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Cardiovascular implants — Endovascular devices —

Part 2: Vascular stents

Implants cardiovasculaires — Dispositifs endovasculaires —

Partie 2: Endoprothèses vasculaires

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Foreword

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

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 25539-2 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

ISO 25539 consists of the following parts, under the general title *Cardiovascular implants — Endovascular devices*:

— *Part 1: Endovascular prostheses*

— *Part 2: Vascular stents*

Introduction

This part of ISO 25539 has been prepared in order to provide minimum requirements for endovascular devices and the methods of test that will enable their evaluation. It is the second part of a proposed three-part standard. ISO 25539-1 addresses endovascular prostheses and ISO 25539-3 will address vena cava filters. ISO/TS 15539, from which this part of ISO 25539 is derived, serves as a rationale for the requirements of this document. The Technical Specification ISO/TS 15539 was developed by first identifying the design requirements for these devices and listing the potential device and clinical failure modes. Tests were then identified to address each of the failure modes. The requirements provided in this part of ISO 25539 are based on that assessment.

Cardiovascular implants — Endovascular devices —

Part 2: Vascular stents

1 Scope

1.1 This part of ISO 25539 specifies requirements for vascular stents, based upon current medical knowledge. With regard to safety, it gives requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization, packaging and information supplied by the manufacturer. It should be considered as a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants.

NOTE Due to the variations in the design of implants covered by this part of ISO 25539 and in some cases due to the relatively recent development of some of these implants (e.g. bioabsorbable stents, polymeric 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.

1.2 The scope of this part of ISO 25539 includes vascular stents used to treat vascular lesions or stenoses, or other vascular abnormalities. These devices might or might not incorporate surface modifications of the stent such as drug and/or other coatings. Stents covered with materials that significantly modify the permeability of the uncovered stent are within the scope of ISO 25539-1. The stent design might dictate the need to address functional requirements identified in both ISO 25539-1 and this part of ISO 25539.

1.3 Delivery systems are included in this part of ISO 25539 if they comprise an integral component of the deployment of the vascular stent.

1.4 Procedures and devices used prior to the introduction of the vascular stent, such as balloon angioplasty devices, are excluded from the scope of this part of ISO 25539.

1.5 Some pharmacological aspects of drug eluting stents are addressed in this part of ISO 25539, but this document is not comprehensive with respect to the pharmacological evaluation of drug eluting stents.

1.6 Degradation and other time-dependent aspects of bioabsorbable and polymeric stents and coatings are not addressed by this part of ISO 25539.

1.7 With the exception of sterilization, this part of ISO 25539 does not address requirements for the evaluation of animal tissue products.

2 Normative references

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

ISO 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 11137-1, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11607 (both parts), *Packaging for terminally sterilized medical devices*

ISO 14155 (both parts), *Clinical investigation of medical devices for human subjects*

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

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*

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*

3 Terms and definitions

For the purposes of this document, the terms and definitions in ISO 14630 and the following apply.

NOTE Bench and analytical tests are described in Annex B. Reportable clinical events are defined in Annex C.

3.1
balloon-assisted deployment
use of a balloon to facilitate the complete deployment (or expansion) of a self-expanding stent

3.2
balloon winging
cross-sectional shape of the balloon when deflated which can cause problems during withdrawal

NOTE Examples include stent migration, damage to host vessel or balloon, and inability to remove the balloon.

3.3
delivery system
system or mechanism used to deliver the stent to the targeted position and to deploy the stent

NOTE The delivery system is removed after stent placement. Examples of delivery systems include balloon catheters or mechanically activated systems.

3.4
determine
to quantitatively appraise or analyse

NOTE Also see **evaluate (3.8)**.

3.5
dogboning
dumbbell-shaped balloon observed during stent deployment when the unconstrained ends of the balloon expand beyond the dilated stent outer diameter

3.6
coating
organic or inorganic material, other than living cells, intentionally applied by a manufacturer to a substrate

NOTE This coating can be intended to be permanent or temporary, and can be applied to the external and/or internal surface.

3.7
drug content
amount of drug present on the surface(s) of a coating, as part of a coating or within the stent

3.8
evaluate
to qualitatively appraise or analyse

NOTE Also see **determine (3.4)**.

3.9
lumen reduction
reduction of diameter or cross sectional area as observed by imaging

3.10
reportable clinical events
complications, failures or device-related observations, including all adverse events and adverse device effects, that might be observed with clinical use of the stent system

NOTE Examples are listed in Annex C. These events might not have clinical significance and might not be attributable to the device.

3.11
stent configuration
stent shape (e.g. cylindrical, tapered, flared, coiled, segmented, bifurcated)

3.12
stent outer surface area
contact area between the stent and the vessel

3.13
stent-free surface area
percentage of surface area of cylinder formed by the implant frame, which is not covered by implant material

3.14
stent system
vascular stent and its delivery system or a vascular stent mounted on the delivery balloon as specified in the instructions for use (IFU)

3.15
vascular stent
stent
implant
transluminally placed balloon-expandable or self-expanding implant, which is used to treat vascular lesions by providing a mechanical support after deployment to maintain or restore vessel integrity

NOTE 1 Stents can or cannot incorporate surface modifications of the stent such as drug and/or other coatings.

NOTE 2 The following stent types are within the Scope of this part of ISO 25539.

3.15.1
articulated stent
stent constructed of segments with distinct connections

3.15.2
bare stent
stent without a coating or covering

NOTE Bare stents can be constructed of single or multiple materials.

3.15.3
bioabsorbable stent
stent that is designed to be a temporary structure without requiring explantation

3.15.4
balloon-expandable stent
stent where the diameter is increased from its pre-deployed size to its post-deployed size with the aid of a balloon catheter

3.15.5
coated stent
stent with a surface layer of an additional material(s) that does not provide significant (e.g. more than 5 %) structural support or appreciably reduce the permeability or stent-free surface area of the bare stent

3.15.6
composite stent
stent consisting of more than one material or material compound that provides significant (e.g. more than 5 %) overall structural support upon deployment

3.15.7
covered stent
stent covered with an additional material(s) that appreciably reduces the permeability and/or eliminates the stent-free surface area of the bare stent

NOTE Covered stents are within the Scope of ISO 25539-1. The stent design might dictate the need to address functional requirements identified in both parts 1 and 2 of ISO 25539.

3.15.8
drug eluting stent
DES
stent that delivers a drug(s) over time

3.15.9
self-expanding stent
stent where the diameter increases from its pre-deployed size to its post-deployed size when released from the delivery mechanism in absence of balloon inflation or other mechanical assistance

NOTE Self-expanding stents are within the scope of ISO 25539-1. The stent design might dictate the need to address functional requirements identified in both parts 1 and 2 of ISO 25539.

4 General requirements

4.1 Classification

A stent shall be designated by its configuration (see 3.11), type (see 3.15), materials of construction, and any surface modifications, coatings, and/or drugs.

4.2 Size

The size of a stent shall be designated by the following characteristics:

a) external diameter;

   1) self-expanding:

      i) unconstrained external diameter of the device, expressed in millimetres;

      ii) intended vessel lumen diameter range, expressed in millimetres;

   2) balloon expandable: range of intended expanded internal diameters;

b) minimum and maximum usable length, expressed in millimetres or centimetres.

4.3 Intended clinical use designation

The intended clinical use shall be designated by one or more of the following:

a) abdominal aorta;

b) arterio-venous shunt for vascular access;

c) carotid;

d) coronary;

e) femoral;

f) iliac;

g) popliteal;

h) renal;

i) thoracic aorta;

j) thoraco-abdominal aorta;

k) tibial;

l) other arterial vessels to be specified;

m) other venous vessels to be specified.

5 Intended performance

The requirements for intended performance of ISO 14630 shall apply.

6 Design attributes

6.1 General

The requirements for design attributes of ISO 14630 apply. In addition, the following shall be taken into account:

a) oxidation-potential, the possibility of crevice corrosion, passivation over the relevant parts;

b) fretting, galvanic and pitting corrosion;

c) interface between implant and body:

   1) fixation hooks if present;

   2) relative movement between stent and tissue;

   3) forces exerted by the stent on the surrounding tissue;

   4) forces required to deform the stent if the deformation is permanent;

d) expected ingrowth, penetration, perforation, tilting and migration; introduction and delivery systems.

NOTE These additional items are adapted from Clause 5 of EN 12006-3:1998[15].

The design attributes for vascular stents (with or without delivery system) are listed in Table A.2 with reference to the test sections for the evaluation of the design (Clause 8). It is recognised that not all tests identified in a category will be necessary or practical for any given stent and/or delivery system. The tests considered and the rationale for selection and/or waiving of tests shall be recorded.

6.2 Delivery system and stent system

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

a) the ability of the system to permit consistent, accurate and safe access to the intended location;

b) the ability of the system to permit consistent, accurate and safe deployment of the stent;

c) the ability of the system to permit consistent and safe withdrawal of the delivery system;

d) the compliance of the system with the requirements of ISO 10993-1 and appropriate other parts of the ISO 10993 series of International Standards (biocompatibility);

e) the ability of the system to minimise blood loss (haemostasis);

f) the visibility of the system under fluoroscopy or other technologies.

6.3 Implant

6.3.1 Stent

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

a) the ability of the stent to be consistently, accurately and safely deployed;

b) the ability of the stent to ensure effective fixation and apposition in the intended location within the vasculature;

c) the ability of the stent to maintain adequate integrity;

d) the consistency of the stent dimensions and its design for compatibility for use in specified vessel diameters;

e) the ability of the stent to maintain adequate blood flow through the lumen (patency);

f) the compatibility of the stent with exposure to magnetic resonance imaging (MRI) fields;

g) the compliance of the stent with the requirements of ISO 10993-1 and appropriate other parts of the ISO 10993 series of International Standards (biocompatibility);

h) the visibility of the stent under fluoroscopy or other technologies.

6.3.2 Coating

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

a) the ability of the coating to maintain adequate integrity over time according to design specifications (e.g. freedom from significant delamination, flaps and bare spots);

b) the appropriate interaction between the coating and the stent (e.g. coating influenced corrosion of the substrate);

c) the ability of the coating to maintain adequate resistance to unintended particulate generation;

d) the conformance of the coating dimensions and other coating parameters (e.g. porosity, density, distribution) to the design requirements;

e) the effect of MRI on the coating of a coated stent (e.g. heating).

6.3.3 Drug

The design attributes to meet the intended performance of the stent if the coating is a drug or if a drug is incorporated into the stent or coating shall additionally take into account at least the following:

a) the ability to reproducibly apply the desired drug type and amount to the stent;

b) the ability to release the desired amount of drug over the specified amount of time;

c) the conformance of the residual drug quantity to design specifications;

d) the freedom of the drug(s) from deleterious impurity and degradant levels at manufacture and with storage;

e) the appropriate interaction between the drug and the coating and/or the stent to which the drug is applied;

f) the effect of MRI on the drug of a drug-eluting stent (e.g. heating).

7 Materials

The requirements for materials of ISO 14630 apply. Additional testing specific to certain materials (e.g. metals, polymers, drugs) shall be performed to determine the appropriateness of the material for use in the design. For example, Nitinol materials dependent on shape memory properties shall be subjected to testing in order to assess transformation properties. In addition, for drug-eluting stents 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.

8 Design evaluation

8.1 General

The requirements for design evaluation of ISO 14630 apply. A risk assessment shall be carried out and the requirements of ISO 14971 shall apply.

Justification shall be provided for the properties not measured.

NOTE 1 All testing might not be appropriate for all stent system designs.

It is impossible to take into consideration all future and emerging technologies. The stent systems based on these new technologies will need to be evaluated following the basic requirements of this part of ISO 25539. Testing beyond the scope of this part of ISO 25539 might also be necessary in order to characterize these stent systems. Consideration shall be given to the failure modes of the stent systems and their effects on the performance of the implant in identifying the appropriate testing.

Whenever changes are made in materials, construction, configuration, application or processing methods, an appropriate analysis of the potential impact of the change on the failure modes and performance of the stent system shall be performed. Appropriate testing shall be conducted as deemed necessary.

The use of a control device for comparison should be considered in the evaluation of certain design attributes.

If overlapping of stents can be anticipated in clinical use (e.g. superficial femoral artery, coronary), integrity of the stent under study in overlapping configurations should be evaluated, unless justification can be provided for testing of individual stents. If overlapping with a different device is specifically indicated, testing should include evaluation with the indicated device.

Testing to establish the labelled shelf-life shall be conducted by repeating appropriate tests. Justification for the selection of tests shall be provided. For drug eluting stents, real time and accelerated testing conditions should be used to define drug attributes for product shelf life.

NOTE 2 Additional guidance for stability testing of drug products can be found in ICH[1)] Q1A[35] (R2), ICH Q1B[36], and ICH Q1D[37].

8.2 Sampling

A sampling plan shall be utilized which will ensure that adequate representation of the data has been obtained for each parameter measured. The design characteristics of the stent (including any drugs and/or coatings), delivery system and stent system shall be verified to be representative of the devices to be released for distribution, including all sizes, configurations and components.

The sampling shall fully represent the range of device designs and might not necessarily require the testing of each size. The stent sizes selected for testing shall represent the worst case combination(s) of diameter and length for each test. A rationale shall be provided for sample selection. It might be necessary to conduct an assessment to identify the size(s) of the device with the greatest potential for failure.

Sampling shall ensure adequate representation of the expected variability in the manufacture of devices.

For those tests with specified confidence and reliability parameters, the sample size shall have a statistical basis. For all tests, the number of samples shall be justified.

1) International Conference on Harmonisation guidelines.

8.3 Conditioning of test samples

All samples shall be subjected to sterilization, including multiple sterilizations, if appropriate, unless justification is provided for use of nonsterilized products.

Samples shall be subjected to conditions that are normally encountered which might affect the test results. Conditioning might include loading the stent on or inside the delivery catheter, preconditioning of the stent system as recommended in the instructions for use (IFU), single or multiple passes through an anatomical model, and deployment of the stent.

A simulated physiological environment (e.g. a temperature-controlled water bath) shall be used when appropriate.

8.4 Reporting

For the purposes of this part of ISO 25539, reporting relates to requests from a national regulatory authority or from a body responsible for assessing conformity.

The test report for the preclinical *in vitro* testing shall include an executive summary of all testing. This summary should include identification of tests, with the rationale for the omission of any tests identified in Annex B or the selection of alternative tests. The information provided in each test report should be based upon a prospectively defined test protocol.

A summary of results, with acceptance criteria and any potential clinical significance of the results, should be included and can be in tabular form. Consideration shall be given to the anatomical, physiological, and morphological conditions of the intended use in establishing the acceptance criteria. Justification and clinical applicability of acceptance criteria for each test shall be provided. A table of contents should be provided and pages should be numbered sequentially.

Individual test reports should include the following information:

a) purpose: state the purpose of the test as it corresponds to this part of ISO 25539;

b) materials: list all materials (e.g. test articles with lot/serial numbers or other appropriate means of traceability, equipment) used in performing the test, using figures and diagrams as appropriate;

c) sampling: state the sampling plan, including the basis for and the number of samples tested; selection of test article shall be justified (e.g. sizes, conditioning);

d) acceptance criteria: state the acceptance criteria for the test results;

e) test method: describe in detail the method used to perform the test, including any prospectively defined inspection procedures, and provide a justification for critical test parameters;

f) protocol deviations: describe any deviations and their potential significance on the interpretation of the results;

g) expression of results: describe testing results expressed in units as indicated in the test method;

h) conclusion: state conclusions, based on comparing results to acceptance criteria, including any potential clinical significance of these results.