



BSI Standards Publication

Cardiovascular implants – Endovascular devices

Part 2: Vascular stents

National foreword

This British Standard is the UK implementation of EN ISO 25539-2:2020. It is identical to ISO 25539-2:2020. It supersedes BS EN ISO 25539-2:2012, which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/150/2, Cardiovascular implants.

A list of organizations represented on this committee can be obtained on request to its committee manager.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

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(ISO 25539-2:2020)

Kardiovaskuläre Implantate - Endovaskuläre
Implantate - Teil 2: Gefäßstents (ISO 25539-2:2020)

This European Standard was approved by CEN on 20 August 2020.

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European foreword

This document (EN ISO 25539-2:2020) has been prepared by Technical Committee ISO/TC 150 "Implants for surgery" in collaboration with Technical Committee CEN/TC 285 "Non-active surgical implants" the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by March 2021, and conflicting national standards shall be withdrawn at the latest by March 2021.

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

This document supersedes EN ISO 25539-2:2012.

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Endorsement notice

The text of ISO 25539-2:2020 has been approved by CEN as EN ISO 25539-2:2020 without any modification.

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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 (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*, 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 third edition cancels and replaces the second edition (ISO 25539-2:2012), which has been technically revised.

The main changes compared to the previous edition are updates to the testing and clinical use of vascular stents as well as improved consistency in nomenclature and reporting requirements.

A list of all parts in the ISO 25539 series can be found on the ISO website.

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

This document was prepared to provide minimum requirements for vascular stents. The rationale for the requirements for bench tests and analyses to assess device performance, guidance on the identification of appropriate testing to evaluate a specific device design, and guidance for developing test methods are provided in informative annexes. Further clarification of terminology is provided in additional informative annexes.

This document has been updated to reflect current knowledge regarding the testing and clinical use of vascular stents, reflected in modifications to the requirements in the main body and in the guidance for developing test methods in [Annex D](#). In addition, revisions have been made to improve consistency in nomenclature and reporting and to enhance the utility of this document.

Requirements particular to the evaluation of specific characteristics of stents (e.g. coatings, drug-elution, absorption) are incorporated by reference to appropriate standards. However, not all tests listed in the referenced standards are applicable to vascular stents. Only tests that address the design attributes specified in [Clause 6](#) are required for compliance to this document.

This revised document introduces methodology to identify appropriate testing and analyses for a specific vascular stent, designated as the device evaluation strategy. The requirement regarding the device evaluation strategy is in the main body. [Annex A](#) provides guidance for developing a focused device evaluation strategy table that is specific to the unique characteristics of a device, device design modifications, or changes in intended use. [Annex A](#) also provides guidance for the development of a comprehensive device evaluation strategy table that may be used when it is not sufficient to focus only on the unique characteristics or changes.

NOTE ISO 25539-1:2017 includes tables that can be used to justify the testing needed for device design modifications and changes in intended use in [Annex A](#). In this document, this concept is called a focused device evaluation strategy table and can be applied to a new device as well as device design modifications or changes in the intended use.

The other significant modifications in the requirements include the addition of non-radial durability testing, with guidance on the selection of appropriate testing, and specific requirements for testing to evaluate patency-related characteristics. Guidance for the development of appropriate tests to meet these requirements is included in [Annex D](#).

The guidance on the development of methods to address the requirement for evaluating fatigue and durability through computational analyses has been modified significantly to include recommendations regarding verification of the solution and validation of the computational model, as well as reporting. The guidance on the model development for simulated use has also been significantly revised to improve the clinical relevance of this testing.

The specific requirements to evaluate pushability, flexibility, torquability, trackability, and deployment accuracy of a stent system have been removed and incorporated within the simulated use evaluation requirement to better reflect how these attributes are evaluated. Similarly, the requirement to evaluate tubing tensile strength has been removed and incorporated within the evaluation of tensile bond strength.

In addition to modifications to specific design evaluation requirements, guidance has been provided regarding the assessment of the acceptability of test results. When the requirement is to quantitatively appraise or analyse a parameter, test results generally may be compared to a quantitative value (i.e. acceptance criteria). For characterization tests it is appropriate to provide an explanation of the relevance of the results. Additionally, some testing may include comparison to test data or existing data from a previously evaluated device.

For design evaluation, requirements regarding sampling, conditioning of test samples, and reporting have been incorporated in the main body. Guidance on these elements of testing and documentation were previously only included in [Annex D](#).

The revisions to the annexes to this document are as follows:

Annex of ISO 25539-2:2012	Revision
Annex A — Attributes of endovascular devices — Vascular stents — Technical and clinical considerations	Annex A now includes the relationship between testing requirements, device attributes, and potential failure modes and guidance for the creation of a device evaluation strategy.
Annex B — Bench and analytical tests	The list of tests is included in Table D.1. Annex B now includes a description of potential clinical effects of failure. Effects of failure for stents used with endovascular prostheses are included.
Annex C — Definitions of reportable clinical events	The term “reportable” clinical events is no longer used in this document. Annex C now includes a description of potential device effects of failure. Effects of failure for stents used with endovascular prostheses are included.
Annex D — Test methods	This edition incorporates the sample equations as a supplement to the radial fatigue durability test from ISO 25539-2:2012, Annex E in Annex D .
Annex E — Supplement to the radial fatigue and durability test analytical approach	There is no longer an Annex E as the sample equations as a supplement to the fatigue durability test have been incorporated in Annex D .

It is recognized by this ISO committee that many stent systems have been shown to be safe and effective in clinical use. This update is not intended to require additional evaluation of these devices to remain in compliance with this document as the testing would not provide useful information regarding the expected clinical performance of the device. Manufacturers may rely on historical data gathered under the guidance of the previous edition of ISO 25539-2. Similarly, for device modifications or changes in intended clinical use, this update is not intended to require additional evaluation of any aspects of the device that are not expected to change clinical performance.

NOTE The relationship between testing requirements, device attributes, and potential failure modes is provided in [Clause A.1](#). [Clause A.1](#) also provides general information regarding device evaluation strategies. [Tables A.2](#) and [A.3](#) provide the rationale for the requirements specified in this document for bench tests and analyses to assess device performance. An explanation of the table headings for [A.2](#) and [A.3](#) are described in [Table A.1](#).

Guidance for the creation of a device-specific evaluation strategy is provided in [Clause A.2](#). Two approaches to create a device-specific evaluation strategy are provided: 1) focused device evaluation strategy in [A.2.1](#); and 2) comprehensive device evaluation strategy in [A.2.2](#).

[Annex B](#) provides a description of the potential clinical effects of failure identified in [Annex A](#).

[Annex C](#) provides a description of the potential device effects of failure identified in [Annex A](#).

Additional descriptions of clinical and device effects of failure are included in [Annexes B](#) and [C](#), respectively.

[Annex D](#) provides information to consider in developing appropriate bench test and analytical methods.

Cardiovascular implants — Endovascular devices —

Part 2: Vascular stents

1 Scope

This document specifies requirements for the evaluation of stent systems (vascular stents and delivery systems) and requirements with respect to nomenclature, design attributes and information supplied by the manufacturer, based upon current medical knowledge. Guidance for the development of *in vitro* test methods is included in [Annex D](#). This document is supplemental to ISO 14630, which specifies general requirements for the performance of non-active surgical implants.

NOTE 1 Due to the variations in the design of implants covered by this document, and in some cases due to the emergence of novel types of such implants, 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.

This document is applicable to vascular stents and vascular scaffolds (e.g. absorbable vascular scaffolds) used to treat vascular stenoses or other vascular abnormalities or pathologies. Some of the requirements are specific to endovascular treatment of arterial stenoses. Although uses of stent systems other than treatment of arterial stenoses (e.g. venous stenting) are within the scope of this document, comprehensive requirements and testing are not described for these uses. Similarly, specific stent configurations (e.g. bifurcation stents) are within the scope, but comprehensive requirements and testing are not described for these devices.

Stents used in combination with an endovascular prosthesis to complete the treatment of a lesion, including bridging stents (e.g. stents placed in the renal arteries after deployment of a fenestrated endovascular prosthesis), are within the scope of this document, but test methods are not described for the combination. ISO 25539-1 also provides information relevant to the preclinical *in vivo* and clinical evaluations of such stents.

Vascular stents that have surface modifications, such as drug and/or other coatings, are within the scope of this document. Stents covered with materials that significantly modify the permeability of the uncovered stent (e.g. by covering the stent-free-surface area) are within the scope of ISO 25539-1. The stent design or intended use might dictate the need to address functional requirements identified in both ISO 25539-1 and this document (e.g. stents used in combination with endovascular prostheses, stents used to treat aortic aneurysms).

Balloons integral to the stent system are within the scope of this document. This document provides requirements beyond the requirements of ISO 10555-4, which are specific to the use of balloons with vascular stents.

This document is not applicable to procedures and devices used prior to the introduction of the vascular stent, such as balloon angioplasty devices.

Tacking devices intended to spot treat post-angioplasty dissections, coil supporting devices, and flow diverters are within the scope of this document, but comprehensive requirements and testing are not described for these devices.

Although drug-eluting stents are within the scope of this document, this document is not comprehensive with respect to the drug-eluting properties of these devices.

NOTE 2 Vascular device-drug combination products are within the scope of ISO 12417-1.

Although absorbable stents and stents with absorbable coatings are within the scope of this document, this document is not comprehensive with respect to the absorbable properties of these devices.

NOTE 3 Absorbable implants are within the scope of ISO/TS 17137.

Although coated stents and coated stent systems are within the scope of this document, this document is not comprehensive with respect to coatings.

NOTE 4 Some coating properties are within the scope of ISO 17327-1.

This document does not address the requirements for, and the evaluation of, viable tissues and non-viable biologic materials used in the construction of vascular stents.

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 (all parts), *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

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 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

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 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*

ASTM F2503, *Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14630 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**adverse event**

unfavorable change in health that occurs in a subject who participates in a study while receiving the treatment or within a specified time after receiving treatment

Note 1 to entry: For the purpose of this document, clinical effects of failure are a subset of adverse events and are described separately.

Note 2 to entry: Adverse events are categorized by the system affected (e.g. cardiac, vascular, respiratory, neurological, renal, gastro-intestinal) and the severity of the event.

3.2**post-dilation**

use of a balloon to facilitate the complete deployment (or expansion) of a *self-expanding stent* ([3.22.9](#))

3.3**bridging stent**

vascular stent used in combination with an endovascular prosthesis to complete the treatment of a lesion

Note 1 to entry: See [3.22](#) for vascular stent.

3.4**clinical effect of failure**

specific clinical observations potentially associated with device failures

Note 1 to entry: Clinical effects of failure are described in [Annex B](#).

3.5**coating**

additional layer of organic or inorganic material, other than living cells, on the surface of a substrate that modifies its surface properties

Note 1 to entry: This coating can be intended to be permanent or temporary and can be applied to the external and/or internal surface.

3.5.1**absorbable coating**

coating ([3.5](#)) that is intended to be absorbed

Note 1 to entry: Drugs are excluded from this definition of absorbable coatings.

3.6**delivery system**

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

Note 1 to entry: The delivery system is removed after stent placement. Examples of delivery systems include balloon catheters or mechanically activated systems.

3.7**determine**

appraise or analyse quantitatively

Note 1 to entry: Also see *evaluate* ([3.14](#)).

3.8**device effects of failure**

consequence to the device potentially associated with device failures

Note 1 to entry: Device effects of failure are described in [Annex C](#).

3.9

device evaluation strategy

rationale for the testing selected for a specific stent system, based on the requirements of the device design and potential failure modes

3.10

comprehensive device evaluation strategy table

optional communication tool to present the device evaluation strategy for a specific stent system that addresses all attributes and *failure modes* ([3.15](#))

3.11

focused device evaluation strategy table

optional communication tool to present the device evaluation strategy for a specific stent system that focuses on the unique characteristics of the device design or procedure and unique aspects of the intended use

3.12

dogboning

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

3.13

drug

active pharmaceutical ingredient [pharmacologically active (drug or medicinal) substance used as a raw material, which is coated on, bound to, or incorporated into the device to achieve an ancillary device function (e.g. minimizing vascular restenosis)] in its final form for administration to the patient (e.g. tablet, solution, spray), that is intended to prevent, diagnose, or treat disease and that achieves its principal intended action in or on the body by pharmacological, immunological, or metabolic means

3.14

evaluate

qualitatively appraise or analyse

Note 1 to entry: Also see *determine* ([3.7](#)).

3.15

failure mode

difficulty or failure of the stent system that can be encountered (hazards) in preclinical *in vivo* or clinical use of a vascular stent and could result in consequences (harm) to the subject

3.16

nominal diameter

primary labelled diameter of the stent

3.17

rated burst pressure

RBP

pressure at which a balloon would not be expected to burst based on appropriate confidence and reliability

3.18

stent configuration

stent shape and geometry

Note 1 to entry: Examples include cylindrical, tapered, flared, coiled, segmented, bifurcated, articulated, closed cell, open cell.

3.19**stent outer surface area**

maximum contact area between the stent and the vessel

Note 1 to entry: Although the entire stent may not contact the vessel wall depending on the conformance to the vessel wall and the intended clinical use (e.g. for treatment of aneurysms), the stent outer surface area would include the maximum potential area along the entire length of the stent.

3.20**stent-free surface area**

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

3.21**stent system**

vascular stent and its *delivery system* (3.6)

Note 1 to entry: If a stent is to be mounted on a delivery balloon, as specified in the instructions for use (IFU), the balloon catheter is not considered part of the stent system with respect to the design requirements and evaluation specified in this document, with the exception of the simulated use, *in vivo* animal, and clinical study requirements. The balloon catheter would be part of the stent system for testing that evaluates the stent only where the stent system is needed to conduct the testing.

3.22**vascular stent****vascular scaffold****stent****implant**

transluminally placed balloon-expandable or self-expanding implant intended to maintain or restore vessel patency or function

Note 1 to entry: Stents can have surface modifications, such as drug and/or other coatings.

Note 2 to entry: The requirements of this document include vascular stents and vascular scaffolds (e.g. absorbable vascular scaffolds) and both are covered by the term stent for simplicity.

Note 3 to entry: The following stent types are within the scope of this document.

3.22.1**absorbable stent**

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

3.22.2**articulated stent**

stent constructed of segments with distinct connections

3.22.3**balloon-expandable stent**

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

3.22.4**bare stent**

stent without a coating or covering

Note 1 to entry: Bare stents can be constructed of a single or multiple materials.

Note 2 to entry: Bare stents can contain a metal oxide layer.

3.22.5

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 of the bare stent [e.g. by covering the *stent-free surface area* (3.20)]

Note 1 to entry: Stents containing only a metal oxide layer are not considered a coated stent for the purposes of this document.

3.22.6

covered stent

stent covered with an additional material(s) that appreciably reduces permeability of the bare stent [e.g. by covering the *stent-free surface area* (3.20)]

Note 1 to entry: Covered stents 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 document.

3.22.7

drug-containing stent

stent that has a drug coating that is not intended to release the drug

Note 1 to entry: For the purposes of this document, drug-eluting refers to both drug-eluting and drug-containing stents, unless otherwise noted.

3.22.8

drug-eluting stent

DES

stent that releases a drug

3.22.9

self-expanding stent

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

4 General requirements for stent systems

4.1 General

The following requirements shall apply to all stent systems.

4.2 Type of stent

The type of stent shall be designated by balloon-expandable, self-expanding, or other.

4.3 Materials of construction for stent system

Materials of the stent system (e.g. wire, imaging markers, coatings, drugs) shall be described by their generic or chemical names.

4.4 Configuration and size designation for stents and stent systems

The configuration of a stent shall be designated by its shape and geometry (e.g. cylindrical, tapered, flared, coiled, segmented, bifurcated, articulated, closed cell, open cell).

The size of the stent system shall be designated by the outer diameter of the stent system and the appropriate lengths.

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

- self-expanding:
 - unconstrained outer diameter of the stent, expressed in millimetres;
 - intended vessel lumen diameter range, expressed in millimetres;
 - usable length, expressed in millimetres or centimetres.
- balloon-expandable:
 - pressure to achieve nominal diameter
 - range of intended inner stent diameters, expressed in millimetres, and associated pressures;
 - intended vessel lumen diameter range, expressed in millimetres;
 - usable length, expressed in millimetres or centimetres.

4.5 Intended clinical use designation

Anatomic limitations (e.g. vessel diameter ranges, lesion lengths) and indicated vessel or graft type (e.g. artery, vein, synthetic vascular graft, saphenous vein graft, AV access graft) shall be specified.

For vascular stents intended to be used in combination with endovascular prostheses, the intended clinical use shall be designated by the intended implant site(s), the type of endovascular prosthesis it may be used with (e.g. aortic fenestrated, aortic branched, aorto-iliac bifurcated), and the purpose of the use of the stent, such as:

- a) bridging between the endovascular prosthesis and a branch artery;
- b) smoothing the transition between the endovascular prosthesis and a blood vessel;
- c) improving the endovascular graft conformance to the vessel wall;
- d) preventing migration of an endovascular prosthesis.

For all other stents, the intended clinical use shall be designated by arterial, venous, or arterio-venous, the disease state or lesion type to be treated (e.g. *de novo* stenosis, restenosis, in-stent restenosis, dissection, external compression, coarctation) and the intended implant site, such as:

- arterial:
 - e) carotid;
 - f) coronary;
 - g) aortic;
 - h) renal;
 - i) iliac;
 - j) superficial femoral;
 - k) proximal popliteal;
 - l) popliteal;
 - m) other arteries to be specified;
- venous:

- n) inferior vena cava;
- o) ilio-femoral;
- p) other veins to be specified;
- arterio-venous: shunts for vascular access.

4.6 Balloon designation

Balloons integral to the stent system shall be designated by the nominal diameter, diameter(s) as a function of the inflation pressure(s), the maximum recommended inflation pressure, and the rated burst pressure (RBP).

NOTE The maximum recommended inflation pressure can be less than or the same as the rated burst pressure.

5 Intended performance

The requirements for intended performance specified in ISO 14630:2012, Clause 4, shall apply.

6 Design attributes

6.1 General

The requirements for design attributes in [6.2](#) to [6.4](#) below, and of ISO 14630:2012, Clause 5, apply. The requirements for the design attributes in [6.5](#) to [6.8](#) apply as relevant to the device design (e.g. [6.5](#) applies if the delivery system or stent is coated, [6.6](#) applies if the stent is coated, [6.7](#) applies if the stents is absorbable or has an absorbable coating, [6.8](#) applies if the stent is drug-eluting).

6.2 Stent system

In addition to the requirements ISO 14630:2012, Clause 5, the design attributes of the stent system shall at least take into account the following:

- a) ability to consistently, accurately and safely access the intended location;
- b) ability to consistently, accurately and safely deploy the stent;
- c) ability to consistently and safely withdraw the delivery system;
- d) ability to minimize blood loss (haemostasis).

6.3 Stent

In addition to the general requirements, the design attributes of the stent shall at least take into account the following:

- a) ability of the stent to be consistently, accurately and safely deployed;
- b) ability of the stent to maintain position and apposition in the intended location within the vasculature, graft, or endovascular prosthesis, as per the intended clinical use;
- c) ability of the stent to maintain adequate integrity;
- d) appropriate interactions between overlapping stents, if applicable;
- e) for stents used in combination with endovascular prostheses, appropriate interactions between the stent and endovascular prosthesis;

- f) compatibility of the stent dimensions for use in specified vessel, graft, or endovascular prosthesis diameters;
- g) ability of the stent to maintain adequate blood flow through the lumen (patency);
- h) ability to safely use magnetic resonance imaging (MRI) on a patient with an implanted stent.

6.4 Stent system and stent

In addition to the general requirements, the design attributes of the stent system and stent shall at least take into account the following:

- a) visibility of the stent system, delivery system, and stent under fluoroscopy or other technologies;
- b) compliance of the delivery system and stent with the requirements of ISO 10993-1 and other appropriate parts of the ISO 10993 series;
- c) sterility of the stent system and stent;
- d) ability of the stent and stent system to maintain adequate resistance to unintended particulate generation;
- e) ability of the stent and stent system to meet specifications under conditions of transit and storage.

6.5 Coating on delivery system or stent

The design attributes of a coating on a delivery system or stent shall at least take into account the following:

- a) ability of the coating to maintain adequate integrity according to design specifications (e.g. freedom from significant delamination, flaps and bare spots);
- b) ability of the coating to maintain adequate resistance to unintended particulate generation;
- c) conformance of the coating dimensions, functional requirements (e.g. lubricity), and other coating parameters (e.g. porosity, density, distribution) to the design requirements.

6.6 Coating on stent

A coating on a stent shall at least take into account the following:

- a) appropriate interaction between a stent coating and the stent (e.g. freedom from coating-influenced damage to the substrate);
- b) ability to safely use MRI on a patient with a coated stent without negatively affecting the coating-related attributes of the stent (e.g. associated with heating).

6.7 Absorbable stent or coating

The design attributes of an absorbable stent or a stent containing an absorbable coating shall at least take into account the following:

- a) ability to degrade or absorb as designed over time;
- b) appropriate mechanical properties over time;
- c) ability of the absorbable stent or absorbable coating to maintain adequate resistance to unintended particulate generation over time;
- d) potential biological effects of degradants;

- e) ability to safely use MRI on a patient with an absorbable stent or stent with absorbable coating without negatively affecting the absorbable properties of the stent (e.g. associated with heating).

6.8 Drug-eluting stent

A drug-eluting stent shall at least take into account the following:

- a) ability of the stent to consistently contain the desired type and amount of drug;
- b) ability to release the desired amount of drug over the specified amount of time for drug-eluting stents and not for drug-containing stents;
- c) conformance of the residual drug quantity to design specifications for drug-eluting stents and not for drug-containing stents;
- d) freedom of the drug(s) from deleterious impurity and degradant levels at manufacture and with storage;
- e) appropriate interaction between the drug and the coating and/or the stent to which the drug is applied;
- f) potential non-target drug effects;
- g) ability to safely use MRI on a patient with a drug-eluting stent without negatively affecting the drug-related attributes of the stent (e.g. associated with heating).

7 Materials

The requirements for materials of ISO 14630:2012, Clause 6, apply. Additional testing specific to certain materials (e.g. metals, polymers, drugs) should be performed to determine the appropriateness of the material for use in the design. For example, nitinol materials dependent on shape-memory properties should be subjected to testing in order to assess transformation properties; electro-chemical potentials of differing metals might require additional testing.

8 Design evaluation

8.1 General

The requirements for design evaluation of ISO 14630:2012, Clause 7, apply. A risk analysis shall be carried out in accordance with the requirements of ISO 14971.

The requirements and testing described in ISO 10555-1 may apply to the design evaluation of a delivery system.

The device design concept shall be considered in the selection of appropriate tests and associated test methods. The device design concept includes the:

- device description (e.g. physical description, materials of construction), what the device key design features are intended to do, and how the key design features accomplish the intended objective;
- intended clinical use (see [4.4](#));
- device implantation procedures;
- conditions of use/intended *in vivo* environment;
- minimum design life of the device.

A device evaluation strategy shall be created. A device evaluation strategy provides the rationale for the testing selected to evaluate the stent system based on the requirements of the device design.

and potential failure modes. The device evaluation strategy may be communicated in a table (device evaluation strategy table) as described in [Annex A](#). Alternative methods for presenting the device evaluation strategy may be used (e.g. a non-tabular presentation of the rationale for the testing based on the potential risks and benefits of the stent system for the intended clinical use).

Emerging-technology stent systems should be evaluated following the requirements of this document, where appropriate. The device evaluation strategy should identify any testing needed beyond the scope of this document to characterize these stent systems.

NOTE 1 All testing in this document might not be appropriate for all stent system designs or intended clinical uses.

Coated, drug-eluting and absorbable stent systems should also be evaluated following the basic requirements of the respective standards, as appropriate to address the design attributes specified in [Clause 6](#).

Whenever changes are made in materials, construction, configuration, intended clinical use, or processing methods, an appropriate analysis of the potential impact of the change on the potential failure modes and performance of the stent system shall be performed. This evaluation may be communicated using appropriate tables as described in [Clause A.2](#). Appropriate testing shall be conducted as deemed necessary, considering the potential impact on device performance of the change.

The use of a control device for comparison may be considered in the evaluation of certain design attributes, particularly for design iterations.

The device design evaluation should be appropriate for the conditions of use described in the design concept and in the instructions for use (IFU). Though not required for the design evaluation, testing beyond these limits may be considered to characterize the changes in device performance (e.g. kink resistance; durability; proper positioning, orientation) as a function of use outside of the recommended conditions (e.g. angles, sizing). Information obtained from such testing might be useful in establishing acceptance criteria and in identifying appropriate warnings or precautions in the IFU for physician users.

Testing to establish the labelled shelf-life shall be conducted by repeating appropriate tests. Justification for the selection of tests shall be provided. Generally, this will not include long-term durability testing, unless the materials of construction are susceptible to degradation that cannot be evaluated through shorter-term testing, or other tests that measure parameters that are not expected to be affected by aging (e.g. MRI safety testing, corrosion testing).

NOTE 2 Additional information regarding shelf-life can be found in ASTM F2914.

8.2 Sampling

A sampling plan should be utilized which will ensure that adequate representation of the data has been obtained for each characteristic measured. It should be verified that the design attributes of the stent system, including any drugs and/or coatings, are representative of the devices to be released for distribution, including all sizes, configurations and components.

The sampling should fully represent the range of device sizes and may not necessarily require the testing of each size. It may be necessary to conduct an analysis to identify the size(s) of the device with the greatest potential for failure.

Multiple approaches to sample selection should be considered, depending on whether there are differences in relevant attributes of different device sizes (e.g. strut thickness, stent length, stent diameter) and the parameter under test (e.g. radial force). For example, four corners sampling may be appropriate for balloon fatigue, if there are no differences in the balloon thickness. Four corners testing may not be necessary for balloon deflation time as the largest size balloon can be justified as the worst case. A rationale shall be provided for sample selection.

If the purpose of the test is to evaluate the interaction between overlapping stents or between an endovascular graft and a stent (e.g. separation force), or if the attribute under test could (e.g. durability)

be significantly affected by the overlap or interaction with the endovascular graft, the test articles should include overlapped stents or the endovascular graft and the stent.

Segments or portions of complete stents or delivery systems may be used as the test articles if appropriately justified.

The need for testing of more than one portion of the stent or more than one deployed diameter should be considered in establishing the sampling plan to ensure adequate characterization for some parameters (e.g. proximal and distal diameters in a tapered stent, radial force in flared regions and the non-flared region of a flared stent)

For all tests, the number of samples should be justified.

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 non-sterilized products.

Samples shall be subjected to conditions that are normally encountered that can affect the performance of the device and test results. Examples of conditioning are preparation of the stent system, loading the stent on or inside the delivery catheter, passage through simulated tortuous vasculature, warming the system to body temperature, and deployment of the stent.

8.4 Reporting

For the purposes of this document, reporting refers to submission to a national regulatory authority.

The design evaluation report should include an appropriate table of contents and four main sections: (a) a background, (b) an executive summary, (c) individual test summaries, and (d) appendices that include the device evaluation strategy and the detailed reports. Pages should be numbered sequentially throughout the document (including appendices).

- a) The background section should describe the device design concept.
- b) The executive summary should include:
 - a description of the bench testing and analyses that have been performed;
 - a summary of the device evaluation strategy, including justification for the omission of tests identified in this document;
 - a table to summarize the testing completed, with the following columns: name of test, test purpose, test; sample description, number of samples, acceptance criteria, summary of results and conclusions, and cross references to the test summary and full test report
 - a summary conclusion statement.
- c) Individual test summaries should include:
 - a brief summary of the purpose, methods, and results;
 - the significance of the test results:
 - for tests with acceptance criteria, justification for the criteria; or
 - for characterization tests, an explanation of the relevance of the results.

d) Individual test reports should include the following information:

- purpose: state the purpose of the test as it corresponds to this document;
- materials: list significant materials (e.g. test articles with lot/serial numbers or other appropriate means of traceability, critical equipment) used in performing the test, using figures and diagrams as appropriate;
- sampling: state the sampling plan, including the basis for and the number of samples tested; selection of test articles shall be justified (e.g. sizes, conditioning);
- acceptance criteria, if applicable: state the criteria for the test results, including justification and/or clinical relevance; clinical applicability of the acceptance criteria shall take into consideration the anatomical and physiological conditions of the intended use;
- test method: describe in detail the method used to perform the test, including any prospectively defined inspection procedures, and provide a justification for relevant test parameters;
- protocol deviations: describe any deviations and their potential significance on the interpretation of the results;
- expression of results: report testing results expressed in units as indicated in the test method;
- discussion, if applicable: include a discussion on the potential clinical significance of the results;
- conclusions: state conclusions, based on comparing results to acceptance criteria or provide an explanation of the relevance of the results for characterization tests.

8.5 Bench and analytical tests

8.5.1 Stent system and delivery system

Testing of the stent system, delivery system, and stent shall be conducted to evaluate the design attributes described in [Clause 6](#), as applicable. The appropriate tests to evaluate each design attribute are based on the potential associated failure modes, device effects of failure, and clinical effects of failure. The rationale for the requirements specified in this document for the bench tests and analytical analyses to assess device performance is described in [Annex A](#).

The ability of the stent system to permit safe and consistent delivery, deployment, and withdrawal, and to provide adequate haemostasis shall be assessed. Sterility, biocompatibility, and visualization shall also be evaluated.

The associated device/procedure related functions, potential failure modes, and potential device effects of failure and clinical effects of failure to be considered are listed in [Tables A.2](#) and [A.3](#).

Testing shall include the items listed in [8.5.1.1](#) to [8.5.1.13](#), as appropriate to the design of the stent system.

8.5.1.1 Balloon testing

The following requirements apply to balloons integral to the stent system.

This subclause is not applicable to commercially available balloons used to achieve adequate apposition or post-dilation of the stent.

8.5.1.1.1 Balloon deflation time

Determine the time required to deflate the balloon when inside of the stent.

8.5.1.1.2 Balloon rated burst pressure

Determine the rated burst pressure (RBP) of the balloon when inside of the stent.

8.5.1.1.3 Balloon rated fatigue

Evaluate the ability of the balloon, when inside of the stent, to withstand repeated inflation cycles to the rated burst pressure, taking into consideration the number of inflation cycles expected clinically.

8.5.1.1.4 Dogboning

Determine the diameters of the balloon extending beyond the ends of the stent that are greater than the stent outer diameters at the maximum recommended inflation pressure (e.g. rated burst pressure).

NOTE This test provides information on potential damage to the vessel beyond the stent.

8.5.1.2 Dimensional verification of stent system

Determine the stent system dimensions, including the usable or working length, profile, and all other appropriate dimensions, for conformance with design specifications.

8.5.1.3 Dislodgement force (pre-mounted, balloon-expandable stents)

Determine the force required to displace the pre-mounted stent from its position on the non-expanded balloon.

8.5.1.4 Force to deploy (self-expanding stents)

Determine the force to deploy the stent by the operator under simulated anatomical conditions. All applicable steps of the deployment process as specified per the IFU should be evaluated (e.g. tether wire release, rotation of thumbwheel, sheath pull back).

NOTE The force to deploy can be used to help establish relevant tensile strength acceptance criteria.

8.5.1.5 Particulate generation

Consider the potential for particulate generation and likely clinical significance that could be associated with the clinical use of the stent system through a risk assessment. The risk assessment should consider potential occurrence of significant adverse clinical events associated with particulate generation (e.g. stroke, myocardial infarct, kidney infarct, pulmonary embolism, lower limb necrosis) based on several factors, including the tolerance for ischemia of the end organ. For intended implant locations with more tolerant end organs, the risk assessment should consider whether there are device design features that are susceptible to particulate generation (e.g. presence of an absorbable coating, hydrophilic coating) or if there is an observation during testing to indicate that there may be a higher risk of having significant particulates generated in either size or quantity (e.g. generation of visible particles during simulated use, observation of particulates, or particle effects in downstream tissue beds during *in vivo* studies).

Document the risk assessment. If the risk assessment indicates that either acute and/or chronic particulate generation does not require further evaluation based on the level of risk, the risk assessment documentation is sufficient to address the particulate generation requirement. If the risk assessment indicates that the potential for acute and/or chronic particulate generation and likely clinical significance exists, acute and/or chronic testing shall be conducted, as applicable. It is not expected that particulates will always need to be characterized beyond size and quantity. Depending on the quantified particulate test results and associated clinical risk, additional particulate characterization (e.g. chemical identification, crystallinity, morphology) and identification of the particulate source might be appropriate.

8.5.1.5.1 Acute particulate generation

Characterize the particles generated acutely from the stent system that could be associated with advancement, deployment and withdrawal.

8.5.1.5.2 Chronic particulate generation

Characterize the particles generated over time from the stent that could be associated with designs that are susceptible to particulate generation over time (e.g. drug-eluting, absorbable, coated).

8.5.1.6 Profile effect/flaring (balloon-expandable stents)

Determine the difference between the outer diameters of the stent and the outer diameters of the balloon as manufactured and after tracking through a tortuous path.

8.5.1.7 Simulated use

Evaluate the performance of the stent system with accessory devices specified in the IFU and determine deployment accuracy using a model(s) that simulate(s) the intended use conditions.

Evaluate the ability to access, deploy, and withdraw the stent system, including pushability, flexibility, torquability, and trackability, and determine deployment accuracy, using an anatomical model(s) that is (are) representative of the anatomy(ies) in the intended patient population. Evaluate the compatibility of the stent system with accessory devices. Evaluate the delivery catheter for delivery system failure. Evaluate the conformability of the deployed stent to the vessel wall, positioning (including orientation, if applicable), and absence of anomalies (e.g. kinks, twists, non-uniform expansion, stent damage). Subsequent to the assessment of device deployment, evaluate the effect of post-dilation if anticipated during clinical use.

8.5.1.8 Tensile bond strength

Determine the tensile bond strength of the joints and/or fixed connections of the delivery system. Evaluate the strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing) separately or concurrently with the bond strength determination.

The acceptance criteria for the bond strength(s) should take into consideration the expected forces applied to the delivery system during clinical use [e.g. tracking (access and withdrawal) and deployment].

NOTE The force to deploy can be used to help establish relevant bond strength acceptance criteria.

8.5.1.9 Torsional bond strength

Evaluate the torsional strength of the joints and/or fixed connections in the segments of the delivery system that are subjected to torsion during clinical use. Evaluate the torsional strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing) separately or concurrently with the torsional bond strength evaluation. The results shall be evaluated in relation to the torque necessary to access, deploy and withdraw the system.

8.5.1.10 Haemostasis

Evaluate the ability of any haemostatic seal or valve in the delivery system to minimize leakage of blood. This requirement is not applicable to systems that do not contain a haemostatic seal or valve.

8.5.1.11 Biocompatibility

The biocompatibility of the delivery system and the vascular stent shall be evaluated in accordance with ISO 10993-1 and appropriate other parts of the ISO 10993 series. The stent should generally be tested separately from the delivery system. However, there may be some tests (e.g.  Documents

implantation) where the stent and delivery system are used or tested together for at least part of the test, and these should be appropriately justified.

8.5.1.12 Sterilization assurance

Sterilization shall be assured in accordance with appropriate international standards.

8.5.1.13 Visibility

Evaluate the ability to visualize the stent system and stent using the imaging techniques specified in the IFU.

8.5.2 Stent

8.5.2.1 General and corrosion

The ability of the vascular stent to function as intended shall be assessed.

The associated device/procedure related functions, potential failure modes, and potential device and clinical effects of failure to be considered are listed in [Table A.1](#).

Testing shall include the items listed in [8.5.2.1](#) to [8.5.2.6](#), as appropriate to the design of the vascular stent. The tests are grouped based on similarities in the objectives of the testing; however, tests are not repeated within multiple categories. Refer to [Annex A](#) for a complete listing of the tests applicable to each design attribute.

Evaluate the susceptibility of a stent with metallic materials to corrosion.

The corrosion mechanisms can include pitting, fretting, crevice and galvanic corrosion. Each corrosion mechanism should be evaluated for specific stent designs, as appropriate. For example, fretting corrosion should be evaluated for stents that may be used in an overlapped condition.

Presence of a coating, coating artefacts and coating manufacturing processes might affect the corrosion susceptibility of the final product and should be considered.

8.5.2.2 Fatigue and durability — Computational analyses

Calculate the magnitude and location of the maximum stresses and/or strains for each appropriate loading scenario based upon the intended clinical application and device design. Appropriate computational analysis tools, such as finite element analysis (FEA), can be used to calculate the stresses and/or strains. The cyclic stresses and/or strains can be compared to material characteristics to calculate the fatigue safety factor.

For absorbable stents the calculation of a stress and/or strain-based fatigue safety factor might not be appropriate.

Computational analyses may also be used to establish appropriate test conditions and to select test articles for fatigue and durability testing.

8.5.2.3 Fatigue and durability — *in vitro* testing

Evaluate the long-term structural integrity of the stent under cyclic loading conditions that represent the *in vivo* environment. This can require several different test configurations.

Potential integrity failures to be assessed include fractures, abrasion, bonding failures, and coating delamination.

In vitro fatigue testing of the stent or appropriately justified test article shall be performed to demonstrate a minimum design life of 10 years. For pulsatile-related (i.e. loading caused by the cardiac cycle) test configurations, a minimum of 380 million cycles is generally required. For non-pulsatile

related test configurations, the minimum number of cycles required to demonstrate a design life of 10 years shall be justified. If the intended design life is less than 10 years, then shorter duration fatigue testing may be appropriate and shall be justified.

If fatigue testing is performed to compare the durability of a vascular stent to a stent with clinically demonstrated durability or clinically known problems with durability, the duration of test shall be justified.

8.5.2.3.1 General considerations

In identifying the appropriate durability tests, developing test methods, and establishing acceptance criteria, consideration of the device design (e.g. geometry, material selection) and intended clinical use (e.g. implantation location, disease state, lesion type) is necessary.

Pulsatile and non-pulsatile loading are associated with several modes of deformation. Pulsatile loading results in radial dilation [i.e. uniform or non-uniform (e.g. perpendicular compression)] and can also produce non-radial (i.e. bending, torsional, axial) deformation. Non-pulsatile loading (e.g. loading from respiration, walking, compression associated with native anatomy) can result in non-radial deformation. Examples of clinical uses, with their associated modes of loading (e.g. bending, axial, torsion, radial) which may occur separately or in combination, include:

- arterial stents are generally subject to radial loading;
- non-aortic stents can also be subject to compression, axial loading, bending and torsion, especially if placed near or across articulating or rotating body joints;
- ascending aortic stents can also be subjected to torsion;
- descending thoracic aortic stents can also be subject to bending;
- venous stents are generally not subject to radial loading;
- venous stents can be subjected to axial loading, bending, torsion, and compression (e.g. associated with respiration, indirect pulsatile deformation when compressed between an artery and a bone/ligaments associated with May-Thurner syndrome).

8.5.2.3.2 Radial fatigue and durability

Evaluate the long-term structural integrity of the stent when subjected to cyclic radial loading conditions, if applicable.

8.5.2.3.3 Axial fatigue and durability

Evaluate the long-term structural integrity of the stent when subjected to cyclic axial loading conditions, if applicable.

8.5.2.3.4 Bending fatigue and durability

Evaluate the long-term structural integrity of the stent when subjected to cyclic bending loading conditions, if applicable.

8.5.2.3.5 Torsional fatigue and durability

Evaluate the long-term structural integrity of the stent when subjected to cyclic torsional loading conditions, if applicable.

8.5.2.3.6 Compression fatigue and durability

Evaluate the long-term structural integrity of the stent when subjected to cyclic compressive loading conditions perpendicular to the stent axis (e.g. compression along the entire length, local compression), if applicable.

8.5.2.4 Patency-related tests

8.5.2.4.1 General and compression resistance to a perpendicularly-applied load (self-expanding stent for a venous or non-aortic, non-coronary or non-renal arterial implant location)

Crush resistance, compression resistance, and radial force characterize different patency-related attributes of the vascular stent and are applicable for specific device types and implant locations. Kink resistance (flexibility) is applicable to all vascular stents. Stent-free surface area is applicable only to intended clinical uses where this measure is relevant to maintaining branch circulation or healing of the stent into the vasculature.

[Table 1](#) provides the rationale for crush and compression resistance and radial force requirements for vascular stents. Loading conditions for use of stents with endovascular prostheses are not addressed in the table. For example, renal artery stents used with fenestrated endovascular prostheses are subjected to perpendicularly applied loads due to movement of the endovascular graft with respiration.

Table 1 — Rationale for crush and compression resistance and radial force requirements

Test	Purpose	Rationale for applicability			
		Venous and non-aortic, non-coronary, and non-renal arterial implant locations		Aortic, coronary and renal artery implant locations	
		Balloon-expandable stents	Self-expanding stents	Balloon-expandable stents	Self-expanding stents
Compression resistance to a perpendicularly-applied load (self-expanding stents)	The purpose of this test is to determine the force at which a pre-specified displacement occurs under a load applied perpendicular to the longitudinal axis of the stent.	Not applicable because this test does not evaluate permanent deformation relevant to a balloon-expandable stent.	Applicable because a self-expanding stent in these implant locations might be subjected to compressive forces that can affect patency.	Not applicable because these implant locations are not typically subjected to perpendicularly-applied loads.	Not applicable because these implant locations are not typically subjected to perpendicularly-applied loads.
Crush resistance with a perpendicularly-applied load (balloon-expandable stents)	The purpose of this test is to determine the force at which a pre-specified amount of permanent deformation occurs under a load applied perpendicular to the longitudinal axis of the stent.	Applicable because a balloon-expandable stent in these implant locations may be permanently deformed by an external load.	Not applicable because a self-expanding stent does not typically undergo permanent deformation.	Not applicable because these implant locations are not typically subjected to perpendicularly-applied loads.	Not applicable because these implant locations are not typically subjected to perpendicularly-applied loads.
Crush resistance with a radially-applied load (balloon-expandable stents)	The purpose of this test is to determine the radially applied load at which a pre-specified amount of permanent deformation occurs.	Applicable because a balloon-expandable stent may be permanently deformed by a radially-applied load.	Not applicable because a self-expanding stent does not typically undergo permanent deformation.	Applicable because a balloon-expandable stent may be permanently deformed by a radially-applied load.	Not applicable because a self-expanding stent does not typically undergo permanent deformation.

Table 1 (continued)

Test	Purpose	Rationale for applicability			
		Venous and non-aortic, non-coronary, and non-renal arterial implant locations		Aortic, coronary and renal artery implant locations	
		Balloon-expandable stents	Self-expanding stents	Balloon-expandable stents	Self-expanding stents
Radial force (self-expanding stents)	The purpose of this test is to determine the outward force as a function of the diameter of the stent.	Not applicable because a balloon-expandable stent can exhibit permanent deformation which is not evaluated by this test.	Applicable because a self-expanding stent exerts a radial outward force against the vessel wall.	Not applicable because a balloon-expandable stent can exhibit permanent deformation which is not evaluated by this test.	Applicable because a self-expanding stent exerts a radial outward force against the vessel wall.

Determine the force at which a pre-specified displacement occurs under a load applied perpendicular to the longitudinal axis of the stent. The loading fixture geometry (e.g. compression by two flat plates, cylindrical bar) shall be representative of the anticipated clinical environment (e.g. compression along the entire length). Evaluate whether the stent recovers its original geometry after removal of the load.

8.5.2.4.2 Crush resistance with perpendicularly applied load (balloon-expandable stent for a venous or non-aortic, non-coronary or non-renal arterial implant location)

Determine the force at which a pre-specified amount of permanent deformation occurs under a load applied perpendicular to the longitudinal axis of the stent. The loading fixture geometry (e.g. compression by two flat plates, cylindrical bar) shall be representative of the anticipated clinical environment (e.g. compression along the entire length).

8.5.2.4.3 Crush resistance with radially applied load (balloon-expandable stent for any implant locations)

Determine the radially applied load at which a pre-specified amount of permanent deformation occurs.

8.5.2.4.4 Radial force (self-expanding stent for any implant locations)

Determine the outward force as a function of the diameter of the stent.

8.5.2.4.5 Kink resistance (flexibility)

Determine the minimum radius that the stent can accommodate without kinking.

8.5.2.4.6 Stent-free surface area and stent outer surface area

Determine the proportion of free or open surface area of the stent at minimum and maximum indicated deployed stent diameters and the maximum contact area between the stent and the vessel.

NOTE Although the entire stent might not contact the vessel wall depending on the conformance to the vessel wall and the intended clinical use (e.g. for treatment of aneurysms), the stent outer surface area would include the maximum potential area along the entire length of the stent.

8.5.2.5 Sizing-related testing

Select the appropriate tests from those listed below to aid in the establishment of the sizing recommendations for the stent.

8.5.2.5.1 Dimensional verification of the stent

Determine the deployed stent dimensions including outer diameter(s), wall thickness(es), and all other appropriate dimensions, for verification to design specifications. Length measurement requirements are in [8.5.2.5.3](#).

8.5.2.5.2 Stent diameter to balloon inflation pressure (balloon-expandable stents)

Determine the relationship between the stent diameter and the balloon inflation pressure for balloon-expandable stents.

8.5.2.5.3 Stent length

Determine the relevant lengths of the stent on the delivery system and as deployed.

8.5.2.5.4 Recoil (balloon-expandable stents)

Determine the amount of elastic recoil (percent of the diameter reduction), after the deployment of a balloon-expandable stent. Recoil shall be considered in the sizing recommendations.

8.5.2.6 Magnetic resonance imaging (MRI) safety

Using clinically relevant MR environments (e.g. appropriate static magnetic field and spatial magnetic gradient field), evaluate the potential for 1) magnetically induced displacement force and torque; and 2) radiofrequency-induced (RF) heating of the stent. Determine the appropriate MR safety term (i.e. MR safe, MR conditional, or MR unsafe) as defined in ASTM F2503.

Characterize the MR image artefact produced by the stent. Describe the location and extent of the image artefact effect on the ability to visualize the device and adjacent anatomy.

NOTE No acceptance criterion is needed for image artefact as the effect of the MR artefact on the usefulness of the image depends on the MR environment and the anatomical region being imaged with respect to the location of the stent. For example, although image artefact associated with an abdominal stent can affect the ability to image the lumbar spine, it would not affect the ability to image the head and neck.

Test methods for evaluating magnetically induced displacement, torque, RF heating, and imaging artefact can be found in:

- ASTM F2052;
- ASTM F2213;
- ASTM F2182;
- ASTM F2119.

8.5.2.7 Stent and an endovascular prosthesis in combination

8.5.2.7.1 General and corrosion for a stent and an endovascular prosthesis used in combination

The ability of the stent to function in combination with an endovascular prosthesis shall be assessed.

The appropriate tests to consider for evaluating the design attributes for a stent used in combination with an endovascular prosthesis include those listed in this subclause, but additional testing may be appropriate. The selection of the tests shall be based on the potential associated failure modes, device effects of failure, and clinical effects of failure, taking into consideration the purpose of combination of the stent with the endovascular prosthesis. Potential purposes include bridging between the endovascular prosthesis and a branch artery, smoothing the transition between the endovascular

prosthesis and a blood vessel, improving the endovascular graft conformance to the vessel wall, and preventing migration of an endovascular prosthesis.

For situations where the stent behaviour is impacted by the interaction of the two devices (e.g. pushability/trackability of a stent system into a fenestration of the endovascular prosthesis), testing associated with the interaction of the two devices shall be performed.

If the stent has been previously evaluated for a different intended use, testing from the individual stent may be leveraged as appropriate. There may be situations where the acceptance criteria for a stent used in combination with an endovascular prosthesis differs from the acceptance criteria for the other intended use of the stent (e.g. the required radial force may be greater for a stent used in combination with an endovascular prosthesis to prevent migration). The modification to the acceptance criteria shall take into consideration the differences of the *in vivo* environment for the new intended use.

NOTE The requirements for endovascular prostheses are specified in ISO 25539-1.

Address the combination of the stent and endovascular prosthesis in the evaluation of corrosion resistance (e.g. fretting corrosion, galvanic corrosion).

For additional guidance for corrosion assessment, refer to [8.5.2.1](#).

8.5.2.7.2 Fatigue and durability for a stent and an endovascular prosthesis used in combination

Evaluate the long-term structural integrity of the stent and endovascular prosthesis when used in combination, under cyclic loading conditions that represent the *in vivo* environment.

Potential integrity failures to be assessed include fractures, abrasion, bonding failures, and coating delamination.

In identifying the appropriate durability tests, developing test methods, and establishing acceptance criteria, consideration of the stent/endovascular prosthesis interface and intended clinical use (e.g. implantation location, disease state, lesion type) is necessary. For example, relative motion can exist between an aortic endovascular prosthesis and the branch stents used to treat a juxtarenal aneurysm.

For additional guidance for fatigue and durability assessment refer to [8.5.2.3](#).

8.5.2.7.3 Patency-related tests for a stent used in combination with an endovascular prosthesis

Evaluate the ability of the stent to resist deformation that can negatively affect patency at the stent/endovascular prosthesis interface. Use an appropriate testing methodology for, and interpret the data in the context of, the intended clinical use conditions. It might be appropriate to interpret the results from previously conducted patency related testing to address this requirement.

For additional guidance for patency-related assessments refer to [8.5.2.4](#). Although [Table 1](#) does not provide guidance for the selection of tests for stents used in combination with an endovascular prosthesis, the considerations in [Table 1](#) may be of use in identifying the applicable testing.

8.5.2.7.4 Separation force between a stent and an endovascular prosthesis

Determine the force required to separate a stent from an endovascular prosthesis (e.g. a renal stent from a fenestrated aortic endovascular prosthesis). The evaluation of separation force is not necessary for stent/endovascular prostheses combinations intended for clinical uses where separation is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. the use of a vascular stent to improve the endovascular graft conformance to the vessel wall).

NOTE Additional information regarding separation force can be found in ISO 25539-1:2017, 8.5.2.4.3 and D.5.2.4.3.

8.5.2.7.5 Simulated use for a stent and an endovascular prosthesis used in combination

Evaluate the performance of the combination of the stent system and endovascular prosthesis using a model(s) that simulate(s) the intended use conditions.

For additional guidance for simulated use assessment, refer to [8.5.1.7](#).

8.5.2.7.6 MR for a stent and an endovascular prosthesis used in combination

Address the requirements of MRI safety [8.5.2.6](#) for the stent and endovascular prosthesis in combination.

8.5.2.7.7 Visibility

Include the stent and endovascular prosthesis in the evaluation of visibility.

For additional guidance for visibility assessment refer to [8.5.1.13](#).

8.5.3 Absorbable stents and stents containing an absorbable coating

Based on the potential associated failure modes, device effects of failure, and clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with an absorbable stent or a stent containing an absorbable coating and conduct testing to evaluate the risks identified in the assessment. All testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

Not all testing parameters described in this document are applicable to absorbable stents. Selection of the appropriate tests should take into account this document and ISO/TS 17137 which includes requirements and testing applicable to absorbable implants.

8.5.4 Coating on a delivery system

Based on the potential associated failure modes, device effects of failure, and clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with a coating on a delivery system and conduct testing to evaluate the risks identified in the assessment. All testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

8.5.5 Coating on a stent

Based on the potential associated failure modes, device effects of failure, and clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with a coating on a stent and conduct testing to evaluate the risks identified in the assessment. All testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

Selection of the appropriate tests for a stent coating should take into account the overall requirements described herein as well as the potentially relevant evaluations described in ISO 17327-1, which describes numerous coating varieties and methods of characterization that should be selected based on their relevance to both the utilized coating process and this intended vascular stent application. Although ISO 17327-1 considers an oxide layer to be a coating, it is expected that the testing described in ISO 25539-2 would be adequate to fulfil the requirements described in ISO 17327-1 for a vascular stent with an oxide layer.

8.5.6 Drug-containing stent

Based on the potential associated failure modes, device effects of failure, and clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with a stent containing a drug and conduct testing to evaluate the risks identified in the assessment. All testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

Selection of the appropriate tests should take into account ISO 12417-1 which includes requirements and testing applicable to vascular device-drug combination products.

8.6 Preclinical *in vivo* evaluation

8.6.1 Purpose

The purpose of preclinical *in vivo* testing is to evaluate the deployment of the stent, the biological response of the host to the stent, and the effect of the implant environment on the stent. Preclinical *in vivo* testing should provide data pertaining to safety. If the objective of an animal study can be met through alternative means (e.g. through reference to previously conducted animal and/or clinical studies), the use of previously obtained data or other supportive information shall be justified. The justification should include comment on the relevance of any differences between the subject device and the device used in the previous study and the relevance of any differences in the intended uses. Multiple studies may be conducted to address all of the relevant specific aims for a particular stent system.

NOTE The principles of 8.6 can be applied for the preclinical *in vivo* evaluation of particular configurations of stents (e.g. bifurcated), materials of construction (e.g. absorbable materials, combination products) and vascular uses other than the treatment of arterial stenoses. Additional specific aims, end points, and reporting requirements might be needed to define an appropriate study.

See ISO/TS 17137 for specific requirements and *in vivo* evaluation applicable to absorbable stents. See ISO 12417-1 for specific requirements and *in vivo* evaluation applicable to vascular device-drug combination stents.

8.6.2 Specific aims

Specific aims of the study shall be stated in the protocol. More than one study may be used to address these aims which can include the following:

- a) evaluate the ability to access the target location with the delivery system;
- b) evaluate the handling, ease of use, and visualization of the delivery system and visualization of the stent;
- c) evaluate the accuracy of deployment;
- d) evaluate the compatibility of accessory devices with the stent system, including balloons used post-deployment, if applicable;
- e) evaluate the ability to withdraw the delivery system;
- f) evaluate the functional haemostasis of the delivery system and sheath introducer, if applicable;
- g) evaluate the position, structural integrity, and patency of the stent acutely and at explant;
- h) conduct gross and histopathological evaluation of explants and pertinent tissues/organs including an assessment of local biological responses (e.g. thrombus deposition, inflammation, endothelialisation, necrosis, aneurysm formation) and downstream and systemic effects (e.g. embolism, infarction);
- i) evaluate local effects after implantation, thrombogenicity, or systemic toxicity end points to address the associated requirements of ISO 10993 series;
- j) record failure modes, device and clinical effects of failure (see [Annexes A, B and C](#) for potential failure modes and effects of failure), and adverse events.

Although evaluation of failure modes such as structural failure of the stent or excessive oversizing may not be a specific aim of an animal study, recording and addressing the associated observations is appropriate.

8.6.3 Protocol considerations

Each stent system shall be tested by implantation of the stent at the intended, or at an analogous vascular site in a reasonable number of animals for an adequate duration of time (e.g. 26 weeks) to accomplish the specific aims of the study. A control might be appropriate for comparison purposes. The type and intervals of interim assessments shall be specified and justified. For novel technologies, interim sacrifices and longer implant durations might be indicated. As far as permitted by the limitations of the animal model, all devices used should be of clinical quality and size, and of the design intended for clinical use.

Interpretation of animal study results can be enhanced by the use of at least a small number of control animals or control devices for comparison purposes. A rationale should be provided if a control is not used in the study.

All animals in the study shall be regularly examined. Histological and pathological assessment of explants and appropriate tissues/organs shall be completed. If an animal either dies or must be sacrificed prior to scheduled termination, it shall be subjected to immediate post-mortem examination. The cause of death or illness, and the extent to which the implant was implicated shall be documented. Information for all animals implanted with either test or control prostheses, including those excluded from the final analyses, shall be recorded and included in the test report.

The design of the preclinical *in vivo* testing, including the experimental protocol, measurement methods and data analysis, shall be documented. In addition, the choice of animal model, such as species, gender, age, and whether or not a lesion is created, shall be justified and shall be consistent with the study objectives. Implantation shall be consistent with the recommended deployment instructions, as far as permitted by the limitations of the animal model, including overlap of stents, if applicable.

NOTE Follow appropriate quality management practices and animal welfare protection measures in the execution of an animal study.

8.6.4 Data acquisition

If the control article is not a stent, data similar to that for animals receiving a stent shall be recorded for each control animal, as appropriate.

The following minimum data shall be recorded for each animal receiving a stent:

- a) identification data:
 - 1) source of animal;
 - 2) animal identification;
 - 3) sex;
 - 4) approximate age;
 - 5) mass;
- b) pre-operative data:
 - 1) verification of satisfactory health status;
 - 2) medications (e.g. prophylactic antibiotics);
- c) operative data:
 - 1) date of procedure;
 - 2) name of person(s) performing procedure;

- 3) implant and procedure information, including:
 - i) stent identification;
 - ii) *in situ* length and diameter of stent;
 - iii) diameter(s) of recipient vessel(s);
 - iv) location and length of overlap for overlapping devices;
 - v) use of systemic antiplatelet/anticoagulant therapy;
- 4) assessment of parameters specified in the protocol, such as:
 - i) the ability to access the target vessel location (e.g. pushability, flexibility, torquability, trackability);
 - ii) the ease and ability to accurately deploy the stent;
 - iii) the ability to visualize the delivery system and the stent;
 - iv) the ability to withdraw the delivery system;
 - v) the compatibility with accessory devices (e.g. balloons used during or after deployment);
 - vi) blood loss (e.g. amount and location);
 - vii) position, conformability, and patency of the stent;
 - viii) observed abnormalities (e.g. kinks, overlap separation, non-uniform expansion, stent damage) of the stent;
 - ix) observed device and clinical effects of failure and adverse perioperative events, including severity, management and outcome;
 - x) any significant deviation from the proposed deployment instructions or protocol;
- d) post-operative and follow-up data:
 - 1) post-operative duration at the time of follow-up;
 - 2) medications, including those that affect coagulation;
 - 3) assessments of structural integrity, patency and position of the stent, including the method and date of visualization;
 - 4) observed device and clinical effects of failure and adverse events, including date of occurrence, severity, management and outcome;
 - 5) assessment of other parameters specified in the protocol;
 - 6) any significant deviation from protocol;
- e) termination data:
 - 1) date of sacrifice;
 - 2) reason for early termination or death, if applicable;
 - 3) name of person(s) performing procedures and assessments;
 - 4) assessment of structural integrity, patency and position of stent, including method of visualization;
 - 5) assessment of other parameters specified in the protocol;

- 6) gross alteration in the dimensional properties of the stent;
- 7) gross and histopathological assessment of explants and appropriate surrounding and distal tissues/organs.

8.6.5 Test report and additional information

Results of all animals enrolled in the protocol shall be recorded and reported, even if excluded from the final analysis.

The test report shall include the following:

- a) study protocol;
- b) rationale for selection of the following:
 - 1) animal model;
 - 2) implantation site;
 - 3) control for comparison or rationale for not using a control group, as applicable;
 - 4) implantation periods;
 - 5) methods of assessment;
 - 6) intervals of observation;
 - 7) sample size (i.e. number of animals and implants);
- c) results:
 - 1) animal accountability, including rationale for exclusion of data from the primary analysis;
 - 2) number of stents successfully implanted and the number of stents not successfully implanted;
 - 3) operator assessment of ease of deployment, visualization and handling;
 - 4) discussion of sizing (e.g. diameter as it may relate to overstretch injury, length as it may relate to thrombogenicity) and potential impact on study results;
 - 5) summary of any changes in position, structural and material integrity, and patency of the stent;
 - 6) summary of device and clinical effects of failure and adverse events;
 - 7) summary of unexpected deaths or early terminations, with discussion of post-mortem pathological evaluation, suspected aetiology, and the potential for the death to be related to the device;
 - 8) summary animal health including scheduled examinations, clinical observations, clinical pathology values and weight gain or loss;
 - 9) summary of gross pathology evaluation and histopathology of explants and appropriate tissues/organs, including gross photographs, radiographs of explants, and representative photomicrographs;
 - 10) summary of other information required by the protocol;
 - 11) significant and/or relevant deviations from protocol;
 - 12) comparison of outcomes for test and control groups, if applicable;
 - 13) conclusions from study;

14) summary of quality assurance and data auditing procedures.

8.7 Clinical evaluation

8.7.1 Purpose

The purpose of clinical evaluation is to assess the safety and effectiveness of a stent system. This evaluation is not intended to demonstrate the long-term performance of the stent. An investigation should be carried out for each new stent or new clinical application of a stent using the principles given in ISO 14155 or an equivalent publication. Significant design changes that can impact safety and performance shall require clinical evaluation if determined to be necessary based on an appropriate risk assessment. This evaluation may follow the requirements described in this document or abbreviated requirements as appropriate to address the identified risks. Additional stent sizes outside the previously evaluated range might require clinical evaluation but may not require assessment consistent with all requirements (e.g. multicentre study, statistically powered sample size).

If an objective of a clinical study can be met through alternative means (e.g. through reference to previously conducted clinical studies), the use of previously obtained data or other supportive information shall be justified. The justification should include comment on the relevance of any differences between the subject device and the device used in the previous study and the relevance of any differences in the intended uses.

For stents used in combination with an endovascular graft, the clinical evaluation should follow the requirements specified in ISO 25539-1.

The principles of [8.7](#) may be applied for the clinical evaluation of particular configurations of stents (e.g. bifurcated) and vascular uses other than the treatment of arterial stenoses. Additional specific aims, end points, and reporting requirements might be needed to define an appropriate study.

See ISO/TS 17137 for specific requirements and *in vivo* evaluation applicable to absorbable stents.

See ISO 12417-1 for specific requirements and *in vivo* evaluation applicable to vascular device-drug combination stents.

8.7.2 Specific aims

Specific aims of the study shall be based on an appropriate risk assessment for the stent system and stated in the protocol. The specific aims may include the following:

- a) Evaluate the effectiveness of the stent system, such as the:
 - 1) ability to access the target location with the delivery system;
 - 2) handling and visualization of the delivery system and visualization of the stent;
 - 3) accuracy of deployment;
 - 4) ability to withdraw the delivery system;
 - 5) position, structural integrity and functionality (e.g. patency, freedom from target lesion revascularization) of the stent acutely and over time;
 - 6) lesion characteristics (e.g. restenosis, aortic false lumen perfusion) over time;
 - 7) device effects of failure (see [Annex C](#) for potential device effects of failure);
- b) Evaluate the safety of the stent system, such as the:
 - 1) clinical effects of failure (see [Annex B](#) for potential clinical effects of failure);
 - 2) adverse events.

8.7.3 Protocol considerations

A multicentre study shall be performed at a minimum of three investigational sites. A justification for the number of investigational sites shall be provided.

A specific question or set of questions (i.e. hypotheses) shall be defined prospectively. These questions shall delineate the appropriate safety (e.g. freedom from major adverse events), effectiveness (e.g. primary patency), or combined safety and effectiveness end points to be measured. Definitions of success and failure for each end point and the duration of follow-up needed to assess each end point shall be specified. A definition for the study success shall also be specified (e.g. meeting both the safety and effectiveness primary end points).

A statistical justification for the number of patients studied shall be provided based upon the primary hypotheses. Preferably, no investigational site should enrol more than 35 % of the total number of study subjects.

The duration of patient follow-up shall be determined in relation to the objectives of the clinical investigation. Patient follow-up intervals shall include a minimum of an assessment at discharge and at the specified study duration. A justification will be required for follow-up intervals. All patients enrolled in the study, including those excluded from the primary end point analyses, shall be recorded and reported. The final report may be completed when the required number of patients to test the hypotheses have reached the specified study duration. The report shall include current follow-up data on all patients. Longer-term patient follow-up (e.g. 2 years to 5 years after the last stent has been implanted) may be appropriate for the post-market clinical assessment of device designs with a limited history of clinical use.

A control should be included in the study to appropriately address the questions postulated. If an appropriate control is not or cannot be identified, or a concurrent control is unnecessary, a method for evaluating the clinical outcomes shall be prospectively defined and justified (e.g. performance goals).

The study design shall be designated by appropriate terms [e.g. number of study arms, type of control (randomized, literature, performance goal), blinding, prospective vs retrospective].

The protocol may differ between the control group and the treatment group. If so, a separate protocol for the assessment of the control subjects shall be included.

Patient inclusion and exclusion criteria shall be clearly identified. The criteria shall specify the target population (i.e. those for whom the stent is intended) and the accessible population (i.e. those who agree and are able to participate fully in the study). An appropriate epidemiological approach shall be utilized for recruiting subjects to minimize bias (e.g. encourage sequential enrollment).

Definitions of primary effectiveness (e.g. primary patency), primary safety (e.g. freedom from major adverse events) and secondary clinical end points, measurement methods, and data analysis shall be specified in the clinical protocol. Secondary end points might include the following:

- individual components that make up any composite primary end points;
- change in quality of life status or other relevant patient reported outcomes;
- measure of therapeutic success (e.g. ankle brachial index);
- technical success [e.g. successful placement of all stents at the intended implantation site(s) with patency];
- procedural success (e.g. technical success in absence of serious device-related adverse events at 30 days);
- device and clinical effects of failure;
- repeat procedures (e.g. target vessel revascularization);
- longer-term outcomes (e.g. 12-month safety data if the primary safety end point is at 30 days).