TECHNICAL SPECIFICATION

ISO/TS 17137

Second edition
2019-09

Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants

Implants cardiovasculaires et systèmes extracorporels — Implants cardiovasculaires absorbables

Reference number
ISO/TS 17137:2019(E)

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Published in Switzerland

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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 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 of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition (ISO/TS 17137:2014), which has been technically revised.

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

Absorbable cardiovascular implants are medical devices with various clinical indications for use in the human cardiovascular blood system. An absorbable cardiovascular implant, or at least a portion thereof, is designed to intentionally degrade over time into degradation products that are absorbed by the body through metabolism, assimilation, and/or excretion (elimination). Such implants can be either surgically or interventionally introduced to the site of treatment.

This document outlines requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization, packaging, and information supplied by the manufacturer. This document should be considered as a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants. This document should also be considered as a supplement to relevant device-specific standards such as the ISO 25539 series specifying requirements for endovascular devices, which do not address degradation and other time dependent aspects of absorbable implants and coatings. Additionally, this document should be considered in conjunction with ISO 14155, which specifies proper practices in clinical investigations.

This document is not comprehensive with respect to the pharmacological evaluation of cardiovascular absorbable implants. More detailed safety and performance requirements for pharmacological agents included in the absorbable cardiovascular implant are described in ISO 12417-1.

Only issues related to degradation and absorption combined with the cardiovascular implant are covered by this document. Due to the variations in the design of implants covered by this document and in some cases due to the relatively recent development of some of these implants (e.g. absorbable stents), acceptable standardized *in vitro* tests and clinical results are not always available. As further scientific and clinical data become available, appropriate revision of this document will be necessary.

NOTE For issues related to the common mechanical function of the cardiovascular implant, the reader might find it useful to consider a number of other international standards (see Bibliography).

Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants

1 Scope

This document outlines design evaluation guidelines for absorbable cardiovascular implants used to treat vessels and/or the vascular space within the circulatory system, including the heart and all vasculature. This document is meant to supplement device-specific standards by providing guidelines specific for absorbable implants and/or components

This document is applicable to implants in direct contact with the cardiovascular system, where the intended action is upon the circulatory system. This document does not address the specific evaluation of issues associated with viable tissues, viable cells, and/or implants with non- viable biological materials and their derivatives. Additionally, procedures and devices used prior to and following the introduction of the absorbable cardiovascular implant (e.g. balloon angioplasty devices) are excluded from the scope of This document if they do not affect the absorption aspects of the implant. A cardiovascular absorbable implant may incorporate substance(s) which, if used separately, can be considered to be a medicinal product (drug product) but the action of the medicinal substance is ancillary to that of the implant and supports the primary mode of action of the implant.

NOTE 1 Some aspects of absorbable components of cardiovascular device-drug combination products (e.g. coatings) in their connection with drug-related aspects of the device are addressed in ISO 12417-1.

NOTE 2 An explanation of the nomenclature of absorb, degrade and related terms can be found in Annex A of this document.

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 5840 (all parts), *Cardiovascular implants — Cardiac valve prostheses*

ISO 10993 (all parts), *Biological evaluation of medical devices*

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 (all parts), *Sterilization of health care products — Radiation*

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

ISO 12417-1, *Cardiovascular implants and extracorporeal systems — Vascular device-drug combination products — Part 1: General requirements*

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

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

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 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 25539 (all parts), *Cardiovascular implants — Endovascular devices*

ISO/TR 37137, *Cardiovascular biological evaluation of medical devices —Guidance for absorbable implants*

ASTM F640, *Standard Test Methods for Determining Radiopacity for Medical Use*

3 Terms and definitions

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

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

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

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

3.1
absorb
absorption
<biomaterials> action of a non-endogenous (foreign) material or substance or its degradation products passing through or being assimilated by cells and/or tissue over time

3.2
degradation product
intermediate or final result from the physical, metabolic, and/or chemical decomposition of a material or substance

3.3
degrade
physically, metabolically, and/or chemically decompose a material or substance

3.4
leachable
substance that can be released from a medical device or material during clinical use

Note 1 to entry: In absorbable devices, leachables can be substances released from the as-manufactured product or substances generated and released as a consequence of its degradation (i.e degradation products).

4 Device design, fabrication, packaging, and use considerations

4.1 Classification

A cardiovascular absorbable implant is a product that accomplishes its intended clinical use and performance through primarily physical and/or mechanical means over a defined time period. An absorbable cardiovascular implant may also incorporate a medicinal substance. A cardiovascular absorbable implant accomplishes its intended clinical use and is then fully or partially absorbed by the body over a finite period of time. The implant's temporary nature is provided by its ability to degrade and the resulting degradation products' ability to be metabolized, assimilated, and/or excreted (eliminated) over time.

The manufacturer shall determine the acceptability of the product for clinical use at all stages of the product life cycle.

4.2 Intended clinical performance

The intended performance of an absorbable implant shall be described and documented by addressing at least the following, with particular regard to patient's safety:

a) intended purpose(s);

b) functional lifetime – duration of intended mechanical function;

c) *in vivo* longevity – approximate time to full absorption of the absorbable components; absence of histological (physical) presence in tissue.

4.3 Intended clinical use

The intended clinical use shall, if applicable, be preferentially identified as one or more of the following:

a) abdominal aorta;

b) arterio-venous shunt for vascular access;

c) carotid artery;

d) coronary artery;

e) coronary heart chambers;

f) femoral artery;

g) iliac artery;

h) popliteal artery;

i) intra-cerebral artery;

j) renal artery;

k) thoracic aorta;

l) thoraco-abdominal aorta;

m) tibial artery;

n) heart valve;

o) venous valve;

p) other heart, arterial, or venous anatomy to be specified as appropriate.

4.4 Materials

The requirements of ISO 14630:2012, Clause 6, shall apply.

Additional testing appropriate to specific material types (e.g. metals, polymers, drugs) shall be performed to determine material acceptability for use in the design. For example, guidance for assessing absorbable polymeric implants can be found in ASTM F2902, with ASTM F3160 useful for absorbable metal materials testing. In a more specific example, absorbable materials dependent on shape memory properties should be subjected to testing that assesses transformation properties. For drug-eluting absorbable implants, drug identity testing shall be performed, including the identification of impurities and degradants. Electro-chemical potentials of differing metals (stents, guidewires, other accessory devices) might require additional types of testing.

4.5 Packaging, labelling, and sterilization

4.5.1 Packaging

4.5.1.1 General

The requirements of ISO 11607-1 and ISO 14630:2012, Clause 10 shall apply.

Each device shall be packaged in a unit container with a sterile barrier, or a combination of unit container and an outer container. The unit container (within its outer container if applicable) may be packaged in a shipping container during transit and storage.

The device packaging configuration should be designed to protect the implant during normal conditions of handling, storage and transport such that device specifications are maintained. The sterile barrier shall be maintained throughout its designated shelf-life to permit the contents to be presented for use in an aseptic manner.

4.5.1.2 Considerations for absorbable product

For absorbable products, non-standard packaging attributes may be needed to mitigate or eliminate the effects of environmental factors in order to maintain the physical, chemical and/or mechanical specifications of the implant. Where the absorbable product is susceptible to hydrolytic or corrosive degradation, consideration should be given toward the control and/or removal of moisture from the package interior (e.g. through the use of moisture resistant packaging materials and/or desiccants). In addition, absorbable products may also be susceptible to physical, chemical, and/or mechanical degradation under extreme temperature conditions. For example, storage of polymeric products or components at temperatures that approach or exceed a glass transition temperature could adversely affect the physical and chemical state of the implant. Therefore, storage conditions should specify the acceptable temperature range and limit the duration of packaged product exposure to elevated thermal conditions.

4.5.2 Labelling

4.5.2.1 Label(s)

Each device shall be accompanied by one or more labels, one on each of the containers.

The requirements of ISO 14630:2012, Clause 11, shall apply, with the following information to be supplied as part of the label(s):

a) name or trade name of the device;

b) expiration date (indication of shelf-life) and the recommended storage conditions;

c) description and/or list of the package contents;

d) size and device type, if applicable;

e) dimensions applicable for clinical use;

f) sterilization method and the notification “STERILE”, if applicable;

g) a warning against the use of the device if the package’s sterile barrier is damaged;

h) a written and/or “Do not resterilize” symbol warning against re-sterilizing and/or reusing the device, if applicable;

i) reference to consult Instructions for Use for user information;

j) chemical nature of any storage medium in the unit container, with appropriate hazard warning.

4.5.2.2 Instructions for use (IFU)

The requirements of ISO 14630:2012, Clause 11, shall apply together with the following information to be included:

a) name or trade name of the device;

b) recommendations for storage; the actual modelled storage range determined to be acceptable for the packaged device, taking into consideration the absorbable properties of the implant or components thereof;

c) statement that the device can or cannot be re-sterilized, including the statements “STERILE”, “DO NOT RESTERILIZE” in prominent form, if applicable;

d) the statement “SINGLE USE ONLY” in prominent form;

e) description and/or list of the package contents;

f) available models and sizes applicable for intended clinical use;

g) identification and description of the absorbable device or components thereof;

h) location of the absorbable part of the device, if only a portion of the implant is absorbable;

i) a general description of the principle of degradation along with both the expected time frame for loss of mechanical function and absorption of the implant;

j) intended use/indications for use;

k) contraindications, warnings and precautions;

l) the potential for interaction of the absorbable material with other materials used in the handling, preparation and implantation of the implant, considering direct contact and the effect of procedural fluids;

m) potential adverse events, including known adverse events associated with implant (or portion thereof) degradation and/or *in vivo* absorption process;

n) recommended methods for the aseptic presentation and preparation of the implant considering the potential for interaction of the absorbable material with the environment or materials used;

o) recommended methods for preparation of the implantation site if applicable;

p) recommendations for visualization if applicable;

q) if the implant is metallic, electrically conductive, or contains metallic or electrically conductive components, MRI safety information shall be provided, including any potential impact that an accompanying radio frequency (RF)-induced temperature rise may have on the absorbable properties of the implant or components thereof. Provided information may also include a post-implantation time period after which safety MRI precautions are no longer relevant or needed;

r) date of or reference relating to the publication of the text, indicating if the text has been revised.

4.5.3 Sterilization

4.5.3.1 General

The sterilization requirements of ISO 14630 shall apply.

The entirety of the device and packaging shall be compatible with the chosen sterilization method. The following provides a list of typical sterilization methods and a brief description of their applicability to absorbable implants or components thereof.

4.5.3.2 Radiation sterilization

If devices are to be sterilized by gamma, electron beam or X-ray radiation sterilization, ISO 11137-1, -2, -3 shall apply, including the Part 1 provision that the product meet its performance specifications throughout its intended lifetime at its maximum acceptable dose. Radiation sterilization processes in polymers can generate free radicals and a potential for change in absorbable material properties that could impact product performance.

4.5.3.3 Ethylene oxide sterilization

If devices are to be sterilized by ethylene oxide, ISO 11135 shall apply, including the provision that the product meets its performance specifications at the most challenging parameters. Ethylene oxide sterilization processes involve exposure to heat and humidity parameters that may impact absorbable material properties that could impact product performance.

4.5.3.4 Steam sterilization

If devices are to be sterilized by steam, ISO 17665-1 shall apply. Steam may not be a viable sterilization option for hydrolysable polymers that are highly susceptible to uncontrollable damage under autoclave conditions.

4.5.3.5 Alternative sterilization

If devices are to be sterilized by use of any other sterilization method, such as dry heat sterilization, hydrogen peroxide sterilization, ozone or nitrogen dioxide sterilization, ISO 14937 shall apply.

4.6 Product shelf-life considerations

4.6.1 General information

Shelf-life is the amount of time that a packaged product can be expected to be stored under specified conditions and meet critical performance properties. Establishment of shelf-life should directly or indirectly assess the device's ability to meet its specified functional requirements upon its removal from its packaging after appropriate storage. For absorbable devices, storage conditions can be vitally important (e.g. temperature and humidity) and deserve careful consideration. A detailed understanding of implant susceptibility to degradation under expected storage conditions is paramount to a successful shelf-life program.

Establishment of product shelf-life shall be through evaluation of one or more appropriate implant performance tests conducted on the final product, with justification for the selection of tests provided. Refer to ASTM F2914 for guidance in selecting appropriate tests for the determination of shelf-life in endovascular devices. If different finished product manufacturing sites are used, generation of appropriate batch release/stability data including appropriate performance specifications to ensure the consistency and equivalency of the finished product across manufacturing sites should also be considered.

ISO/IEC Guide 51, ISO/IEC Guide 63, ISO 10993-1, and ISO 11135 (see Clause 2 and the Bibliography) provide guidance regarding shelf-life establishment. It is often unnecessary to assess every device attribute measured at time 0 (i.e. no aging) and after appropriate storage conditions to establish shelf-life. ASTM F2914 provides guidance for determination of the appropriate attributes for testing as part of establishment of shelf-life for endovascular devices. Accelerated aging might be appropriate to establish the shelf-life of an absorbable device in a timely manner. AAMI TIR17 contains guidance regarding accelerated aging programs and provides a brief discussion of aging theory. Also, ASTM F1980 provides guidance on accelerated aging parameters and discusses humidity. Absorbable device shelf-life establishment requires special consideration. ASTM F2902 provides guidance regarding shelf-life of absorbable polymeric implants.

