TECHNICAL SPECIFICATION

ISO/TS 17137

Third edition
2021-09

Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants

Implants cardiovasculaires et systèmes extracorporels — Implants cardiovasculaires absorbables

Reference number
ISO/TS 17137:2021(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).

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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 third edition cancels and replaces the second edition (ISO/TS 17137:2019), which has been technically revised.

The main changes compared to the previous edition are as follows:

— considerations have been added to multiple clauses regarding degradation-induced device fracture and the generation of absorbable particulate matter after mechanical attributes are lost;

— clauses about labelling and instructions for use (IFU) have been modified;

— Figure 2 has been modified to facilitate translation into multiple languages;

— standards with guidance for characterization of absorbable polymers and metals have been elaborated.

— additional guidance regarding animal and clinical study design, limitations, and assessment has been added.

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 either metabolism, assimilation, or excretion (elimination), or all. Such implants can be either surgically introduced or introduced through intervention 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 is intended to be a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants. This document is intended to also be 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, it can be useful to consider a number of other international standards that are given in the Bibliography.

Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants

1 Scope

This document establishes design evaluation requirements and recommendations 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 intended to supplement device-specific standards by providing guidelines specific for either absorbable implants or components, or both.

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 can 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.

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 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 11137-1, *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 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 14630:2012, *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/TS 37137-1, *Biological evaluation of absorbable medical devices — Part 1: General requirements*

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 https://www.electropedia.org/

3.1
absorb
absorption
<biomaterial> action of a non-endogenous (foreign) material or substance or its degradation products passing through or being assimilated by either cells or tissue, or both 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).

3.5
particulate
particle
particulate matter
mobile material (other than gas bubbles) that are either present on or arise from the presence or use of the device

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 either physical or mechanical, or both, 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 the 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) 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[39], with ASTM F3160[42] 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, the requirements of ISO 12417-1 should be addressed. Electrochemical potentials of differing metals (stents, guidewires, other accessory devices) can 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 (T_g) can 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, and the requirements of relevant device-specific standard (e.g. relevant parts of the ISO 25539 series) shall apply, with the following information to be supplied as part of the label(s):

a) identification of the device;

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

c) indication of storage conditions to avoid (i.e. conditions that can have an impact on performance of the absorbable device or components thereof).

4.5.2.2 Instructions for use (IFU)

The requirements of ISO 14630:2012, Clause 11, and the requirements of relevant device-specific standard (e.g. relevant parts of the ISO 25539 series) shall apply together with the following information to be included:

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

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

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

d) 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;

e) intended use or indications for use;

f) contraindications, warnings and precautions;

g) 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;

h) potential adverse events, including known adverse events associated with either implant (or portion thereof) degradation or in vivo absorption process, or both;

i) known device-specific adverse events with potential for increased occurrence due to absorbable material;

j) 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;

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

l) recommendations for visualization, if applicable;

m) if the implant is metallic, electrically conductive, or contains metallic or electrically conductive components, magnetic resonance imaging (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;

n) differences in methods of preparation and implantation of the device when compared to a non-absorbable device of the same type, if applicable;

o) differences in post-implant considerations for the device when compared to a non-absorbable device of the same type, if applicable.

NOTE These post-implant considerations include those during the implantation procedure (e.g. post-implant dilatation of an absorbable vascular stent) or following the implantation procedure (e.g. considerations during follow-up imaging).

p) 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, ISO 11137-2, ISO 11137-3 shall apply, including the provision (which can be found in ISO 11137-1) 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 can 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 can 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[40] 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 and 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 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[40] provides guidance for the determination of the appropriate attributes for testing as part of establishment of shelf-life for endovascular devices. Accelerated aging can be appropriate to establish the shelf-life of an absorbable device in a timely manner. AAMI TIR17[27] contains guidance regarding accelerated aging programs and provides a brief discussion of aging theory. Also, ASTM F1980[30] provides guidance on accelerated aging parameters and discusses humidity. Absorbable device shelf-life establishment requires special consideration. ASTM F2902[39] provides guidance regarding the shelf-life of absorbable polymeric implants.

4.6.2 Real-time aging

Shelf-life assessment of packaged and sterilized absorbable products should include real-time exposure to temperature and humidity challenge conditions that, at minimum, are reflective of the expected storage environment.

Guidance regarding transportation related risk management is provided in 4.7.2.

Real-time testing of the absorbable device's critical attributes under conditions analogous to actual storage conditions is the most definitive means for assessing the shelf-life of a packaged absorbable device. Multiple time points (e.g. 6, 12, and 24 months) are recommended to mitigate risk associated with a failure to meet the requirements at later time points.

4.6.3 Accelerated aging

Accelerated aging allows medical devices to be provided to health care professionals with specified shelf-life in a timely manner. However accelerated aging can lead to an inaccurate assessment of the shelf-life of a product, providing additional risk to the patient. Thus, when accelerated aging programs are designed, conservatism is recommended. Real-time aging studies should be conducted in addition to the accelerated aging studies to validate the shelf-life established by accelerated aging testing.

The testing plan to establish the shelf-life of an absorbable device using accelerated conditions should consider the mechanism of degradation of the implant. The rationale for the accelerated aging factors should be provided. Conservative aging factors should be chosen. AAMI TIR17[27] provides conservative accelerated aging factors. However, these conservative factors might not be appropriate for absorbable devices and should be used with caution.

Exposure to humidity, ultraviolet light, ozone, or other gases can also be used to establish the shelf-life of an absorbable device if the aging process of the materials can be shown to correlate with these environmental factors. It should be noted that aging can be further accelerated when multiple aging processes are involved. One should carefully define the combined effect of aging processes when establishing the test method for accelerated aging.

4.7 Risk management

4.7.1 General

The manufacturer shall define and implement a risk management system in accordance with ISO 14971. The entire system shall provide intended users the ability to safely and effectively perform all required preoperative, intra-operative, and post-operative procedural tasks and achieve all desired objectives.

This shall include all other tools and accessories that intended users will use to complete the procedure.

NOTE For guidance on how to determine and establish design attributes pertaining to the use of the system to conduct the implant procedure, see IEC 62366-1.[8]

4.7.2 Failure modes

There exist three major categories of failure modes. Examples of possible failure within each category specific to absorbable cardiovascular implants include the following:

— Design related: One or more implant design deficiencies (e.g. materials, dimensions, construction) can result in unintended functional failure (e.g. selection of an absorbable material that degrades prematurely). In addition, implant design should provide a safety margin adequate to provide appropriate temporal function in all indicated and reasonably anticipated clinical uses.

— Manufacturing related: Inappropriate manufacturing conditions (e.g. excess moisture), storage (e.g. defective packaging) and/or transport (e.g. excess thermal exposure) can potentially result in functional compromise or failure.

— Application or use related: Situations that can arise from unintended (abnormal) use errors (e.g. over-expansion resulting in excessive particulate generation or fracture at implantation) as described in IEC 62366-1[8] and/or from intended (correct) use errors (e.g. unable to deliver device past tortuous anatomy that was not excluded in the IFU).