISO/IEC 15415).

## 11.3 Label

The information on the label shall be presented in human-readable form and may be supplemented by machine-readable information [e.g. radio frequency identification (RFID) or bar codes].

The label shall bear the following information:

a) the name or trade name of the implant;

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

NOTE 1 In some regulatory jurisdictions, there are requirements to include the name and address of the authorized representative or local agent.

c) a description of the implant (e.g. cardiac valve), the model designation of the implant, including attributes such as material, size, side (i.e. left or right), connector and the batch code or the serial number of the implant preceded by an appropriate identification;

EXAMPLE 1 "LOT", "SN" or the lot, or serial number symbols ISO 7000-2492 and ISO 7000-2498, respectively; see ISO 15223-1:2021, 5.1.5 and 5.1.7.

NOTE 2 In some regulatory jurisdictions, there are requirements to include a unique device identifier (UDI).

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

e) if applicable, an indication that the implant incorporates:

— any drug or biological product,

— any non-viable human or animal cells or tissues or their derivatives (e.g. intact tissue, highly-purified derivative),

— any radioactive substance, including the type and activity of the radioactive substance;

f) for terminally sterilized implants, 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; see ISO 15223-1:2021, 5.2.1 or 5.2.2, 5.2.3, 5.2.4 and 5.2.5.

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

EXAMPLE 3 The “non-sterile” symbol ISO 7000-2609; see ISO 15223-1:2021, 5.2.7.

NOTE 3 Some regulatory authorities require all implants supplied in a non-sterile condition to be labelled as non-sterile.

h) if applicable, the “use by date”, expressed as year and month, and, if appropriate, day;

EXAMPLE 4 The “use by date” symbol ISO 7000-2607; see ISO 15223-1:2021, 5.1.4.

i) if there is no “use by date”, the date of manufacture;

NOTE 4 In some regulatory jurisdictions, the date of manufacture can be included as part of the batch code or serial number provided the date is clearly identifiable.

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

EXAMPLE 5 The “do not re-use” symbol ISO 7000-1051; see ISO 15223-1:2021, 5.4.2.

k) any required special storage (e.g. temperature, humidity, UV environment, pressure) and/or handling conditions;

l) any special instructions;

EXAMPLE 6 The symbol "LEFT" or "L" for implants to be used on the left side or "RIGHT" or "R" for implants to be used on the right side.

m) warnings or precautions that need to be brought to the immediate attention of the intended user. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use;

n) an indication to check the instructions for use;

EXAMPLE 7 The "Consult instructions for use" symbol ISO 7000-1641; see ISO 15223-1:2021, 5.4.3.

o) an indication that the implant shall not be used if the package is damaged or unintentionally opened;

EXAMPLE 8 The "Do not use if package is damaged" symbol ISO 7000-2606; see ISO 15223-1:2021, 5.2.8.

p) If applicable, a clear indication that the instructions for use for the implant are supplied in electronic form instead of in paper form, information on how to access the instructions for use in electronic form and information for obtaining the instructions for use in paper form.

Information on the label that is intended to facilitate proper implant identification at the point of use shall be legible when viewed under illumination of 215 lux using normal vision, corrected, if necessary, at a distance of 1 m.

NOTE 5 Providing clear and accurate information can facilitate proper implant identification at the point of use, typically in the operating room. For musculoskeletal implants, ASTM F2943 provides guidance on the content of the label and on the relative location of the information within the label.

## 11.4 Instructions for use

Instructions for use shall be provided in paper format together with the implant or in a non-paper format (e.g. electronic).

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

a) the name and contact details of the manufacturer, including at least the postal address and the country;

NOTE 1 Contact details can include telephone number, email address, website URL, etc.

NOTE 2 In some regulatory jurisdictions, there are requirements to include the name and address of the authorized representative or local agent.

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

c) If the implant is supplied as part of a procedure pack/convenience kit, the description of the contents of the procedure pack/convenience kit;

d) a clear statement of the intended purpose, indications, contra-indications and the patient target group or groups as appropriate;

e) the intended performance described in Clause 4;

f) any residual risks and any undesirable side-effects as well as their likelihood;

g) information allowing the intended user to select a suitable implant (including the correct size), its accessories and related devices (e.g. ancillary implants, associated implants), in order to obtain a safe combination;

h) the recommended surgical technique in regard to the implant, including practical advice on how to avoid or minimize risks associated with implantation;

i) an indication that the contents of the package are sterile and of 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; see ISO 15223-1:2021, 5.2.1 or 5.2.2, 5.2.3, 5.2.4 and 5.2.5.

j) details of any treatment or handling needed before the implant can be used, including information for each applicable processing step (i.e. cleaning, disinfection, drying, packaging and sterilization) as specified in the information to be provided by the medical device manufacturer in ISO 17664-1;

EXAMPLE 2 Final assembly.

EXAMPLE 3 Sterilization of the implant provided non-sterile.

EXAMPLE 4 If permitted, the cleaning, disinfection and sterilization of a non-used implant.

NOTE 3 ISO 17664-1 requires at least one validated method be specified for each applicable processing step.

k) instructions for dealing with the contents of a sterile package that has been damaged or has been previously opened;

l) if the implant is suitable for re-sterilization, suitable method(s) with cycle parameters and either the maximum number of re-sterilization cycles that may be performed or a description of other end-of-life indicators if specified (see 9.3);

m) statement that the implant is intended for single use, including information on known characteristics and technical factors that can pose a risk if the implant was to be re-used;

EXAMPLE 5 The “do not re-use” symbol ISO 7000-1051; see ISO 15223-1:2021, 5.4.2.

n) any special storage (e.g. temperature, humidity, UV environment, pressure) and/or handling conditions;