TECHNICAL SPECIFICATION

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Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants

Implants cardiovasculaires et systèmes extracorporels — Implants cardiovasculaires absorbables

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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. www.iso.org/directives

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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

The committee responsible for this document is ISO/TC 150, *Implants for surgery*, sous-comité SC 2, *Cardiovascular implants and extracorporeal systems*.

The following definitions apply in understanding how to implement an ISO International Standard and other normative ISO deliverables (TS, PAS, IWA):

— “shall” indicates a requirement;

— “should” indicates a recommendation;

— “may” is used to indicate that something is permitted;

— “can” is used to indicate that something is possible, for example, that an organization or individual is able to do something.

3.3.1 of the ISO/IEC Directives, Part 2 (sixth edition, 2011) defines a requirement as an “expression in the content of a document conveying criteria to be fulfilled if compliance with the document is to be claimed and from which no deviation is permitted.”

3.3.2 of the ISO/IEC Directives, Part 2 (sixth edition, 2011) defines a recommendation as an “expression in the content of a document conveying that among several possibilities one is recommended as particularly suitable, without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action is deprecated but not prohibited.”

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 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 Technical Specification outlines requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization, packaging, and information supplied by the manufacturer. This Technical Specification should be considered as a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants. This Technical Specification 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.

This Technical Specification 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/TS 12417.

Only issues related to absorption combined with the cardiovascular implant are covered by this Technical Specification.

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 Technical Specification outlines design verification and validation considerations for absorbable cardiovascular implants.

NOTE Due to the variations in the design of implants covered by this Technical Specification 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 Technical Specification will be necessary.

For the purpose of this Technical Specification the terms "vessel and/or vascular space" refer to the entire circulatory system, including the heart and all vasculature.

This Technical Specification is applicable to implants in direct contact with the cardiovascular system, where the intended action is upon the circulatory system. This technical specification 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 Technical Specification 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 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/TS 12417.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

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

ISO 11137 (all parts), *Sterilization of health care products — Radiation*

ISO/TS 12417, *Cardiovascular implants and extracorporeal systems—Vascular device-drug combination products*

ISO 14155:2011, *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 14971:2007, *Medical devices — Application of risk management to medical devices*

ISO/TR 15499, *Biological evaluation of medical devices — Guidance on the conduct of biological evaluation within a risk management process*

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 25539-2:2008, *Cardiovascular implants — Endovascular devices — Part 2: Vascular stents*

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

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

IEC 62366, *Medical devices — Application of usability engineering to medical devices*

ASTM F2394-07(2013), *Standard Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System*

3 Terms and definitions

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

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

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

3.3
degrade (verb)
to physically, metabolically, and/or chemically decompose a material or substance

3.4
leachable (adjective)
substances that can be released from a medical device or material during clinical use

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

4 Implant considerations

4.1 Classification

A cardiovascular absorbable implant is a product that is considered to be a medical device that accomplishes its intended clinical use and performance over a defined time period. A cardiovascular absorbable implant accomplishes its intended clinical use and is then 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 products' ability to be metabolized, assimilated, and/or excreted (eliminated) over time.

An absorbable cardiovascular implant may also incorporate a medicinal substance. However, for the purposes of this Technical Specification, if the action of the medicinal substance is ancillary to a device's primary mode of action, the product is considered to be a surgical implant.

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) intended lifetime.

4.3 Intended clinical use

The intended clinical location shall be 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) other arterial or venous vessels to be specified.

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, a general guide for assessing absorbable polymeric implants can be found in ASTM F2902. 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 11607-1:2006 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.

For devices that are supplied sterile, the sterile barrier shall be maintained 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 at temperatures that approach or exceed the glass transition temperature of absorbable polymeric products might adversely affect the physical and chemical state of the implant. Therefore, storage conditions should be specified that limit the temperature range and time limit of implant exposure.

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):

NOTE Items with particular relevance to absorbable implants are italicised.

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 device or components thereof;

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) for implants supplied sterile, a warning against the use of the device if the package is damaged;

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

i) 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, if applicable:

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 there-of;

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, if applicable;

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 properties and *in vivo* 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 requirements of ISO 14630:2012, Clause 9, 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 Parts 1, 2 and 3 shall apply, including the Part 1 provision that the product meet its performance specifications throughout its intended lifetime at its maximum acceptable dose.

NOTE Radiation sterilization (of polymers) commonly results in a residual presence of free radicals and an increase in the rate of degradation.

4.5.3.3 Ethylene oxide sterilization

If devices are to be sterilized by ethylene oxide, ISO 11135-1 shall apply, including the provision that the product meet 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 in turn impact product performance specifications.

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 since hydrolysable polymers 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 Risk management

4.6.1 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 ANSI/AAMI HE74 and IEC 62366.

4.6.2 Failure modes

There exist three groups of failure modes. Examples of possible failure within each group 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 functional integrity in all clinical indications (e.g. force differences in the coronary vs tibial artery).

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/User Interface related: Unintended (abnormal) use errors (e.g. over-expansion resulting in excessive particulate/fragment generation at implantation) as described in IEC 62366. Intended

