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Cardiovascular implants — Endovascular devices —

Part 2: Vascular stents

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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. thrombogenicity,

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 that 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).

Consideration should be given to the use of independent core laboratories and event adjudication committees, as appropriate. The sources of the data to be included in reporting (e.g. site, core lab, adjudication committee) should be specified in the protocol.

8.7.4 Data acquisition

Data similar to that for patients in the study arm shall be recorded for each patient in the control arm, as appropriate.

At a minimum, the following data shall be recorded for each patient in the study arm:

a) Identification and demographic data:

   1) patient identification;

   2) indication for treatment (e.g. critical limb ischemia, claudication, post-thrombotic syndrome, acute coronary syndrome, stable angina) and associated medical diagnosis (e.g. occlusion, stenosis, venous insufficiency);

   3) demographics

      i) date of birth;

      ii) sex;

      iii) weight or body mass index;

      iv) height;

   4) race, as appropriate (i.e. when this information can be legally obtained);

   5) name of investigator;

   6) name of institution;

b) pre-procedural data:

   1) risk factors, such as hypertension, diabetes mellitus, renal insufficiency, prior deep venous thrombosis, pulmonary embolic disease, hyperlipidemia, tobacco use, obesity, anaesthesia risk and any other cardiovascular risk factors;

   2) summary of previous vascular interventions at the same or other relevant vascular sites and adjunctive vascular interventions (e.g. atherectomy, thrombolysis, ballooning of distal vessels), including non-surgical interventions and previously implanted vascular devices (e.g. stents, endovascular prostheses, surgically placed vascular prostheses);

   3) relevant medications;

   4) diagnostic criteria:

      i) clinical assessment;

      ii) objective assessment of lesion and access vessel characteristics and other relevant factors (e.g. sizes, degree of calcification and tortuosity, presence of collateral vessels, lesion length);

c) procedural data:

   1) name of implanting physician;

   2) date of procedure;

3) identification data for the stent(s) [e.g. unique device identifier, model number and implant traceability (e.g. lot number), size, configuration];

4) urgency of intervention (e.g. planned, bailout, abrupt and threatened closure);

5) information regarding the procedure (e.g. adjunctive vascular procedures performed);

6) relevant medications (e.g. antiplatelets, anticoagulants);

7) position of stent (e.g. distance from anatomical landmarks);

8) vascular segment treated length;

9) luminal diameter of stent;

10) assessment of procedural outcome (e.g. technical success, residual stenosis, patency, stent integrity);

11) record device and clinical effects of failure and adverse events [see 8.7.4, e)];

12) date of hospital discharge, if applicable;

13) ability to visualize the delivery system and stent on imaging;

d) follow-up data:

1) interval of follow-up (e.g. discharge, 30-day, 12-month);

2) date of follow-up visit;

3) relevant interventions or surgeries since last follow-up;

4) clinical and imaging evaluation:

i) clinical assessment (e.g. target lesion revascularization);

ii) presence or absence of planned imaging surveillance and modality;

iii) objective assessment of targeted lesion characteristics (e.g. patency, percentage of diameter stenosis) and method of assessment (e.g. duplex ultrasound, angiography);

iv) objective assessment of stent positioning (i.e. for venous stenting) and stent integrity and method of assessment;

5) relevant medications, such as anticoagulants or antiplatelets;

6) record device and clinical effects of failure and adverse events [see 8.7.4, e)];

e) device and clinical effects of failure, and adverse events:

1) type of effect or event, date of occurrence, severity, management (e.g. none, medical treatment, secondary endovascular procedure, open surgical procedure), outcome (e.g. continuing, resolved, unknown, death);

2) documentation of stent involvement;

3) documentation of probable causative factors (e.g. caused by the stent, patient factors, technical factors);

f) secondary procedures associated with the treated segment:

1) date;

2) reason for reintervention;

3) type of reintervention;

4) outcome of reintervention;

g) death:

1) date;

2) whether autopsy was performed, and if so, the findings;

3) cause of death;

i) whether or not the death was related to the stent or procedure;

ii) summary of explant analyses, if applicable;

h) patient withdrawal:

1) date;

2) months of study completed;

3) reason for withdrawal (e.g. lost to follow-up, withdrew consent, removed from study per physician recommendation).

8.7.5 Final report

The final report shall include the following:

a) study protocol, including at a minimum:

1) study description (e.g. study design, designation, control arm, number of sites, number of patients);

2) primary and secondary end points, hypotheses and definitions of success;

3) source of the data (e.g. site, core lab);

4) definition of study success;

5) subject population (i.e. selection criteria);

6) follow-up intervals;

7) methods of assessment [e.g. clinical, computed tomography angiography (CTA), magnetic resonance angiography (MRA), duplex ultrasound];

8) data analysis plan including methods to address missing data;

9) definitions of technical and procedural success, device and clinical effects of failure, and adverse events;

b) rationale, based on the risk assessment and questions to be answered, for selection of the following:

1) study size;

2) choice of control;

3) measurement methods;

4) statistical analyses employed;

5) patient follow-up intervals;

c) number of patients treated at each investigational site;

d) follow-up accountability (e.g. numbers of patients eligible for each follow-up interval and the number with specified follow-up data), including a rationale for the exclusion of data from the primary end point analyses;

e) demographics, risk factors, and relevant vascular lesion characteristics (e.g. lengths of the stenotic lesions);

f) numbers of devices per patient and sizes of devices used;

g) significant and/or relevant deviations from the clinical protocol and the manner in which deviations were addressed in the data presentation;

h) results:

   1) technical success;

   2) procedural success;

   3) safety:

      i) primary and secondary end point outcomes;

      ii) summary of peri-procedural (less than or equal to 30 days, or prior to hospital discharge) and late conversions to open surgery;

      iii) summary of peri-procedural and late deaths;

   4) effectiveness:

      i) primary and secondary end point outcomes;

      ii) summary of secondary interventions;

   5) conclusions from study, including results of hypothesis testing and achievement of success as defined by the protocol.

9 Post-market surveillance

A systematic procedure to review post-market experience gained from implants shall be in place using the principles given in ISO 14630:2012, 7.4, and ISO 14971, or equivalent publications.

10 Manufacturing

Stent systems shall be manufactured in such a way that the design attributes are achieved. Requirements are specified in other related international standards.

The requirements of ISO 13485 and ISO 14630:2012, Clause 8 shall apply.

11 Sterilization

11.1 Products supplied sterile

11.1.1 Stents and/or stent systems that are labelled “Sterile” shall comply with international, national or regional standards and have a sterility assurance level (SAL) of 10^{-6}. Sterilization processes shall be validated and routinely controlled.

a) For stents and/or stent systems that are to be sterilized by ethylene oxide, ISO 11135, shall apply.

b) For stents and/or stent systems that are to be sterilized by moist heat, ISO 17665-1 shall apply.

c) For stents and/or stent systems that are to be sterilized by radiation, ISO 11137 (all parts) shall apply.

d) For stents and/or stent systems incorporating animal tissue that are to be sterilized using liquid chemical sterilants, ISO 14160 shall apply.

e) For stents and/or stent systems that are to be sterilized by other sterilization processes, ISO 14937 shall apply.

11.2 Sterilization residuals

The requirements of ISO 14630:2012, 9.4, shall apply.

12 Packaging

12.1 General

12.1.1 General

The requirements of ISO 14630:2012, Clause 10, shall apply.

12.1.2 Unit container

Each stent and/or stent system shall be packaged in a unit container providing a sterile barrier, if applicable. It shall be readily apparent if the unit container has been opened.

12.1.3 Outer container

Each unit container shall be packaged in an outer container. This outer container shall be designed so as to protect the unit container from damage due to storage.

12.1.4 Shipping container

Each outer container, or a number of outer containers not necessarily of the same type, shall be packaged in a shipping container designed to protect the contents under normal conditions of handling, transit and storage.

12.1.5 Maintenance of sterility in transit

For stents and/or stent systems supplied sterile, the unit container shall be designed to maintain the sterility of the stent and/or stent system under normal conditions of handling, transit and storage, and to permit the contents to be presented for use in an aseptic manner.

The packaging shall conform to ISO 11607-1.

12.2 Labelling

12.2.1 Container label

Each stent and/or stent system shall be accompanied by a label(s) on an appropriate container(s).

12.2.2 Stents without delivery systems

At least the following information shall be provided in words, phrases, symbols or drawings on the label(s):

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

b) name and/or trademark, address and contact information of the manufacturer;

c) product name;

d) the type of stent (e.g. balloon-expandable, self-expanding)

e) the material(s) of construction;

f) configuration (see 4.4), if applicable;

g) dimensions: designated length and diameter(s) after expansion;

h) model/reference number;

i) lot/serial number;

j) sterilization method and the word “STERILE”;

k) single use;

l) expiry/expiration date;

m) warnings or reference to read the manual (symbol);

n) warning against the use of the stent if the package is open or damaged;

o) manufacturer’s recommendation for storage, if applicable;

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

12.2.3 Stent systems (stents with delivery system)

At least the following information shall be provided in words, phrases, symbols or drawings on the label(s):

a) information as described in 12.2.2;

b) delivery system information, at least:

   1) dimensions: minimum required size of introducer (internal diameter), maximum size of guidewire and usable, working or effective length of the catheter;

   2) RBP and maximum recommended inflation pressure, if applicable.

12.2.4 Record label

Each stent and/or stent system should be supplied with transferable record labels suitable for attachment to the records of the patient receiving the stent. The record label should include the following information:

a) manufacturer's identification;

b) product name;

c) manufacturer's batch and/or sterile lot number;

d) part or model number (manufacturer's catalogue number).

12.3 Information supplied by the manufacturer

12.3.1 General

The requirements of ISO 14630:2012, Clause 11.3, shall apply.

12.3.2 Information and instructions for use for stents and/or stent systems

Each unit container or outer container of which the contents are identical shall be supplied with instructions for the use (IFU) of the stent and/or stent system, or instructions on how to access an electronic version of the IFU. The instructions shall include the following information to use the stent/stent system safely and properly, taking into account the training and knowledge of the potential users:

a) name and/or trademark and address of the manufacturer;

b) product name;

c) device description and materials of construction, including, but not limited to:

   1) material of construction of the stent;

   2) description of the location(s) of markers for visualization, if applicable;

   3) identity of the coating material(s), if applicable;

   4) identity and amount of drug(s), if applicable;

   5) type of construction (self-expanding or balloon-expandable).

d) indications for use;

e) contraindications, cautions and warnings;

f) for drug-eluting stents, the potential for drug interactions with the drug delivered by the stent;

g) recommendations for stent sizing, including vessel diameters, lesion lengths, and stent diameter as a function of inflation pressure, as applicable;

h) potential adverse events;

i) data from clinical studies, if applicable;

j) recommended methods for the aseptic presentation and the preparation of the stent and delivery system;

k) recommended methods for vessel preparations, such as pre-dilation, and methods for access, delivery of the stent and withdrawal of the delivery system;

l) the applicable information regarding the sterility of the device, in prominent form:

   1) NON-STERILE;

   2) STERILE;

   3) STERILE — DO NOT RESTERILIZE;

m) specify that the device is single use only in prominent form;

n) resterilization information, if applicable;

o) notification of additives and/or leachable components, if applicable;

p) recommendations for storage, if applicable;

q) date of or reference relating to the publication of the IFU, indicating when the IFU was last revised;

r) recommendations for visualization;

s) MRI safety information.

Annex A
(informative)

Relationship between testing requirements, device attributes, and potential failure modes and guidance for the creation of a device evaluation strategy

A.1 Device evaluation strategy introduction and rationale for bench testing and analyses

A device evaluation strategy provides the rationale for the evaluation plan for a device. The rationale for the evaluations required by this document that are applicable to most vascular stents is described in Tables A.2 and A.3. Identification of the appropriate testing for a device evaluation strategy involves describing each device-related and procedure-related function needed to achieve the desired performance (i.e. device attributes) and the associated relationships between device attributes, potential failure modes, and testing requirements.

Potential device effects of failure are categorized into two categories: initial effects and subsequent effects of failure. Subsequent effects are defined as a secondary effect of device failure after an initial effect. For example, stent fracture might lead to stent embolization. In this example, stent fracture would be listed under “initial effect(s)” and stent embolization would be listed under “subsequent effect(s).”

The known potential clinical effects of death and re-intervention are not listed in the tables because additional intervention and death are a reflection of the severity of the failure and not helpful in identifying tests to evaluate device function.

To reduce redundancy, some potential failure modes associated with individual device and procedure related functions are not repeated if covered under previously identified functions (e.g. deployment related failure modes that may affect patency are listed under the device function “ability to deploy” and not repeated under “patency”).

Table A.1 — Explanation of Tables A.2 and A.3 column headings

Device attributes/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Each individual device-related and procedure-related function required for the device to achieve the overall desired performance. Functions should be attributes of the device or procedure and therefore should be stated in the positive.	The specific failures that might occur and could result in consequences (effects) to the device or patient if the function is not attained. Individual failure modes should be addressed separately. They should be presented in separate rows for an attribute, as they may have different effects of failure and may be mitigated with different testing.	The potential effect(s) of the failure mode on the device. Device effects of failure describe what happens to the device as a result of the failure and may be important to capture, whether or not there is an associated clinical effect of failure.	The potential additional device effect(s), if any, resulting from one of the effects listed in the previous column.	The potential effect(s) of the failure mode on the patient.	Bench tests and analyses of the device to evaluate the function and the potential failure mode.

Table A.2 — Rationale for bench testing and analyses for the stent system

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Ability to access	Stent system is incompatible with accessory devices	— Access failure — Accessory device failure — Delivery system damage — Stent damage	— None	— Access vessel injury — Failure to complete device implantation	— Dimensional verification of stent system — Simulated use
	Inability to advance stent system to target site	— Access failure — Delivery system damage — Stent damage	— None	— Access vessel injury — Access vessel rupture — Failure to complete device implantation — Vascular trauma — procedural dissection	— Simulated use
	Stent dislodgement from the delivery system	— Stent dislodgement from the delivery system	— Stent embolization	— Failure to complete device implantation — Foreign body embolization — Ischaemia — Lumen obstruction	— Dislodgement force — Simulated use
	Unable to cross lesion with stent system	— Access failure	— Stent dislodgement from the delivery system	— Failure to complete device implantation — Foreign body embolization — Vascular trauma — procedural dissection	— Profile effect/ flaring — Simulated use

Table A.2 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Ability to deploy	Inability to activate deployment mechanism or procedure	— Balloon-related deployment failure — Delivery system-related deployment failure — Inability to deploy	— None	— Failure to complete device implantation	— Force to deploy — Simulated use
	Improper positioning or orientation	— Inaccurate deployment — Lack of apposition to the vessel wall	— Stent dislodgement — Stent embolization	— Amputation — Ischaemia — Lumen obstruction — Cardiac dysfunction — Stent occlusion — Restenosis — Thrombosis — Dissection creation or extension — Vascular injury — stent related	— Balloon testing — Dogboning — Stent length — Profile effect/ flaring — Simulated use
	Excessive balloon inflation	— Balloon rupture	— None	— Dissection creation or extension — Foreign body embolization (balloon fragments) — Restenosis — Thrombosis — Vascular trauma — procedural dissection — Vessel rupture — Vessel thrombosis	— Balloon rated burst pressure for balloons

Table A.2 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Ability to withdraw	Incomplete balloon deflation	— Stent displacement	— Stent embolization	— Ischaemia — Lumen obstruction — Access vessel injury — Access vessel rupture — Vascular trauma — procedural dissection	— Balloon deflation time — Simulated use
	Damage of implant components by other components (e.g. delivery system snagging on the stent)	— Stent damage — Stent displacement	— Stent migration — Stent embolization	— Stented branch vessel loss of patency — Branch vessel obstruction — Ischaemia — Lumen obstruction — Cardiac dysfunction — Foreign body embolization	— Dimensional verification of stent system — Simulated use
Atraumatic introduction, tracking and withdrawal	Emboli generation	— None	— None	— Embolism — Ischaemia	— None
	Particulate generation	Particulate generation	— None	— Adverse biological response — Ischaemia	— Acute particulate generation

Table A.2 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
	Trauma to vasculature	— None	— None	— Access vessel injury — Access vessel rupture — Unintentional dissection septum perforation — Vascular trauma — procedural dissection	— Dimensional verification of stent system — Simulated use
Delivery system integrity	Separation of delivery system components (e.g. bond failures, complete tip separation)	— Delivery system damage	— Balloon-related deployment failure — Delivery system-related deployment failure	— Failure to complete device implantation — Foreign body embolization — Vascular trauma — procedural dissection	— Simulated use — Tensile bond strength — Torsional bond strength
	Tubing material failure	— Delivery system damage	— Balloon-related deployment failure — Delivery system-related deployment failure	— Failure to complete device implantation — Foreign body embolization — Vascular trauma — procedural dissection	— Simulated use — Tensile bond strength — Torsional bond strength
	Loss of balloon integrity	— Balloon-related deployment failure — Balloon rupture — Inaccurate deployment — Lack of apposition to the vessel wall	— Stent dislodgement — Stent embolization	— Failure to complete device implantation — Foreign body embolization (e.g. balloon fragments)	— Balloon rated fatigue — Balloon rated burst pressure
Haemostasis	Inadequate haemostasis	— None	— None	— Blood loss	— Dimensional verification of stent system — Haemostasis
Sterility	Non-sterile product	— None	— None	— Insertion site infection — Stent infection	— Sterilization assurance
Biocompatibility	Non-biocompatible	— None	— None	— Adverse biological response	— Biocompatibility

Table A.2 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Visualization	Inability to safely and effectively access, deploy, or withdraw	— All device effects associated with access, deployment and withdrawal	— None	— All clinical effects of failure associated with inability to access, deploy, or withdraw	— Visibility
	Inadequate visibility of the stent	— None	— None	— Inability to monitor the stent over time	— Visibility

Table A.3 — Rationale for bench testing and analyses for the stent

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Atraumatic apposition of stent to the vessel wall	Excessive radial force	None	None	— Dissection creation or extension — Erosion leading to fistula formation — Vascular injury — stent related	— Radial force (self-expanding stents)
	Trauma to vasculature (includes trauma due to any cause, such as, inadequate flexibility, over-dilating)	None	None	— Vascular injury — stent related	— Simulated use
	Structural failure of stent (includes loss of integrity due to any cause, such as, wear between overlapping stents, fatigue)	— Strut fracture	— Lack of apposition to the vessel wall — Stent embolization	— Ischaemia — Lumen obstruction — Cardiac dysfunction — Foreign body embolization — Restenosis — Thrombosis — Vascular injury — stent related	— Fatigue and durability - computational analyses — Fatigue and durability — Simulated use
		— Bond fracture	— Stent embolization	— Ischaemia — Lumen obstruction — Foreign body embolization — Vascular injury — stent related	— Fatigue and durability - computational analyses — Fatigue and durability — Simulated use

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Stent integrity		— Connector or link break or fracture	— Stent embolization	— Ischaemia — Lumen obstruction — Restenosis — Thrombosis — Foreign body embolization	— Fatigue and durability - computational analyses — Fatigue and durability — Simulated use
		— Active fixation element (hook/ barb) fracture	— Stent migration — Stent embolization	— Ischaemia — Lumen obstruction — Cardiac dysfunction — Restenosis — Thrombosis — Foreign body embolization	— Fatigue and durability - computational analyses — Fatigue and durability — Simulated use
	Corrosion	— Bond fracture — Stent fracture	— Lack of apposition to the vessel wall — Stent embolization	— Adverse biological response — Foreign body embolization — Ischaemia — Lumen obstruction — Cardiac dysfunction — Restenosis — Thrombosis — Vascular injury — stent related	— Corrosion

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Appropriate interaction between a stent and an endovascular prosthesis (e.g. for stents used in branch arteries with an aortic endovascular prosthesis or for stents used to cover dissected vessels after coverage of the primary entry tear with an endovascular prosthesis)	Dimensional mismatch between stent and endovascular prosthesis	— Component separation — Poor apposition between components	— None	— Branch vessel loss of patency — Ischaemia — Lumen obstruction	— Simulated use
	Inaccurate positioning or orientation of the stent with respect to the endovascular prosthesis	— Branch vessel stent compression or kink — Component separation	— None	— Branch vessel loss of patency — Ischaemia — Lumen obstruction	— Patency-related tests for a stent used in combination with an endovascular prosthesis — Simulated use
	Separation between the stent and the endovascular prosthesis	— Component separation	— None	— Branch vessel loss of patency — Ischaemia — Lumen obstruction — Type IIIa endoleak	— Patency-related tests for a stent used in combination with an endovascular prosthesis — Separation force between a stent and an endovascular prosthesis — Simulated use

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
	Development of angulation or kink between stent and endovascular prosthesis	— Stent compression, collapse, kink or infolding	— None	— Amputation — Ischaemia — Lumen obstruction — Stent occlusion — Restenosis — Thrombosis — Branch vessel blockage — Branch vessel coverage	— Patency-related tests for a stent used in combination with an endovascular prosthesis — Fatigue and durability for a stent and an endovascular prosthesis used in combination — Simulated use
	Loss of stent or endovascular prosthesis integrity due to interactions between components	— Stent-related graft material holes — Stent fracture — Support structure fracture (e.g. fixation system of the endovascular prosthesis)	— Stent embolization — Component separation	— Branch vessel loss of patency — Ischaemia — Lumen obstruction — Branch vessel blockage — Branch vessel coverage — Vascular injury — stent related — Type IIIb endoleak	— Fatigue and durability for a stent and an endovascular prosthesis used in combination — Simulated use
	Corrosion due to interactions between components	— Bond fracture — Stent fracture	— Lack of apposition to the vessel wall — Stent embolization — Component separation	— Adverse biological response — Foreign body embolization — Ischaemia — Lumen obstruction — Restenosis — Thrombosis — Vascular injury — stent related	— Corrosion for a stent used in combination with an endovascular prosthesis
	Inadequate visibility of the stent	— None	— None	— Inability to monitor the stent over time	— Visibility
Safe overlapping of stents	Dimensional mismatch between stents	— Stent separation — Poor apposition between stents	— None	— Ischaemia — Restenosis — Thrombosis	— Dimensional verification of stent

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
	Excessive stiffness or radial force in overlap region	— None	— None	— Dissection creation or extension — Erosion leading to fistula formation — Vascular injury — stent related	— Simulated use
	Inaccurate positioning or orientation	— Stent separation	— None	— Ischaemia — Restenosis — Thrombosis — Lumen obstruction	— Simulated use
	Angulation or kink at the margin of the overlap	— Stent kink	— None	— Ischaemia — Lumen obstruction — Restenosis — Thrombosis	— Kink resistance — Simulated use
	Loss of stent integrity due to overlapping	— Stent fracture	— None	— Ischaemia — Lumen obstruction — Vascular injury –stent related	— Fatigue and durability — Simulated use
Appropriate sizing recommendations	Excessive oversizing	— Stent compression, collapse, kink or infolding		— Ischaemia — Lumen obstruction — Stent occlusion — Restenosis — Dissection creation or extension — Thrombosis — Vascular injury — vascular stent related	— Dimensional verification of stent — Radial force (self-expanding stents) — Simulated use

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
	Undersizing	— Lack of apposition to vessel wall	— Stent migration — Stent embolization	— Branch vessel obstruction — Ischaemia — Lumen obstruction — Cardiac dysfunction	— Dimensional verification of stent — Radial force (self-expanding stents) — Simulated use
	Excessive recoil	— Lack of apposition to the vessel wall	— Stent migration — Stent embolization	— Branch vessel obstruction — Ischaemia — Lumen obstruction	— Dimensional verification of stent — Recoil — Simulated use
	Inappropriate device size selection	—	—	—	— Dimensional verification of stent — Stent diameter to balloon inflation pressure (balloon-expandable stents) — Stent length
Patency	Kinking	— Stent kink	— None	— Ischaemia — Lumen obstruction — Stent occlusion — Restenosis — Thrombosis embolism	— Kink resistance — Simulated use
	Improper positioning or orientation	— Lack of apposition to the vessel wall	— None		— Simulated use
	Stent compression, collapse, kink or infolding	— Stent compression, collapse, kink or infolding	— Stent fracture		— Crush resistance, compression resistance, radial force, as appropriate — Simulated use
	Inadequate treatment of the lesion (e.g. dissection, residual stenosis, occlusion)	— None	— None	— Vessel thrombosis — Dissection creation or extension — Foreign body embolization — Restenosis — Thrombosis — False lumen patency — False lumen perfusion	— Simulated use — Kink resistance — Crush resistance, compression resistance, radial force, as appropriate — Stent-free surface area and stent outer surface area

Table A.3 *(continued)*

Device/ procedure related function(s)	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing
		Device effect(s) of failure		Clinical effect(s) of failure	
		Initial effect(s)	Subsequent effect(s)		
Magnetic resonance imaging (MRI) safety	Heating	— None	— None	— Vascular injury — MR related	— MR safety — MR for a stent used in combination with an endovascular prosthesis
	Lack of quality MR imaging	— None	— None	— Inability to monitor stent over time with MR imaging — Inadequate MR imaging	
	Movement of stent	— Stent migration	— None	— Vascular injury — MR related	

A.2 Device-specific evaluation strategy table

A.2.1 General and focused device evaluation strategy

For a specific device design either a focused device evaluation strategy or a comprehensive device evaluation strategy table may be used to provide the rationale for the testing strategy for the device. The focused device evaluation strategy table may be more efficient for device designs when there are discrete design characteristics that may affect device performance that may require specific testing, or for modifications in the device design or intended use resulting in the need to conduct testing associated with the modifications, rather than repeating all of the testing listed in this document. The comprehensive device evaluation strategy table is recommended for device designs that are significantly different from available technology.

The information provided in Tables A.2 and A.3 may be of use in populating the device-specific evaluation strategy table. The nonclinical testing column may include information on preclinical *in vivo* evaluation of the device as related to the evaluation of a particular attribute or potential failure mode, as well as bench tests and analyses as shown in Tables A.2 and A.3.

For a new device, it may be most efficient to provide a device evaluation strategy table that is focused on the unique aspects of a device design. This would involve first describing the potential effect of the *in vivo* environment on the device (Table A.5) and presenting a device evaluation strategy table that only includes information specific to the unique aspects of the device and the proposed intended use (Table A.8).

For a device design modification or change in intended use, a similar approach can be taken, describing the change in the device and/or intended use (Table A.6 and/or Table A.7, as applicable) and presenting a device evaluation strategy table (Table A.8) that only includes information specific to the modifications.

The three categories of focused device evaluation strategy and the associated evaluation guidance tables are described in Table A.4.

Table A.4 — Focused device evaluation strategy of table applicability

	Table A.5 — Effects of the *in vivo* environment on the device evaluation	Table A.6 — Design comparison between a previously evaluated device and the modified device	Table A.7 — Indication for use comparison of a previously evaluated device and the study device	Table A.8 — Focused device evaluation strategy table
New device	☑			☑
Device design modification		☑		☑
Change in intended use			☑	☑

A.2.1.1 Identification of potentially affected attributes for focused device evaluation strategy

Information to support the focused device evaluation strategy table should include identification of unique or changed parameters and the associated procedure-related functions or performance-related functions required for the device to achieve the desired performance that could be affected by the parameters. For a new device, this would involve addressing the *in vivo* environment per A.2.1.1.1. For a device design modification or change in intended use, this would involve addressing the differences between the modified and previously evaluated device per A.2.1.1.2.

The respective tables should be complemented by a rationale to explain why other attributes would not likely be affected by the unique device characteristics or changes in the device and/or the indications for use.

A.2.1.1.1 *In vivo* environment

To aid in explaining why the testing strategy for a device is adequate, it may be helpful to identify the unique aspects of the proposed intended use that could have an impact on the device evaluation strategy, the specific parameters that are associated with each aspect, the attributes of the device and procedure that could be affected by the parameter, and the test methods that could be impacted by the *in vivo* conditions. This helps to explain why some testing is needed and how tests are designed to simulate *in vivo* conditions. An example of this table is provided in Table A.5.

Table A.5 — Effects of the *in vivo* environment on the device evaluation

Unique aspects of the intended use	*In vivo* parameters	Potentially affected attributes	Affected test methods
List each unique aspect associated with the intended use (e.g. implant location, disease state, lesion type) that may be important in assessing device performance.	Identify each *in vivo* parameter that could be affected by the unique aspect. Examples of in vivo parameters include blood vessel sizes, angulation, movement, tortuosity, compliance, and flow characteristics.	List each procedure-related function or performance-related function required for the device to achieve the desired performance that could be affected by the *in vivo* parameter.	List the tests associated with the evaluation of the attributes that would be affected by the *in vivo* parameters.

A.2.1.1.2 Device design or intended use comparison

For a device design modification or change in the intended use, any design differences and differences in the intended *in vivo* environment should be described with identification of the attributes of the device and procedure that could be affected by the differences and the tests that would be associated with the evaluation of the attribute. Examples of these tables are provided in Tables A.6 and A.7.

Table A.6 — Design comparison between a previously evaluated device and the modified device

Device design rationale	Design difference	Comparison of design feature characteristics		Potentially affected device/procedure-related functions	Affected tests
		Previously evaluated device name	Modified device name		
State the expected benefits of the modified device design as compared to the previously evaluated device. Examples of expected benefits of design differences include reduced crossing profile, improved apposition, and improved deployment accuracy.	List each design feature that is different between the previously evaluated device and modified device to achieve the benefit. Examples of design feature differences include stent material and stent geometry.	Provide a detailed description of relevant design feature characteristics of the previously evaluated device, including quantitative values as appropriate. Examples of design feature characteristics that may be associated with a stent material and geometry include stent material processing, stent wall thickness, and cell design.	Provide a detailed description of the design feature characteristics of the modified device, including appropriate quantitative values.	List each device-related and procedure-related function that could be affected by the design difference.	List the tests associated with the evaluation of the attributes that would be affected by the design difference.

Table A.7 — Indication for use comparison of a previously evaluated device and the study device

Differences in the *in vivo* environment	Comparison of *in vivo* parameters		Potentially affected device/procedure-related functions	Affected tests
	Prior intended use	New intended use		
List each *in vivo* parameter associated with the different intended use (e.g. implant location, anatomical dimensional requirements, disease state, lesion type) that may be important in assessing device performance. Examples of *in vivo* parameters include blood vessel sizes, angulation, movement, tortuosity, compliance, and flow characteristics.	Describe the *in vivo* parameter for the previously evaluated intended use.	Describe the *in vivo* parameter for the new intended use.	Identify each individual device-related and procedure-related function that could be affected by the difference of the *in vivo* parameter.	List the tests associated with the evaluation of the attributes that would be affected by the difference of the *in vivo* parameters.

A.2.1.2 Focused device evaluation strategy table

A focused device evaluation table should address the device-related and procedure-related attributes identified in the tables described in A.2.1.1, as applicable, as well as attributes that are relevant to the unique aspects of the device design.

The columns for a device-specific device evaluation strategy table may include those outlined in Table A.1; however, additional columns may be added. For example, a column identifying the unique or modified device characteristics is needed to focus the table on relevant attributes. In addition, a column on device design information may be included that identifies the key design characteristics intended to provide the function or to address or mitigate the potential failure mode. This column may also include relevant information about the design of the device (i.e. design input) that will aid in understanding

the testing selected to address the attribute or potential failure mode. An example of the columns for a focused device evaluation strategy table is provided in Table A.8.

Table A.8 — Focused device evaluation strategy table

Unique or modified design feature or difference in the *in vivo* environment	Device or procedure-related attribute that could potentially be impacted by the unique characteristics or differences or the new intended use	Potential failure modes	Potential effects of failure		Device design information	Value of information from previously evaluated device for modified devices	Nonclinical device testing
			Potential device effects of failure	Potential clinical effects of failure			
Identify each unique or modified design feature or each difference in the *in vivo* environment, as applicable.	List each device-related and procedure-related function or feature that could be affected by the device design or the difference(s) identified in A.2.1.	State the failures that might occur and could result in consequences (effects) to the device or patient if the function is not maintained or improved.	List the potential effect(s) of the failure mode on the device. Describe any potential difference in the type or severity of the device effects of failure as compared to the previously evaluated device for modified devices.	List the potential effect(s) of the failure mode on the patients. Describe any potential differences in the type and severity of the clinical effects of failure as compared to the previously evaluated device for modified devices.	Discuss the relevant information considered in the design of the device to provide the function or mitigate the potential failure mode or to explain why the function will be maintained or improved for a modified device.	Provide an explanation regarding how information obtained from the assessment of the previously evaluated device is informative.[a]	Identify the bench tests and analyses appropriate to evaluate the function and the potential failure mode(s). Take into consideration the information available from a previously evaluated device, if applicable.

[a] For example, explain how the information from the previously evaluated device reflects on:

— the potential for the device to achieve the desired function,

— the likelihood of the device to pose a significant safety risk, or

— the appropriate testing to address the desired function of the device (e.g. information may be available to indicate that one or two tests are most relevant to assess a specific attribute to predict clinical performance).

A.2.2 Comprehensive device evaluation strategy

It may be helpful to support a comprehensive device evaluation strategy by providing information on the *in vivo* conditions applicable to the intended use for a device, as described in A.2.1.1.1.

A comprehensive device evaluation strategy should address all device-related and procedure-related attributes applicable to the device. The columns for the comprehensive device evaluation strategy table may include those outlined in Table A.1, with the addition of a column for the device design information.

A.3 Testing summary

It is helpful to clarify the applicability of each test described in this document to a specific device or modification and to state if and how the test protocol was tailored for the device design, implant location or intended use, and to identify any additional tests that have been conducted. This is best presented in tabular format with the following information: the tests (i.e. standard testing and additional tests); the purpose of the test; an explanation of the applicability of each standard test to the device; and a brief

description of how a test has been designed to incorporate unique aspects of the device design or the intended use/implant location. An example of this table is provided in Table A.9.

Table A.9 — Test summary

Test	Purpose of test	Applicability	Impact of device design or implant location
List the tests from this document (see Annex D) and any additional tests.	State the purpose of each test.	Discuss if each of the standard tests are applicable to the device or modification.	Discuss if the test protocol for each standard test has been modified or how each new test has been designed to incorporate the device design or implant location/intended use.

Annex B
(informative)

Description of clinical effects of failure

NOTE Table B.1 includes effects of failure that can be relevant to a stent depending on the stent design and intended clinical use. Table B.2 includes additional effects of failure that can be relevant to a stent used with an endovascular prosthesis or for the treatment of aneurysms or aortic dissections.

Table B.1 — Descriptions of clinical effects of failure

Event	Description
Adverse biological response	Unspecified clinical adverse event caused by use of a non-biocompatible material. NOTE This clinical effect is not commonly reported. It is often not possible to link an adverse event to a particular material. These events are mitigated through appropriate biocompatibility testing.
Amputation	Removal of a body part due to a failure of the effectiveness of the device.
Aneurysm/ pseudoaneurysm formation	Pseudoaneurysm formation at the implantation site due to delayed healing around the stent.
Blood loss	Any blood loss requiring intervention (i.e. transfusion, medical therapy, surgical repair).
Branch vessel obstruction	Clinically significant, unplanned obstruction of blood flow of a major branch vessel.
— Arterial branch vessel obstruction	Clinically significant, unplanned obstruction of blood flow of an arterial branch vessel.
— Tributary branch vessel obstruction	Clinically significant, unplanned obstruction of blood flow of a venous branch vessel.
Cardiac dysfunction	Right heart dysfunction due to stent embolization.
Embolism	Migration of intraluminal debris (e.g. thrombus, atheromas material) in the presence of clinical sequelae.
Failure to complete device implantation	Inability to implant a stent due to an inability to access the intended implantation site or to deploy the stent.
Foreign body embolization	Intraluminal migration of a stent, fragments of the stent, or pieces of the stent system (e.g. balloon fragments, pieces of a delivery system).
Inability to monitor stent over time	Inability to monitor device integrity and position over time due to an inability to visualize the stent.
Inadequate MR imaging	Inability to obtain quality MR imaging due to distortion or imaging artefact caused by the stent.
Insertion site infection	Development of an infection at the insertion site of the stent system.
Revascularization	A repeat procedure (percutaneous or surgical) to restore blood flow.
— Clinically-driven target lesion revascularization	A repeat procedure (percutaneous or surgical) of the original lesion site due to worsening clinical symptoms (e.g. pain, wounds).
— Target lesion revascularization	A repeat procedure (percutaneous or surgical) of the original lesion site.
— Target vessel revascularization	A repeat procedure (percutaneous or surgical) of a lesion in the target vessel.
Stent patency loss or reduction	Limited or no flow through the stent.
— Lumen obstruction	Blockage of the lumen of a stent by physical (e.g. kink, twist, collapse), rather than physiological, means.

Table B.1 *(continued)*

Event	Description
— Restenosis	Significant reduction in luminal diameter when compared to the reference diameter.
— In-segment restenosis	Significant reduction in luminal diameter at any point along the length of the stent in addition to any reduction in luminal diameter within the non-stented adjacent sections of the vessel, when compared to the post-procedural reference diameter.
— In-stent restenosis	Significant reduction in luminal diameter at any point along the length of the stent when compared to the post-procedural reference diameter.
— Stent occlusion	Complete blockage of the stent lumen.
— Thrombosis	Haemodynamically significant thrombus formation within the lumen of the stent.
— Acute thrombosis	Haemodynamically significant thrombus formation within the lumen of the stent up to 24 h after stent implantation.
— Subacute thrombosis	Haemodynamically significant thrombus formation within the lumen of the stent between 24 h and 30 d after stent implantation.
— Late stent thrombosis	Haemodynamically significant thrombus formation within the lumen of the stent between 30 d and 1 year after stent implantation.
— Very late thrombosis	Haemodynamically significant thrombus formation within the lumen of the stent beyond 1 year after stent implantation.
Vascular trauma	Injury to a vessel as a result of the stent procedure.
— Access vessel trauma	Injury to a vessel at the access site during the stent procedure which may result in hematoma, false aneurysm or arteriovenous fistula.
— Procedural dissection	Tear of the vessel wall during the stenting procedure.
— Vascular injury — MR related	Injury to a vessel due to heating or device movement during MR imaging.
— Vessel rupture	Rupture of a vessel due to excessive ballooning.

Table B.2 — Additional descriptions of clinical effects of failure specific to a stent used in combination with an endovascular prosthesis or a stent used to treat an aneurysm or aortic dissection

Event	Description
Aneurysm enlargement	Any enlargement of the diameter or volume of the aneurysm sac greater than documented measurement error, as determined by contrast-enhanced CT or other appropriate modality.
Aneurysm rupture	Rupture of the treated, native aneurysm sac.
Aortic enlargement	An increase in aortic diameter in a specific segment greater than documented measurement error as compared to the baseline measurement after treatment. Examples of segments include the aneurysm neck and, for the treatment of dissections, the treated segment.
Dissection creation or extension	Creation or extension of a tear within the vessel wall. A dissection can propagate antegrade, retrograde or in both directions.
— Procedural dissection	Creation or extension of a dissection during the stenting procedure.
— Post-procedural dissection	Creation or extension of a dissection due to the creation of a new entry tear at the margins of the stent post procedure.
False lumen patency	Persistence of blood flow into the false lumen after treatment of dissection resulting in lack of complete thrombosis.
— Patent false lumen	Flow present throughout the aortic false lumen in the absence of evidence of thrombus, within a specific segment of the aorta.

Table B.2 *(continued)*

Event	Description
— Partially thrombosed false lumen	Thrombus within the aortic false lumen that has a residual patent flow channel, within a specific segment of the aorta.
False lumen perfusion (FLP)	Persistence of blood flow into the false lumen from any source after treatment of a dissection, analogous to endoleaks for the treatment of aneurysms.
— Primary intimal tear (PIT FLP)	Flow from a proximal aortic source through the primary intimal tear (PIT), into the aortic false lumen (similar to a Type Ia endoleak after treatment of aneurysms).
— Proximal aorta (PA FLP)	Flow from an aortic source proximal to the treated segment, through an entry tear proximal to the PIT, into the aortic false lumen.
— Distal aorta (DA FLP)	Flow from an aortic source distal to the primary entry tear through fenestrations in the dissection septum, secondary aortic tears, or re-entry points, into the aortic false lumen.
— Distal aorta (DA FLP)a	Flow from an aortic source through fenestrations in the dissection septum, secondary aortic tears, or re-entry points, into the aortic false lumen within the treated segment.
— Distal aorta (DA FLP)b	Flow from an aortic source through fenestrations in the dissection septum, secondary aortic tears, or re-entry points, into the aortic false lumen distal to the treated segment.
— Proximal branch (PB FLP)	Flow into the aortic false lumen via retrograde flow from aortic arch branch vessels.
— Distal branch (DB FLP)	Flow into the aortic false lumen via retrograde flow from distal branch vessels in the chest (intercostals), abdomen (e.g. mesenteric, renal), or pelvis (iliac).
Stented branch vessel loss of patency	Reduction of blood flow in a stented branch vessel when the stent is used in combination with an endovascular prosthesis.
Stent-related endoleak	Persistence of blood flow abluminal to the endovascular prosthesis.
— Stent-related type IIIa	An endoleak arising from an inadequate seal between a stent and the endovascular prosthesis (e.g. an endoleak at the junction of a renal stent and the fenestration in an endovascular prosthesis).
— Stent-related type IIIb	An endoleak arising from holes in the graft material due to wear between a stent and an endovascular prosthesis.

Annex C
(informative)

Description of device effects of failure

NOTE Table C.1 includes effects of failure that can be relevant to a stent depending on the stent design and intended clinical use. Table C.2 includes additional effects of failure that can be relevant to a stent used with an endovascular prosthesis or for the treatment of aneurysms or aortic dissections.

Table C.1 — Description of device effects of failure

Event	Description
Access failure	Failure to reach the intended site with the stent system due to mechanical failure or patient anatomy.
Accessory device failure	Inability to use the accessory device as intended due to mechanical failure.
Active fixation element (hook/barb) fracture	Fracture or breakage of a positive fixation element (e.g. hook, barb).
Balloon rupture	Bursting of a balloon used in the deployment, post-dilation or touch-up of a stent.
Delivery system damage	Damage incurred to the delivery system (e.g. kink, bond failures, complete tip separation).
Deployment failure	Inability to deploy the stent per the instructions for use.
— Balloon-related deployment failure	Inability to fully deploy the stent due to balloon failure.
— Delivery system-related deployment failure	Inability to deploy the stent at the intended site due to mechanical failure.
— Inability to deploy	Inability to deploy the stent at the intended site due to patient anatomy.
Inaccurate deployment	Improper positioning, configuration or orientation of the stent during deployment.
Lack of apposition to the vessel wall	Incomplete or a loss of contact of the stent to the vessel wall.
Loss of stent integrity	Fracture or breakage of the stent.
— Bond fracture	Fracture or breakage of bonds (e.g. welds) between support structure components.
— Connector or link break or fracture	Fracture or breakage of connectors or links between stent rings or stent struts.
— Strut fracture	Fracture or breakage of stent struts.
Particulate generation	Embolization of particles or particulate matter associated with the stent system.
— Acute particulate generation	Embolization of particles during stent advancement, deployment, and withdrawal.
— Chronic particulate generation	Embolization of particles over time from the stent.
Poor apposition between stents	Incomplete apposition between overlapping stents (e.g. shelving).
Stent compression, collapse, kink or infolding	Significant reduction in luminal diameter due to compression, collapse, kink or infolding. Contributing factors may include excessive oversizing, local compression or increased stiffness at the overlap region between stents.
Stent damage	Damage to the stent incurred during access or withdrawal of the delivery system.
Stent displacement	Movement of the expanded stent from its intended implantation site during withdrawal of the delivery system.
Stent dislodgement from the delivery system	Inability to deploy a stent at the intended site due to movement of a pre-mounted stent from the crimped position on a nonexpanded balloon.

Table C.1 *(continued)*

Event	Description
Stent embolization	Embolization of the stent from the intended implantation site that affects a downstream organ (e.g. heart).
Stent migration	Movement of the stent from the intended implantation site.
Stent separation	Separation between overlapping stents.

Table C.2 — Additional descriptions of device effects of failure specific to a stent used in combination with an endovascular prosthesis or a stent used to treat an aneurysm or aortic dissection

Event	Description
Branch vessel stent compression or kink	Clinically relevant reduction in luminal diameter of a stent due to compression or kink (e.g. due to migration of the main body component of an endovascular prosthesis).
Component separation	Separation between a stent and an endovascular prosthesis.
Poor apposition between components	Incomplete apposition between a stent and an endovascular prosthesis.
Stent-related graft material holes	Holes in the graft material due to wear between a stent and an endovascular prosthesis.
Support structure fracture	Fracture or breakage of the support structure of an endovascular prosthesis (e.g. fixation system) due to wear between a stent and an endovascular prosthesis.

Annex D
(informative)

Test methods

D.1 General

The information included in this annex is intended to provide guidance for preclinical *in vitro* testing performed in order to verify the design of the stent system. Guidance for reporting the test results is also provided. It is recognized that not all of the tests described in this annex are applicable to all system designs. It is also recognized that testing intended to ensure that the device meets specifications during manufacture may be conducted in accordance with the details outlined in this annex.

NOTE 1 Specific guidance for preclinical *in vitro* testing of stents used in combination with endovascular prostheses are not included in this annex or in ISO 25539-1:2017, Annex D. Methods presented in these annexes can be used to develop appropriate tests to verify the design of stents and endovascular prostheses used in combination.

Guidance for developing appropriate test methods is included in this annex allowing flexibility in designing appropriate methodologies for specific device designs and indications for use. To ensure consistency in the testing of devices, use of the methods developed based on the steps and concepts outlined in this annex is recommended. If alternative methods are employed, these methods should be justified. It is recognized that some tests listed in this annex can be combined. For combined tests, the report should provide the individual test results for each of the tests listed in this annex, if appropriate.

As identified in Table D.1, some requirements in the body of this document do not have an associated test method guidance in this annex, as the methodologies are better addressed by other standards (e.g. MRI safety).

Modifications to existing test methods or inclusion of additional test methods might be required for various stent system designs. When identifying testing conditions, attention should be paid to the relevant physiological conditions. A simulated physiological environment (e.g. a temperature-controlled water bath) should be used when appropriate.

To ensure valid results, measurement equipment used during testing should have appropriate accuracy, and be calibrated or verified against traceable measurement standards, as appropriate. The accuracy should be adequate to determine the measured value relative to the acceptance criteria.

NOTE 2 Although this is an informative annex, the terms “should” and “shall” are used to differentiate between considerations and critical components of the methods, respectively.

D.2 Sampling

A sampling plan should be utilized which ensures 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 are representative of the devices to be released for distribution, including all sizes, configurations and components.

If the purpose of the test is to evaluate the interaction between modular components (e.g. separation force between a stent and an endovascular prosthesis used in combination) or overlapping stents or if the attribute under test could be significantly affected by the overlap (e.g. kink resistance), the test articles should include overlapped stents.

The sampling should fully represent the range of device sizes and might 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. A rationale should be provided for sample selection.

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

The need for testing of more than one area in a stent to ensure adequate characterization for some parameters (e.g. flared end of stent) should be considered in establishing the sampling plan.

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

Additional recommendations regarding sampling may be included in individual test methods, as appropriate.

NOTE Additional guidance regarding sampling can be found in ASTM F3172.

D.3 Conditioning of test samples

All samples should be subjected to sterilization, including multiple sterilizations, if appropriate, unless justification is provided for use of non-sterilized products.

Samples should be subjected to conditions that are normally encountered and that can affect the 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, and deployment of the stent in an environment with physiologically relevant temperature.

D.4 Reporting

For the purposes of this annex, reporting relates to requests from a national regulatory authority.

The design evaluation report should include an appropriate table of contents and four main sections: (1) background, (2) an executive summary, (3) individual test summaries, and (4) 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 and justification for the selection of test articles (e.g. sizes, conditioning);
- acceptance criteria, if applicable:
  - the International Standard used (i.e. ISO 25539-2:2020);
  - the method used (if the standard includes several);
  - the result(s), including a reference to the clause which explains how the results were calculated;
  - any deviations from the procedure;
  - any unusual features observed;
  - the date of the test.
  - 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.

D.5 Test method development guidance

D.5.1 General

Clause D.5 lists guidelines for tests where appropriate. An index of test methods is given in Table D.1. Additional guidance for developing test methods can be found in the informative standards listed in Table D.1. These standards are included for reference purposes and are not required for conformance to this document.

Table D.1 — Index of test methods

Design evaluation subclause	Tests	Annex D subclause	Informative reference
8.5.1	Stent system and delivery system	D.5.2	
8.5.1.1	Balloon testing	D.5.2.2	

Table D.1 *(continued)*

Design evaluation subclause	Tests	Annex D subclause	Informative reference
8.5.1.1.1	Balloon deflation time	D.5.2.2.2	
8.5.1.1.2	Balloon rated burst pressure	D.5.2.2.3	
8.5.1.1.3	Balloon rated fatigue	D.5.2.2.4	ISO 10555-4
8.5.1.1.4	Dogboning	D.5.2.2.5	
8.5.1.2	Dimensional verification of the stent system	D.5.2.3	ASTM F2081
8.5.1.3	Dislodgement force (pre-mounted, balloon-expandable stents)	D.5.2.4	ASTM F2394
8.5.1.4	Force to deploy (self-expanding stents)	D.5.2.5	
8.5.1.5	Acute particulate generation	D.5.2.6	For drug-eluting, absorbable, and coated stents: ASTM F2743 AAMI TIR42 ISO 12417-1 ISO/TS 17137 ISO 17327-1
8.5.1.6	Profile effect/flaring (balloon-expandable stents)	D.5.2.7	
8.5.1.7	Simulated use	D.5.2.8	
8.5.1.8	Tensile bond strength	D.5.2.9	ISO 10555-1
8.5.1.9	Torsional bond strength	D.5.2.10	ISO 10555-1
8.5.1.10	Haemostasis	No test method proposed. May evaluate as part of *in vivo* animal study or alternative.	
8.5.1.11	Biocompatibility	See ISO 10993-1 and other appropriate parts.	
8.5.1.12	Sterilization assurance	See appropriate international standards.	
8.5.1.13	Visibility	D.5.2.11	ASTM F640
8.5.2	Stent	D.5.3	
8.5.2.1	Corrosion	D.5.3.1	See test method D.5.3.1.5.
8.5.2.2	Fatigue and durability —computational analyses	D.5.3.2	ASTM F2514 ASTM F3211 ASME V&V40
8.5.2.3	Fatigue and durability — *in vitro* testing	D.5.3.3	
8.5.2.3.1	General	D.5.3.3.1	ASTM F2477 ASTM F2942 ISO/TS 17137 ASTM F3211
8.5.2.3.2	Radial fatigue and durability	D.5.3.3.2	ASTM F2477
8.5.2.3.3	Axial fatigue and durability	D.5.3.3.3	ASTM F2942
8.5.2.3.4	Bending fatigue and durability	D.5.3.3.4	ASTM F2942
8.5.2.3.5	Torsional fatigue and durability	D.5.3.3.5	ASTM F2942
8.5.2.3.6	Compression fatigue and durability	D.5.3.3.6	
8.5.2.4	Patency-related tests	D.5.3.4	

Table D.1 *(continued)*

Design evaluation subclause	Tests	Annex D subclause	Informative reference
8.5.2.4.1	Compression resistance to perpendicularly-applied load (self-expanding stents)	D.5.3.4.1	
8.5.2.4.2	Crush resistance with perpendicularly-applied load (balloon-expandable stents)	D.5.3.4.2	
8.5.2.4.3	Crush resistance with radially-applied load (balloon-expandable stents)	D.5.3.4.3	ASTM F3067
8.5.2.4.4	Radial force (self-expanding stents)	D.5.3.4.4	ASTM F3067
8.5.2.4.5	Kink resistance (flexibility)	D.5.3.4.5	
8.5.2.4.6	Stent-free surface area and stent outer surface area	D.5.3.4.6	ASTM F2081
8.5.2.5	Sizing-related testing	D.5.3.5	
8.5.2.5.1	Dimensional verification of stent	D.5.3.5.1	ASTM F2081
8.5.2.5.2	Stent diameter to balloon inflation pressure (balloon-expandable stents)	D.5.3.5.2	
8.5.2.5.3	Stent length	D.5.3.5.3	
8.5.2.5.4	Recoil (balloon-expandable stents)	D.5.3.5.4	ASTM F2079
8.5.2.6	Magnetic resonance imaging (MRI) safety	See appropriate international standards.	
8.5.2.7	Stent and an endovascular prosthesis in combination	Parallel methods from this document may be used to aid in developing appropriate test methods. For separation force, additional guidance may be found in ISO 25539-1:2017, 8.5.2.4.3 and D.5.2.4.3.	
8.5.3	Absorbable stents and stents containing an absorbable coating	N/A	ISO/TS 17137
8.5.4	Coating on a delivery system	N/A	
8.5.5	Coating on a stent	N/A	ISO 17327-1
8.5.6	Drug-eluting stent	N/A	ISO 12417-1

D.5.2 Stent system and delivery system

D.5.2.1 General

The subclause D.5.1 describes testing that includes the stent system, the delivery system without the stent, and balloons integral to the stent system.

D.5.2.2 Balloon testing

D.5.2.2.1 General

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

D.5.2.2.2 Balloon deflation time

D.5.2.2.2.1 Purpose

The purpose of this test is to determine the time required to deflate the balloon when inside of the stent.

D.5.2.2.2.2 Materials

The following materials apply:

— stent system;

— recommended guidewire or equivalent;

— temperature-controlled water bath (37 ± 2) °C;

— contrast medium as specified in the IFU or fluid with equivalent viscosity;

— inflation device fitted with a means of measuring pressure, and of maintaining the inflation pressure;

— timer with an accuracy of ±1 s.

D.5.2.2.2.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.2.2.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.2.2.5 Test method

Develop a test method based on the following steps:

a) For balloon-expandable stent, submerge the stent in the water bath and complete any pre-balloon inflation steps per the IFU.

b) Inflate the balloon in accordance with the IFU.

c) Deflate the balloon in accordance with the IFU and record the time it takes to deflate the balloon to the pre-determined end point representative of a deflated condition.

D.5.2.2.2.6 Expression of results

The deflation time should be expressed in seconds (s).

D.5.2.2.2.7 Test report

The test report shall be in accordance with Clause D.4 and include the maximum, minimum, mean and standard deviation of the balloon deflation time. The definition of the deflation end point and the fluid used for inflation shall also be reported.

D.5.2.2.3 Balloon rated burst pressure

D.5.2.2.3.1 Purpose

The purpose of this test is to determine rated burst pressure (RBP) of the balloon when inside of the stent.

D.5.2.2.3.2 Materials

The following materials apply:

— stent system;

— recommended guidewire or equivalent;

— temperature-controlled water bath (37 ± 2) °C;

— fluid for inflation (e.g. room temperature water);

— pressure gage;

— inflation device fitted with a means of measuring pressure and capable of maintaining the inflation pressure;

— timer with an accuracy of ±1 s.

D.5.2.2.3.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.2.3.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.2.3.5 Test method

Develop a test method based on the following steps:

a) For balloon-expandable stents complete any pre-inflation steps per the IFU.

b) Since balloon behaviour might be affected by temperature, submerge the stent system in the water bath for a minimum of 2 min. Initiate inflation of the balloon, bringing the balloon to the nominal inflation pressure.

c) Inflate the balloon using a clinically relevant pre-determined pressure profile versus time (e.g. 10 s at each selected pressure increment).

d) Monitor the system for decrease in pressure due to a persistent leak, rupture, or other failure mode (e.g. shaft failure, seal leak).

e) Repeat steps c) and d) until a decrease in pressure due to a persistent leak, rupture, or other failure mode is detected.

f) Record the burst pressure and describe the location and failure mode [e.g. shaft failure, seal leak, balloon rupture (including orientation of rupture), or fragmentation].

g) Determine the rated burst pressure. The rated burst pressure (P_{rb}) is based upon the results of this testing that shows statistically with at least a 95 % confidence that 99,9 % of the balloons will not burst at or below this pressure. The P_{rb} can be calculated in the following manner using a one-sided tolerance limit for a normal distribution:

$$P_{rb} = X - K(D_s)$$

where

X is the mean balloon burst pressure (P_{mb});

D_s is the standard deviation of balloon burst pressure;

K is the factor of one-sided tolerance limit for a normal distribution (K is found in statistical tables and is dependent on P, C, and N);

P is the 0,999 (99,9 % reliability);

C is the 0,95 (95 % confidence);

N is the number of balloons tested.

D.5.2.2.3.6 Expression of results

The burst pressures should be expressed in atmospheres (atm) or kilopascals (kPa).

D.5.2.2.3.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the mean burst pressure (MBP), the calculated RBP, the maximum, minimum, and standard deviation of the burst data and observed failure modes.

D.5.2.2.4 Balloon rated fatigue

D.5.2.2.4.1 Purpose

The purpose of this test is to 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 for balloon-expandable stents.

D.5.2.2.4.2 Materials

The following materials apply:

— stent system;

— recommended guidewire or equivalent;

— temperature-controlled water bath (37 ± 2) °C;

— fluid for inflation (e.g. room temperature water);

— leak detection mechanism (e.g. dye in the test fluid, pressure gage, flow rate monitor);

— inflation device, fitted with a means of measuring pressure, and capable of maintaining the inflation pressure;

— compliant tube (with a clinically relevant radial compliance) of a diameter which represents the largest recommended vessel diameter for the stent under test, if necessary to keep the stent from moving excessively during the inflation cycles;

— timer with accuracy of ±1 s.

D.5.2.2.4.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.2.4.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.2.4.5 Test method

Develop a test method based on the following steps:

a) Submerge the stent system in the water bath and deploy the stent in the water bath or in the compliant tube, as appropriate, inflating the balloon using a clinically relevant rate, to the rated burst pressure, maintain pressure for a minimum of 10 s or for the length of time stated in the IFU.

b) Deflate the balloon.

c) Repeat steps a) and b), with the balloon inside of the stent, a clinically relevant number of inflation cycles. The number of inflation cycles may be more than the number expected clinically in order to provide an appropriate factor of safety.

d) If any persistent leak or decrease of pressure occurs during testing, record the number of cycles and the mode of failure [e.g. seal leak, balloon rupture (including orientation of rupture), or fragmentation]. Any such leak or decrease in pressure due to failure of the balloon, shaft, proximal seal, or distal seal, should be considered a failure in this test.

D.5.2.2.4.6 Expression of results

Pressure shall be expressed in atmospheres (atm) or kilopascals (kPa).

D.5.2.2.4.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the number of cycles successfully completed, the maximum number of cycles expected clinically, any observed failure modes, and the maximum inflation pressure. The selected tube diameter(s), if used for testing, shall be justified.

NOTE Additional information regarding balloon rated fatigue can be found in ISO 10555-4.

D.5.2.2.5 Dogboning

D.5.2.2.5.1 Purpose

The purpose of this test is to determine the diameter(s) of the balloon extending beyond the ends of the stent that are greater than the stent outer diameter(s) at the maximum recommended inflation pressure (e.g. rated burst pressure).

D.5.2.2.5.2 Materials

The following materials apply:

— stent system;

— recommended guidewire, or equivalent, as appropriate;

— temperature-controlled environment (37 ± 2) °C;

— fluid for inflation (e.g. room temperature water.);

— inflation device fitted with a means of measuring pressure and capable of maintaining the inflation pressure;

— measuring equipment for diameters (e.g. micrometre, optical profile projector, laser-micrometre, appropriate profile hole gauges).

D.5.2.2.5.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.2.5.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.2.5.5 Test method

Develop a test method based on the following steps:

a) Prepare the stent system.

b) Insert the appropriate guidewire in the device, as appropriate, in accordance with the IFU.

c) Place the device in the temperature-controlled environment.

d) Allow to equilibrate to test temperature.

e) Inflate the balloon, using a clinically relevant rate, to the maximum pressure as indicated in the IFU, maintaining pressure for a minimum of 30 s, or for the inflation time stated in the IFU. That is, if the inflation time stated in the IFU is longer than 30 s, that longer time should be used for this test, unless adequate justification is provided for using a shorter duration.

f) While the balloon is at the maximum recommended inflation pressure (e.g. rated burst pressure), measure the maximum balloon outer diameter at both ends; for each end of the stent, measure the outer stent diameter in two perpendicular directions, and determine the average, then calculate the difference between the balloon and stent outer diameter for each end.

D.5.2.2.5.6 Expression of results

Balloon and stent outer diameter (OD) shall be expressed in millimetres (mm). Pressure shall be expressed in atmospheres (atm) or kilopascals (kPa).

D.5.2.2.5.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the maximum, minimum, mean and standard deviation of the measured diameter differences at the balloon ends. The maximum inflation pressure at which measurements were made shall be identified.

D.5.2.3 Dimensional verification of the stent system

D.5.2.3.1 Purpose

The purpose of this test is to determine the stent system dimensions, including the usable or working length, profile, and all other appropriate dimensions, for conformance with design specifications.

D.5.2.3.2 Materials

The following materials apply:

— stent system;

— equipment for establishing the profile of the stent system:

  — measuring equipment for diameters (e.g. micrometre, optical profile projector, laser-micrometre);

  — appropriate profile hole gauges;

— measuring equipment for length.

D.5.2.3.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.3.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.3.5 Test method

Develop a test method based on the following:

a) Establish the profile of the stent system along the usable or working length using one of the following methods:

   1) measure the maximum outer diameter of the stent system using the appropriate measuring instrument; or

   2) verify that the outer diameter fits through the appropriately sized profile hole gauge.

   Consideration should be given to the potential for asymmetry.

b) Measure the usable or working length of the stent system using an appropriate measuring instrument.

c) Measure all other appropriate dimensions.

D.5.2.3.6 Expression of results

Length shall be expressed in centimetres (cm). Other dimensions shall be expressed in millimetres (mm).

D.5.2.3.7 Test report

The test report shall be in accordance with Clause D.4. The test report shall include the maximum, minimum, mean and standard deviation of all measured dimensions and the results of any verified dimensions (e.g. pass-through hole gauge).

NOTE Additional information regarding dimensional verification can be found in ASTM F2081.

D.5.2.4 Dislodgement force (pre-mounted, balloon-expandable stents)

D.5.2.4.1 Purpose

The purpose of the test is to determine the force required to displace the pre-mounted stent from its position on the non-expanded balloon.

D.5.2.4.2 Materials

The following materials apply:

— stent system;

— temperature-controlled environment (37 ± 2) °C;

   — mechanical testing system equipped with a suitable load cell, a constant rate of traverse and suitable gripping fixture for the balloon catheter;

   — a fixture that allows the stent to be removed from the balloon, while minimizing interaction between the balloon and the fixture;

— recommended guidewire or equivalent;

D.5.2.4.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.4.4 Conditioning

Conditioning shall be in accordance with Clause D.3 and shall include tracking through a tortuous anatomical model in a temperature-controlled water bath using appropriate accessory devices (e.g. introducer sheath).

D.5.2.4.5 Test method

Develop a test method based on the following steps:

a) Insert the guidewire into the stent system.

b) Secure the stent in the stent gripping fixture within the water bath or other appropriately justified test environment.

c) Attach the tip or the shaft of the delivery system to the other grip of the testing system.

d) Activate the test system to separate the stent from the delivery system using a constant crosshead speed (e.g. 200 mm/min).

e) Record the force until the stent moves beyond a pre-specified critical distance (e.g. the margin of the balloon) or until a clinically acceptable load is achieved.

f) Repeat steps a) to e), using a new sample, reversing the direction of load application (i.e. evaluate both proximal and distal dislodgement forces).

D.5.2.4.6 Expression of results

Force shall be expressed in newtons (N).

D.5.2.4.7 Test report

The test report shall be in accordance with Clause D.4 and include the maximum, minimum, mean and standard deviation of the peak force, for both proximal and distal dislodgement.

NOTE Additional information regarding dislodgement force can be found in ASTM F2394.

D.5.2.5 Force to deploy (self-expanding stents)

D.5.2.5.1 Purpose

The purpose of this test is to determine the force to deploy the stent by the operator under simulated anatomical conditions. All applicable steps of the deployment process should be evaluated.

D.5.2.5.2 Materials

The following materials apply:

— stent system;

— accessory devices necessary to accomplish deployment in accordance with the IFU;

— anatomical model that includes a delivery pathway and a deployment location; the angulation, and tortuosity and diameter of the intended stent deployment location and delivery pathway (including access pathway) should be representative of a challenging anatomical configuration.

An assessment of the parameters that affect the force to deploy a particular system design shall be considered in designing an appropriate anatomical model. Literature and patient data are appropriate sources to identify challenging anatomy. Selection of the model material and model geometry should take into consideration the compliance of the vasculature being represented by the model. The expected response of the *in vivo* vessel to the insertion of accessory devices (e.g. guidewire, introducer sheath) and the stent system, and the friction associated with the model material, should also be considered in selecting the model material and test fluid:

— force measuring mechanism (e.g. force gauge, mechanical testing system);

— gripping fixture;

— temperature-controlled water bath (37 ± 2) °C.

D.5.2.5.3 Sampling

Sampling shall be in accordance with Clause D.2. Stent systems to be tested should be representative of the devices that have the potential for the highest deployment force. The effect of diameters and lengths should be taken into consideration in the selection of devices for testing.

D.5.2.5.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.5.5 Test method

Develop a test method based on the following steps:

a) Prepare the stent system per the IFU.

b) Insert the stent system into the anatomical model.

c) Attach the deployment mechanism to the load measuring equipment.

d) Allow the device to stabilize at physiological temperatures.

e) Initiate and complete the deployment per the IFU at a rate that simulates clinical use while measuring the force to deploy the stent. If multiple mechanisms are required for deploying a stent (e.g. tether wire release, rotation of thumbwheel, sheath pull back), the force to deploy should be measured for each of these relevant deployment steps.

f) Record any anomalous observations (e.g. buckling) for each test sample.

D.5.2.5.6 Expression of results

For each deployment mechanism, the maximum force required to deploy the stent is recorded in newtons (N) or newton-meters (N·m), as appropriate. Record any anomalous observations (e.g. buckling) for each test sample.

D.5.2.5.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the maximum, minimum, mean and standard deviation of the deployment forces and any anomalous observations. The report shall include a description of and justification for the anatomical model used (e.g. angulation, tortuosity, diameter and construction material of the model).

D.5.2.6 Acute particulate generation

D.5.2.6.1 Purpose

The purpose of this test is to evaluate the number of particles generated acutely from the stent system that could be associated with advancement, deployment, and withdrawal.

D.5.2.6.2 Materials

The following materials apply:

— stent system;

— accessory devices necessary to accomplish deployment in accordance with the IFU (e.g. guidewire, introducer sheath, balloons used to achieve adequate apposition of the stent);

— anatomical model that includes a delivery pathway and a deployment location;

— fixture capable of delivering or maintaining particle-free water or appropriate fluid at physiological temperature (37 ± 2) °C;

— particle counting system with applicable equipment (e.g. particulate analyser, microscope) capable of achieving a ≥90 % recovery demonstrated for ≥10 µm and ≥25 µm and a ≥ 75 % recovery for ≥50 µm particle size ranges.

D.5.2.6.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.6.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.6.5 Test method

NOTE Acute particulate testing of stent systems for drug-eluting, absorbable, and coated stents is not within the scope of this test method and guidance can be found in ASTM F2743, AAMI TIR42, ISO 12417-1, ISO/TS 17137 and ISO 17327-1.

Develop a test method based on the following steps:

a) Connect the anatomical model to the fluid system and allow the test system to stabilize at temperature and other relevant conditions; or alternatively, fill the anatomical model with fluid and allow the test system to stabilize at temperature.

b) Determine the baseline number and size of particles from the test apparatus.

c) Following the IFU and using the appropriate accessory devices, advance, deploy and withdraw the stent system and count the number of particles in each size range.

d) Flush the anatomical model and when appropriate, other associated fluid contact regions of the test apparatus until the detected particle counts match the baseline or other test termination criteria.

D.5.2.6.6 Expression of results

Particle size shall be expressed in micrometres (µm) and should be presented in appropriate size bins (e.g. ≥10 µm, ≥25 µm, ≥50 µm).

D.5.2.6.7 Test report

The test report shall be in accordance with Clause D.4. The maximum, minimum, mean and standard deviation of the particle counts in each size bin shall be reported.

D.5.2.7 Profile effect/flaring (balloon-expandable stents)

D.5.2.7.1 Purpose

The purpose of this test is to 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.

D.5.2.7.2 Materials

The following materials apply:

— stent system;

— anatomical model that includes a delivery pathway and a deployment location; the tortuosity and dimensions of the intended implant location and delivery pathway should be considered in the design of the model; the use of a compliant model should be considered;

— measuring equipment for diameters (e.g. micrometre, optical profile projector, laser-micrometre, calibrated callipers);

— accessory devices, necessary to accomplish deployment in accordance with the IFU;

— temperature-controlled water bath (37 ± 2) °C or other appropriately justified test environment (e.g. pre-soaked at (37 ± 2) °C). for stents and balloons with dimensions that are sensitive to changes between ambient and physiological temperatures;

— appropriate inspection equipment, e.g. light microscope with camera;

— cylindrical gage or template of known radius.

D.5.2.7.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.7.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.7.5 Test method

Develop a test method based on the following:

a) Measure the outer diameter of the stent mounted on the balloon at the proximal and distal ends and the outer diameter of the uninflated balloon proximal and distal to the stent, using the appropriate dimensional measurement instrument; profile measurements should be obtained for at least two axes perpendicular to the longitudinal axis of the test article or by rotating the stent system until the maximum diameter of both the stent and uninflated balloon are obtained.

b) Record profile measurements and calculate the difference between the stent diameter and the balloon diameter (proximal and distal) for each device.

c) Insert the appropriate accessory devices (e.g. guidewire, introducer sheath) into the anatomical model.

d) Advance the stent system through the anatomical model and withdraw the system back through the modelled bend and repeat this process for a justified number of cycles.

e) Repeat steps a) and b) and calculate the change in pre- and post-tracking measurements.

f) Bend the stent system to a known (and justified) radius of curvature and measure the distance between the outer diameter of the stent and the outer diameter of the uninflated balloon at the proximal and distal ends of the stent.

g) Record any anomalous observations (e.g. kinking, dislodgement) for each test article.

D.5.2.7.6 Expression of results

Diameters, distances and radii shall be expressed in millimetres (mm).

D.5.2.7.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the critical dimensions of the tortuous anatomical model and the maximum, minimum, mean and standard deviation of all measured and calculated values. Any anomalous observations shall be reported.

D.5.2.8 Simulated use

D.5.2.8.1 Purpose

The purpose of this test is to 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 anatomical variation in the intended patient population. This test is also intended to evaluate the compatibility of the stent system with accessory devices and delivery system failure. Additionally, this test is intended to evaluate the conformability of the deployed stent to the vessel wall, positioning (including orientation, if applicable), and absence of anomalies (e.g. kinks, twists, component separation, non-uniform expansion, stent damage). Evaluate the effect of post-dilation, if post-dilation is anticipated in clinical use.

D.5.2.8.2 Materials

The following materials apply:

— stent system(s);

— accessory devices necessary to accomplish deployment in accordance with the IFU (e.g. guidewire, introducer sheath, balloons used to achieve adequate apposition of the stent);

— anatomical model that includes a delivery pathway and a deployment location. The angulation, tortuosity and diameter of the intended implant location and delivery pathway (including access pathway) of the model should be based on the expected anatomy in the intended patient population and can include three-dimensional tortuosity. Multiple models with varied anatomy or materials of construction might be necessary to sufficiently challenge the relevant characteristics of the device.

Literature and patient data are appropriate sources to identify the expected anatomy. The limits set in the IFU regarding anatomy are also important to consider when selecting the anatomical model(s). Selection of the model material and model geometry(ies) should take into consideration the compliance of the vasculature being represented by the model. The expected response of the *in vivo* vessel to the insertion of accessory devices (e.g. guidewire, introducer sheath) and the stent system and the friction associated with the model material should also be considered in selecting the model material and test fluid:

— temperature-controlled fluid environment (37 ± 2) °C;

— measuring equipment for distance.

D.5.2.8.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.8.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.8.5 Test method

Develop a test method based on the following steps:

a) Connect the anatomical model to or immerse in the fluid system and allow the test system temperature to stabilize.

b) Following the IFU and using the appropriate accessory devices (e.g. guidewire, introducer sheath), insert, deliver and deploy the stent, while evaluating the following:

   1) Evaluate the ability of the stent system to be advanced to, and positioned in, the targeted deployment location of the anatomical model(s) without compromising the function of the delivery system. This testing shall include, during advancement of the system, the evaluation of pushability, flexibility, trackability and, if appropriate, the ability to torque the system without negatively affecting the ability to deploy. Note any anomalies and their impact on the performance of the stent system.

   2) For stents requiring rotational orientation for appropriate position, evaluate the ability of the stent system to provide sufficient rotation to the distal (leading) end in order to position the stent in the target orientation.

   3) Evaluate the ease and ability to deploy the stents.

   4) Determine the accuracy of deployment by identifying the target deployment location and measuring the post deployment location relative to the target location using a pre-defined coordinate system to indicate directionality.

   5) Evaluate the ability to withdraw the delivery system and accessory devices from the anatomical model(s) and note any anomalies, such as delivery system failure, stent dislodgment or stent damage.

   6) Evaluate the compatibility of the stent system with the accessory devices (e.g. guidewire, introducer sheath) and when appropriate, the compatibility of the accessory devices with the stent (e.g. balloons used post-deployment).

c) Visually inspect the deployed stent in the anatomical model. Evaluate and record the conformability of the stent to the model vessel wall, positioning (including orientation, if applicable), absence of anomalies (e.g. kinks, undesired twisting, component separation, non-uniform expansion, stent damage) and the type and location of any stent damage or any other anomalies. Visually inspect the delivery system and record the type and location of any damage or any other anomalies.

d) Visually inspect the accessory devices and record the type and location of any clinically relevant damage or other anomalies.

e) If anticipated in clinical use, evaluate the effect of post-dilation.

NOTE 1 Simulated use can be evaluated through a combination of tests, provided that all of the steps in the IFU are followed.

NOTE 2 It can be appropriate to evaluate post-dilation effects in a separate test.

D.5.2.8.6 Expression of results

Results of the evaluation in the simulated use test shall be expressed descriptively. Distances shall be expressed in millimetres (mm).

D.5.2.8.7 Test report

The test report shall be in accordance with Clause D.4 and shall include all results and abnormal observations. The report shall include a description of the anatomical model(s) used and justification of how the model(s) is representative of the anatomical variation in the intended patient population (i.e. angulation, tortuosity and diameter). The test fluid and the model material of construction shall be reported and justified. The results for pushability, flexibility, torquability, trackability, and compatibility between the accessory devices and the stent system shall each be reported. Additionally, observed anomalies identified during deployment, the conformability of the deployed stent to the vessel wall, stent positioning (including orientation, if applicable), and observed stent anomalies shall be reported. Deployment accuracy shall be reported taking into account directionality, including maximum, minimum, mean, and standard deviation. The type and location of any stent or delivery system damage and any clinically relevant accessory device damage shall be reported.

D.5.2.9 Tensile bond strength

D.5.2.9.1 Purpose

The purpose of this test is to determine the bond strength of all joints and/or fixed connections of the delivery system (e.g. distal tip, hub bond). The strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing) shall be evaluated separately or concurrently with the bond strength determination.

D.5.2.9.2 Materials

The following materials apply:

— delivery system or appropriate component joints and/or fixed connections;

— recommended guidewire or equivalent, if appropriate;

— mechanical testing system with a constant crosshead speed, a suitable load cell and appropriate gripping fixtures;

— temperature-controlled environment (37 ± 2) °C, as appropriate.

D.5.2.9.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.9.4 Conditioning

Conditioning shall be in accordance with Clause D.3. Conditioning of the test samples should include loading, tracking (access and withdrawal) and deployment. Multiple tracking cycles through an appropriate anatomical model should be considered. Information regarding an appropriate anatomical model is provided in D.5.1.7.2. Delivery systems from completed simulated use testing (see D.5.1.7) may be used for this test.

NOTE Additional information regarding pre-soaking can be found in ISO 10555-1.

D.5.2.9.5 Test method

For bonds that will be subjected to physiological temperatures, testing should be performed at (37 ± 2) °C.

Develop a test method based on the following steps:

a) Insert the delivery system or component over the guidewire, if appropriate.

b) Using a mechanical testing system with an appropriate crosshead speed (e.g. 200 mm/min), apply tension to the bonded joint or to a series of bonded joints until a bond breaks or loses functional integrity. Ensure that the guidewire is not gripped at both ends.

c) Record the peak force at which failure occurs and describe the type and location of the failure.

D.5.2.9.6 Expression of results

Bond strength shall be expressed in newtons (N).

D.5.2.9.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the type and location of the failure and the maximum, minimum, mean and standard deviation of the bond strength(s).

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].

D.5.2.10 Torsional bond strength

D.5.2.10.1 Purpose

The purpose of this test is to 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. The torsional strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing) shall be evaluated separately or concurrently with the torsional bond strength evaluation.

D.5.2.10.2 Materials

The following materials apply:

— delivery system or appropriate component joints and/or fixed connections;

— recommended guidewire or equivalent, if appropriate;

— torque testing system with a suitable torque gauge;

— temperature-controlled environment (37 ± 2) °C, as appropriate.

D.5.2.10.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.10.4 Conditioning

Conditioning shall be in accordance with Clause D.3. Conditioning of the test samples should include loading, tracking (access and withdrawal) and deployment. Multiple tracking cycles through an appropriate anatomical model should be considered. Information regarding an appropriate anatomical model is provided in D.5.1.7.2. Delivery systems from completed simulated use testing (see D.5.1.7) may be used for this test.

NOTE Additional information regarding pre-soaking can be found in ISO 10555-1.

D.5.2.10.5 Test method

For bonds that will be subjected to physiological temperatures, testing should be performed at (37 ± 2) °C.

Develop a test method based on the following steps:

a) Insert the delivery system or component over the guidewire, if appropriate.

b) Affix one end of the test sample in a clamping apparatus.

c) Attach the other end of the test sample to the torque gauge. The test gauge length shall be long enough to avoid influence of the clamping apparatus and short enough to ensure uniform torsional loading.

d) Rotate the sample at a rate characteristic of that used in a typical clinical use to one end of the sample until either of the following predetermined conditions is achieved:

   1) test to failure (i.e. the joint and/or delivery system breaks or loses functional integrity); or

   2) test to predetermined, clinically relevant number of rotations to the stent system.

e) Record either of the following predetermined test end points:

   1) the torque or number of rotations at which failure occurs and the failure mode and location; or

   2) whether the predetermined number of rotations was achieved without failure.

D.5.2.10.6 Expression of results

Torsional bond strength (torque strength) shall be expressed in newton–metres (N·m) or number of rotations.

D.5.2.10.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the mode and location of the failure and the maximum, minimum, mean and standard deviation of the torsional bond strength.

The results shall be evaluated in relation to the torque level necessary to access, deploy and withdraw the system.

D.5.2.11 Visibility

D.5.2.11.1 Purpose

The purpose of this test is to evaluate the ability to visualize the stent system and stent using the imaging techniques specified in the IFU.

D.5.2.11.2 Materials

The following materials apply:

— stent system;

— accessory devices necessary to accomplish deployment in accordance with the IFU;

— phantom tissue model, or equivalent (e.g. water, metal, large animal model);

— imaging machine (e.g. fluoroscopy) capable of operating at clinically relevant power levels.

Visibility is significantly affected by variations in equipment and parameter settings. In the selection of the equipment used for this evaluation, consideration should be given to this variability.

D.5.2.11.3 Sampling

Sampling shall be in accordance with D.2.

D.5.2.11.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.2.11.5 Test method

Develop a test method based on the following steps:

a) Position the stent system in the phantom tissue model.

b) Position the model relative to the imaging machine to simulate clinical conditions.

c) Use the imaging system to visualize the stent system and any identification markers.

d) Evaluate the images for ease of visibility. For example, the degree of visibility may be assessed by locating the exact ends, orientation of critical points and/or parts of the stent system. Alternatively, the degree of visibility may be compared to a specified material or device with known visibility.

e) Repeat steps a) through step d) to evaluate the stent and the delivery system during deployment and withdrawal, and the stent after withdrawal of the delivery system.

D.5.2.11.6 Expression of results

Results of the assessments shall be expressed descriptively, with representative images as appropriate.

D.5.2.11.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the assessment of visibility for all applicable components at the various stages of testing. Describe the results of the assessments and/or include visual results (e.g. representative fluoroscopic images). The test report shall also include the make and model of the imaging equipment, the relevant imaging parameters and details of the phantom tissue model.

NOTE Additional information regarding visibility can be found in ASTM F640.

D.5.3 Stent

D.5.3.1 Corrosion

D.5.3.1.1 Purpose

The purpose of this assessment is to evaluate the susceptibility of a stent with metallic materials to corrosion.

NOTE This annex does not include specific methodology for corrosion testing. Guidance is provided regarding the assessment of corrosion using various sources (e.g. literature, historical clinical data) and through reference to other standards.

D.5.3.1.2 Materials

The following materials apply:

— stent or appropriate test samples of the stent (e.g. segments, sections, components, subassemblies) that have undergone actual or simulated manufacturing processes. Test samples shall be appropriate to the type of corrosion under evaluation (e.g. crevice, pitting, fretting, galvanic);

— materials as specified in the test methods selected for this evaluation;

— reference samples, as appropriate.

D.5.3.1.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.3.1.4 Conditioning

Conditioning shall be in accordance with Clause D.3 and shall include actual or simulated loading and deployment. Additional preconditioning steps might be appropriate for coated stents.

D.5.3.1.5 Test method

The susceptibility of the metallic materials of the stent to corrosion should be assessed. Corrosion assessment includes, but is not limited to, evaluation of test results, review of literature and consideration of the historical clinical performance of the material(s) under assessment. Guidance on corrosion assessment may be found from a variety of sources (e.g. literature, textbooks, standards, regulatory guidance documents).

The following is a partial list of references regarding corrosion terminology, equipment, test procedures and methods:

— ISO 17475, *Corrosion of metals and alloys — Electrochemical test methods — Guidelines for conducting potentiostatic and potentiodynamic polarization measurements*

— ISO 16429, *Implants for surgery — Measurements of open-circuit potential to assess corrosion behaviour of metallic implantable materials and medical devices over extended time periods*

— ASTM F2129, *Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices*

— ASTM F3044, *Test Method for Standard Test Method for Evaluating the Potential for Galvanic Corrosion for Medical Implants*

— ASTM G5, *Standard reference test method for making potentiostatic and Potentiodynamic Anodic Polarization Measurements*

— ASTM G61, *Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements for Localized Corrosion Susceptibility of Iron-, Nickel-, or Cobalt-Based Alloys*

— ASTM G71, *Standard Guide for Conducting and Evaluating Galvanic Corrosion Tests in Electrolytes*

— ASTM G102, *Standard Practice for Calculation of Corrosion Rates and Related Information from Electrochemical Measurements*

D.5.3.1.6 Expression of results

Test data shall be expressed in units appropriate to the methods selected.

D.5.3.1.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the complete corrosion assessment, including a summary of all test data, analyses and referenced information, comparisons to applicable controls, any appropriate comparison between *in vivo* and *in vitro* performance and conclusions regarding the anticipated corrosion resistance of the stent. For quantitative data, the maximum, minimum, mean and standard deviation shall be included. Applicable requirements indicated in the guidance documents used for testing should also be included.

D.5.3.2 Fatigue and durability — Computational analyses

D.5.3.2.1 Purpose

The purpose of the computational analyses is to 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 stresses and/or strains can be compared to material characteristics to calculate the fatigue safety factor.

Computational analyses may also be used to establish appropriate test conditions and to select test articles for fatigue and durability testing. There may also be additional considerations required for computational analyses of absorbable stents.

D.5.3.2.2 Model inputs and tools

The following model inputs and tools apply:

— structural design of the stent and, if appropriate, a representation of the *in vivo* environment (e.g. blood vessel);

— material properties (e.g. modulus, fatigue limit, vessel compliance) and constitutive models (e.g. linear elastic) for all materials under evaluation;

— the information needed to establish boundary conditions related to manufacturing (e.g. compressed diameter required to achieve delivery system profile), deployment (e.g. balloon expansion diameter or implant diameter), and, if appropriate, interaction between the stent and the surrounding tissue;

— the information needed to establish boundary conditions (e.g. constraints and loads) that are representative of the intended clinical use (e.g. vessel diameters, deformation, curvature);

— appropriate modelling tools, such as finite element analysis and computer aided design software to model the stent and, if appropriate, the *in vivo* environment (e.g. blood vessel).

D.5.3.2.3 Analysis

The analyses shall be performed on the sizes and configurations necessary to ensure an adequate evaluation of the stent.

Perform computational analyses based on the following steps.

a) Establish the purpose of each computational analysis.

   1) Establish the purpose of each computational model analysis. For example, the computational analysis may be used to identify the stent size and configuration that is expected to perform with the lowest fatigue safety factor.

   2) Select computational software with the capabilities to perform the analysis.

b) Define the model geometry.

   1) Identify the sizes and configurations of the stents to be evaluated.

   2) Establish the stent geometry, and if appropriate, mock or diseased vessel geometry. The geometry should be representative of the finished product. Analysis may be limited to segments of the stent, and/or vessel, with appropriate justification. Consideration shall be given to the allowed variability of the dimensions when selecting the geometry for analysis.

3) All appropriate deformation modes should be considered in selecting the extent of the stent to be modelled or when applying symmetry assumptions.

c) Establish the material properties.

Determine the properties of the materials of the finished stent necessary to conduct the analysis. If appropriate, establish the material properties for the representative vessel.

d) Define the constitutive model.

1) For each material in the analysis, determine the appropriate constitutive model (i.e. the relationship between stress and strain), such as superelasticity, hyperelasticity, and plasticity. The material properties that are used to develop the constitutive models should represent the final, processed materials (e.g. final heat treatment).

2) Confirm that the constitutive model(s) represents the behaviour of the material within the applicable stress or strain range using an appropriate test method(s) (e.g. tensile, bending).

e) Create the finite element mesh.

Create a mesh and specify the element type(s), shape(s), and formulation(s) (e.g. shape function) to model the stent and, if appropriate, the representative vessel.

f) Apply the constraints to the mesh.

g) Apply the loading conditions.

1) Apply the loading conditions to represent delivery system loading (e.g. compressed diameter required to achieve the delivery system profile) stent deployment (e.g. balloon expansion diameter, implant diameter) and recoil, if applicable.

2) Apply the representative loading conditions (e.g. cyclic deformation, cyclic pressure) that the stent is expected to experience *in vivo*.

h) Apply solution methodology and execute the analysis.

1) Select the appropriate solution techniques and tolerances for the equation(s) being solved.

2) Incorporate any additional boundary conditions necessary to ensure model stability. It is important to ensure that the applied boundary conditions do not over-constrain and/or do not add unintended loadings, rotations or contact.

i) Verify the solution.

Conduct a mesh sensitivity analysis to demonstrate that further mesh refinement does not significantly change the computational results (e.g. the maximum strain does not change significantly when additional elements are used).

j) Validate the computational model.

Obtain test data to allow comparison of the appropriate output(s) of the model to the physical behaviour of the stent.

k) Analyse results.

1) Compute the appropriate stress or strain quantities (e.g. principal stresses, equivalent strains).

2) Calculate fatigue safety factors using the appropriate failure criteria (e.g. constant life diagram). Identify the location associated with the lowest fatigue safety factor (e.g. high stress/strain regions).

D.5.3.2.4 Expression of results

Stress shall be expressed in megapascals (MPa). Strain shall be expressed as a percentage (%) or dimensionless. Locations of critical stresses and/or strains should be depicted in colour figures with legends. Diagrams for fatigue analysis shall be provided (e.g. constant life, Morrow analysis, Goodman analyses).

D.5.3.2.5 Report

NOTE 1 The computational analysis report is intentionally different from the standard test reports described in Clause D.4.

The report shall include the following:

a) background and purpose:

   1) provide a brief device description and the intended use environment;

   2) state the purpose of each analysis;

b) geometry:

   1) report the sizes and configurations of the stents selected for evaluation;

   2) provide diagrams and a brief description of the model(s);

   3) provide a justification for the sizes and configurations of the stents selected for evaluation;

   4) if only a portion of the stent was modelled, provide a justification for the geometry analysed (e.g. the use of symmetry);

   5) provide a justification for how the model geometry is representative of the finished product and, if appropriate, the mock or diseased vessel (e.g. size, disease state);

   6) report the dimensions selected in the context of the expected variability;

c) material properties:

   1) list all the materials in the model and report the relevant material property values (e.g. modulus, yield strength, fatigue limit);

   2) provide and justify the source of the material properties (e.g. literature, test data and conditions) for the stent and, if appropriate, for the representative vessel;

   3) provide a justification for why the material properties are representative of the final, processed material (e.g. final heat treatment) in the intended *in vivo* environment (e.g. 37 °C) if applicable, describe tests conducted to determine the material properties;

d) constitutive model:

   1) for each material, provide the relationship between stress and strain (i.e. constitutive model) including a graphical representation and/or the associated equations;

   2) for each material, discuss how the constitutive model captures the material behaviour (e.g. loading, unloading, plastic deformation);

   3) provide a justification for the assumptions in the constitutive model used to represent each material;

4) provide a summary of the methodology and data for any testing conducted to support the constitutive model;

e) mesh:

1) describe the element type, shape, and formulation for the mesh used in the analysis;

2) provide a representative image of the mesh in the areas of high stress/strain;

3) provide a justification for why the elements selected adequately represent the spatial distribution of the stress/strain under the prescribed loading;

f) constraints:

1) report the boundary conditions (e.g. rigid cylinder for vessel, fixed degrees of freedom), including a graphical representation if appropriate;

2) provide a justification for the boundary conditions used to restrict motion of the model or to isolate specific deformations;

g) loading conditions:

1) report the loading parameters (e.g. location, magnitude and direction of loading, number of cycles) and the sequence of the loads applied to the model to represent delivery system loading, stent deployment and recoil, if appropriate;

2) report the loading conditions (e.g. cyclic deformation, cyclic pressure) applied to the model to represent the deformation(s) or load(s) the stent is expected to experience *in vivo*;

3) provide justification that the delivery system loading and stent deployment simulation are representative of actual delivery system loading (e.g. compressed diameter required to achieve the delivery system profile) in accordance with manufacturing and stent deployment in accordance with the IFU;

4) provide a justification for the values used for the expected *in vivo* loading conditions;

h) solution methodology:

1) report the equation solution techniques and tolerances; describe the software package and any user subroutines that were implemented;

2) provide a justification for any additional boundary conditions used to enhance model stability;

i) solution verification:

1) report the results of the mesh sensitivity analysis, demonstrating that further mesh refinement does not significantly change the computational results (e.g. the maximum strain does not change significantly when additional elements are used);

2) provide a justification for the computational result (e.g. maximum strain) used to establish the adequacy of the mesh density;

j) validation:

1) provide an adequate description of the test method (e.g. radial outward force) used to assess the ability of the computational model to adequately predict the behaviour of the stent; this description may include illustrations to show similarities between the model and the test article in the fixture;

2) provide a comparison of the test results to the values predicted by the computational model over a region relevant to the analysis objectives; provide an assessment of the significance of any relevant differences between the measured and predicted values;

3) provide a justification for the mode of loading used to assess the ability of the computational analysis to adequately predict the behaviour of the stent;

k) results: for each computational analysis, report the magnitude and illustrate the physical location(s) of the relevant quantitative results (e.g. maximum principal stresses, mean and alternating equivalent strain, fatigue safety factors);

l) discussion/conclusions:

1) discuss the results in the context of the stated purpose of the computational model (e.g. identifying the stent configuration and size with, and the location of, the lowest fatigue safety factor, assessing the acceptability of the fatigue safety factors), including any limitations and conservative modelling conditions;

2) when applicable, discuss the implications of the computational analysis with respect to related testing; for example, explain how the computational analysis complements accelerated durability testing conclusions.

NOTE 2 Additional information regarding computational analyses for radial loading can be found in ASTM F2514.

NOTE 3 As a potential alternative or supplement to a traditional 'test-to-success' fatigue testing paradigm, interested readers can find information on the 'fatigue-to-fracture' methodology in ASTM F3211.

NOTE 4 Additional information regarding computational model verification and validation can be found in ASME V&V40.

D.5.3.3 Fatigue and durability — *in vitro* testing

D.5.3.3.1 General

D.5.3.3.1.1 Purpose

Device durability may be evaluated in separate individual tests, tests that apply multiple sequential deformation modes, or tests that apply simultaneous deformation modes. When combining deformation modes under a single test, the relative rate of occurrence of the deformation modes should be considered in developing appropriate test methods, particularly with accelerated testing. These methods do not apply to absorbable stents.

The information included in this subclause are applicable to radial fatigue and durability, axial fatigue and durability, bending fatigue and durability, torsional fatigue and durability and compression fatigue and durability that follow in D.5.2.3.2 to D.5.2.3.6. Specific considerations for the development of test methods are included in the individual clauses.

For the purpose of this subclause, displacement is defined as the movement of a test fixture, a test article, or mock vessel (e.g. diametrical, linear, rotational) in response to the action of a test apparatus. Deformation is defined as the change in shape of a test article or stent in response to a displacement(s) or an applied load(s).

These tests may be modified to evaluate chronic particulate generation.

NOTE 1 Additional information regarding durability testing can be found in ASTM F2477 and ASTM F2942.

NOTE 2 Information regarding durability testing for absorbable stents can be found in ISO/TS 17137.

NOTE 3 As a potential alternative or supplement to a traditional 'test-to-success' fatigue testing paradigm, interested readers can find information on the 'fatigue-to-fracture' methodology in ASTM F3211.

Fatigue and durability testing is intended to evaluate aspects of the long-term structural integrity of the stent under cyclic loading conditions that represent the *in vivo* environment.

Appropriate test methods should be developed to simulate physiological deformations of the stent. These test methods should describe how to attain deformations of the test article through the application of forces and/or displacements to the test fixture or a mock vessel.

Potential failure modes that can be evaluated in these tests include stent fracture, and wear or abrasion between stent components.

The fatigue and durability tests are not intended to fully evaluate potential failure modes related to corrosion, wear between the stent and the recipient vessel, or stent migration. Consideration should be given as to whether such observations during testing indicate an increased potential for these failure modes to occur clinically.

D.5.3.3.1.2 Materials

The following materials apply:

— stent system;

NOTE This test is not designed to evaluate the entire system; however, the system is required to deploy the stent that is under test.

  — if applicable, accessory devices necessary to accomplish deployment in accordance with the IFU (e.g. guidewire, introducer sheath, balloons used to achieve adequate apposition of the stent);

  — if applicable, a mock vessel with a diameter and properties appropriate to enable simulation of the loading mode under study;

  — appropriately sized to represent the vessel diameter for the loading conditions under test;

  — constructed of a material (e.g. silicone) capable of maintaining consistent deformation of the test article under cyclic loading, without creating unwanted deformation of the test article;

  — capable of withstanding the test conditions at the test frequency and temperature for the duration of the test;

  — designed and/or modified to minimize test article migration;

— fatigue test system capable of applying cyclic loads and/or displacement to the test article;

— measurement system(s) (e.g. load cell, strain gauge, high speed camera) capable of quantifying appropriate loads, displacements and/or deformations;

— cycle counting system for measuring the number of cycles applied to the test article;

— fluid fixture capable of maintaining phosphate buffered saline (PBS) (unless testing in a different fluid can be justified) at physiological temperature (37 ± 2) °C;

— inspection equipment [e.g. light microscope, lighted magnifying glass, radiography, scanning electron microscopy (SEM)].

D.5.3.3.1.3 Sampling

Sampling shall be in accordance with Clause D.2.

Sampling shall allow for the evaluation of the structural integrity of all relevant parts of the stent and contact areas between overlapping stents, when applicable.

The stent size(s) with the greatest potential for fatigue failure shall be identified and justified using computational modelling (e.g. finite element analysis), engineering analysis, and/or clinical data. Alternatively, samples representing the range of sizes may be chosen for testing.

Segments or portions of the complete stent may be used as the test article if appropriately justified.

D.5.3.3.1.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

The stent system should be tracked through an anatomical model prior to fatigue and durability testing unless appropriate justification is provided.

D.5.3.3.1.5 Test method

This subclause includes general considerations for the development of all types of fatigue and durability tests:

a) define test conditions:

   1) establish loading conditions; the effect of the stent on the overall deformation expected *in vivo* should be considered when establishing the loading conditions. The direction and magnitude of the applied displacement or force should be justified based on physiologically relevant data (e.g. literature, clinical data) for the specific anatomical location, patient age, or condition being treated. Computational modelling may be used with the physiologically relevant data to determine the appropriate loading conditions;

   2) mock vessel; there is no general guidance beyond those included in the general materials subclause (see D.5.2.3.1.2). See the individual fatigue and durability test methods;

   3) test frequency; the test frequency shall be selected to maintain the test article deformation within the pre-defined limits for the duration of the test and to avoid undesirable harmonics, localized heating of the stent, and rate-dependent effects on material properties;

   4) displacement conditions/control; the gripping technique, slip between the mock vessel (if used) and the test article, or dynamic forces may result in deformations other than intended during testing; establish the method to control displacement or the application of force during testing and verify that each test article achieves the intended deformation during the cyclic loading at the test frequency over the duration of the test;

b) set up:

   1) either deploy the test article according to the IFU directly into the test fixture or deploy the stent according to the IFU and secure the test article (i.e. either the complete stent or a segment or portion of the stent) to the test fixture; if appropriate, deploy additional overlapped stents;

   2) inspect the test article(s) using appropriate visual aids, and record the location and severity of any anomalies (e.g. non-uniform stent expansion);

   3) allow the test articles to reach the pre-defined test temperature before initiating the test;

c) testing: after initiation of testing, at periodic intervals, monitor the test conditions and equipment operation to ensure that the test article does not migrate and experiences the intended displacements or forces; because the relationship between the intended displacements or forces and test article deformation might change over time, it might be necessary to verify that the test article is deforming as intended; the methodology to verify that the displacements and/or deformations are as intended shall be described in the test method; if appropriate, stop the test at periodic intervals for inspection of the test article(s); removing the test article from a mock vessel for the periodic inspection is not recommended. However, if removing the test article from a mock vessel is necessary, care shall be taken to remove and re-deploy in a manner that minimizes the effect on the test article;

d) termination: terminate the test after the desired number of cycles has been achieved or a pre-specified end point has been observed;

e) post-test inspection: carefully remove the test articles from the test apparatus and mock vessel, if applicable; completely visually inspect each test article for evidence of macroscopic damage;

if anomalies are identified, if fractures cannot be visually identified due to the size or design of the stent, or if additional evaluation of regions of interest (e.g. potential areas of high stress/strain or wear) is needed, use appropriate methodologies (e.g. light microscopy, scanning electron microscopy, radiography) to further inspect for evidence of damage; identify and document the presence and location of any anomalies, including the following:

— pre-specified failures modes under evaluation in the test, such as stent fracture, and significant wear between stents;

— additional observations, such as migration of stent within mock vessel;

— failure modes that may be related to corrosion, wear between the stent and the recipient vessel, or stent migration; consideration should be given as to whether such observations indicate an increased potential for these failure modes to appear clinically.

SEM images can be taken of fracture surfaces and fracture locations to characterize the nature and origin of the fracture. When evaluating fractures, consider the potential for artefactual stent fracture related to the test apparatus (e.g. gripping method) or testing parameters.

D.5.3.3.1.6 Expression of results

There is no general guidance. See the expression of results subclause of the individual fatigue and durability test methods.

D.5.3.3.1.7 Test report

The test report should be in accordance with Clause D.4. The intended and measured displacements and/or deformations shall be reported.

Results of all inspections, including the cycle count at which the inspections took place and the number and location of any observed anomalies, including fractures, shall be reported. The test report should include a discussion on the potential causes (e.g. fatigue failure, material inclusion, pre-existing sample damage, mock vessel friction) and clinical relevance of the observations. Results should be considered and interpreted in relation to any applicable *in vivo* data.

D.5.3.3.2 Radial fatigue and durability

D.5.3.3.2.1 Purpose

NOTE The information below is specific to this test and used in conjunction with D.5.2.3.1 which describes general fatigue and durability considerations.

The purpose of this test is to evaluate the long-term structural integrity of the stent when subjected to cyclic radial loading conditions.

D.5.3.3.2.2 Materials

Refer to the materials listed in the general materials subclause (see D.5.2.3.1.2), including the mock vessel.

D.5.3.3.2.3 Sampling

Refer to the information in the general sampling subclause (see D.5.2.3.1.3).

D.5.3.3.2.4 Conditioning

Refer to the information in the general conditioning subclause (see D.5.2.3.1.4).

D.5.3.3.2.5 Test method

Refer to the information in the general test method subclause (see D.5.2.3.1.5) with the following:

This test method describes a radial fatigue and durability test that subjects the test article to a specified amount of cyclic radial deformation. Testing shall be performed using a mock vessel and fatigue tester that induces a physiologically relevant radial deformation of the test article. Each test article is inspected periodically during the test for the occurrence of fracture, and other aspects of structural integrity;

a) define test conditions:

1) establish loading conditions; refer to the information in the general test method, establish loading conditions subclause [see D.5.2.3.1.5, item a), 1)] with the following: the loading conditions of the test, that is, the intended mean and alternating diameters of the test article, are based on the expected clinical vascular pressures, the *in vivo* dynamic radial compliance of the target vessel, and the radial stiffness of the stent; force equilibrium models, finite element analysis or experimental evaluation can be used to establish the target mean and alternating diameters; definitions of compliance reported in the literature vary; the dynamic radial compliance, C_{dr}, should be expressed as a percentage of the diameter change per 100 mmHg and defined per ISO 7198:2016, A.5.9:

$$C_{dr} = \left(D_{p_2} - D_{p_1}\right) \times 10^4 / \left(D_{p_1} \times \left(p_2 - p_1\right)\right)$$

where

D_{p_1} is inner diameter at the pressure of p_1;

D_{p_2} is the inner diameter at the pressure of p_2;

p_1 is the lower pressure value (diastolic), in mmHg;

p_2 is the higher pressure value (systolic), in mmHg;

2) mock vessel: refer to the information regarding the mock vessel in the general materials subclause (see D.5.2.3.1.2) with the following: the mock vessel should allow displacement of the test article at the intended amplitude around the intended mean diameter, at the test frequency and temperature, for the duration of the test;

NOTE Mock vessel diameter, wall thickness and compliance can be appreciably affected by the tube mounting operation.

3) test frequency: refer to the information in the general test method, test frequency subclause [see D.5.2.3.1.5, item a) 3)].

4) displacement conditions/control: refer to the information in the general test method, displacement conditions/control [see D.5.2.3.1.5, item a) 4)] with the following: establish the method to control radial displacement during testing; verify that the test article achieves the intended deformation during the cyclic loading at the test frequency using a representative sample; the results of this verification activity should be used to establish the procedure for controlling the displacement of the test articles; for example, if it can be shown that the outside diameter of the mock vessel as measured by a laser micrometre correlates with the intended deformation of the stent (see D.6), then this may be used to control the applied displacement during testing; there are important considerations for controlling radial displacement during testing that should be identified and addressed in establishing the procedures for controlling displacement; for example, apposition of the test article to the mock vessel should be maintained;

b) set up: refer to the information in the general test method, set up subclause [see D.5.2.3.1.5, items b) 1) to 3)];

c) testing: refer to the information in the general test method, testing subclause [see D.5.2.3.1.5, item c)] with the following:

   1) set the frequency to the established rate and adjust the test system to achieve the intended mean and alternating diameters of the mock vessel or test article; verify that the test article deformations are as intended; after mean and alternating diameter targets are achieved, begin counting the cycles;

   2) verify the test article response (e.g. mean and alternating diameters) at regular time intervals to ensure that the target values are maintained; adjust the test system as necessary to maintain the desired operational target; the method for ensuring the appropriate test article response should be specified and justified; the location evaluated should be specified and justified;

d) termination: refer to the information in the general test method, termination subclause [see D.5.2.3.1.5, item d);

e) post-test inspection: refer to the information in the general test method, post-test inspection subclause [see D.5.2.3.1.5, item e)].

D.5.3.3.2.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). All pressures shall be expressed in kilopascals (kPa) or millimetres of mercury (mmHg). Diameters shall be expressed in millimetres (mm). Radial displacement shall be expressed in millimetres (mm) or as the percent change in diameter (%) of the test articles and is calculated by $100(\Delta D/D_{\text{diastolic}})$ where D refers to the outer diameter of the test articles. The compliance is expressed as a percentage of the diameter change per 100 mm of mercury (%/100 mmHg).

D.5.3.3.2.7 Test report

Refer to the information in the general test method, test report subclause (see D.5.2.3.1.7) with the following: the intended and measured radial displacements of the test article shall be reported.

D.5.3.3.3 Axial fatigue and durability

D.5.3.3.3.1 Purpose

NOTE The information below is specific to this test and used in conjunction with D.5.2.3.1 which describes general fatigue and durability considerations.

The purpose of this test is to evaluate the long-term structural integrity of the stent when subjected to cyclic axial loading conditions appropriate for the device design and intended clinical use.

D.5.3.3.3.2 Materials

Refer to the materials listed in the general materials subclause (see D.5.2.3.1.2).

D.5.3.3.3.3 Sampling

Refer to the information in the general sampling subclause (see D.5.2.3.1.3).

D.5.3.3.3.4 Conditioning

Refer to the information in the general conditioning subclause (see D.5.2.3.1.4).

D.5.3.3.3.5 Test method

Refer to the information in the general test method subclause (see D.5.2.3.1.5) with the following: this test method describes an axial fatigue and durability test that subjects the test article to a specified

amount of cyclic axial displacement. Axial deformation of the test article can be applied by lengthening, shortening, or cycling about a neutral position. Testing is performed with a fatigue tester that induces a physiologically relevant axial deformation of the test article and can be performed with or without a mock vessel. Each test article is inspected periodically during the test for the occurrence of fracture, and other aspects of structural integrity; the test article, with or without a mock vessel, can be directly secured to the test fixture with the load applied directly to the test article, or the test article can be deployed within a mock vessel and the load applied to the mock vessel, with appropriate justification:

a) define test conditions:

   1) Establish loading conditions: refer to the information in the general test method, establish loading conditions subclause [see D.5.2.3.1.5, item a) 1)] with the following: the loading conditions of the test, that is, the intended minimum and maximum axial lengths, are based on the anticipated clinical lengthening and/or shortening; force equilibrium models, finite element analysis or experimental evaluation can be used to establish the target minimum and maximum lengths;

   2) mock vessel (if applicable): refer to the information regarding the mock vessel in the general materials subclause (see D.5.2.3.1.2);

   3) test frequency: refer to the information in the general test method, test frequency subclause [see D.5.2.3.1.5, item a) 3)];

   4) displacement conditions/control: refer to the information in the general test method, displacement conditions/control [see D.5.2.3.1.5, item a) 4)] with the following: establish the method to control axial displacement applied during testing; verify that the test article achieves the intended deformation during the cyclic loading at the test frequency using a representative sample; the results of this verification activity should be used to establish the procedure for controlling the displacement of the test articles; for example, if it can be shown that the cross head displacement of the axial testing apparatus adequately correlates with the intended deformation of the stent, then this may be used to control the applied displacement during testing;

b) set up: refer to the information in the general test method, set up subclause [see D.5.2.3.1.5, items b) 1)–3)] with the following:

   1) if a mock vessel is used, and axial shortening of the test article is being evaluated, it might be appropriate to stretch the mock vessel before deploying the test article;

   2) adjust the test apparatus to yield the desired axial displacement;

   3) when calculating percent axial shortening, the following formula should be used:

$$P_{as} = \left[\frac{(L_{free} - L_{min})}{L_{free}} \right] \times 100$$

where

P_{as} is the percentage of the axial shortening;

L_{free} is the initial unsecured length of the test article as measured on the test apparatus;

L_{min} is the minimum unsecured length of the test article throughout fatigue cycle.

When calculating percent axial lengthening, the following formula should be used:

$$P_{al} = \left[\frac{(L_{max} - L_{free})}{L_{free}} \right] \times 100$$

where

P_{al} is the percentage axial lengthening;

L_{max} is the maximum unsecured length of the test article throughout fatigue cycle;

L_{free} is the initial unsecured length of the test article as measured on the test apparatus;

c) testing: refer to the information in the general test method, testing subclause [see D.5.2.3.1.5, item c)] with the following:

1) set the frequency to the established rate and adjust the test system to achieve the intended minimum and maximum test article length; verify that the test article deformations are as intended; after the minimum and maximum test article length targets are achieved, begin counting the cycles;

2) verify minimum and maximum test article lengths at regular time intervals to ensure that the target values are maintained; adjust the system as necessary to maintain the desired operational target;

d) termination: refer to the information in the general test method, termination subclause [see D.5.2.3.1.5, item d)];

e) post-test inspection: refer to the information in the general test method, post-test inspection subclause [see D.5.2.3.1.5, item e)].

D.5.3.3.3.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). Axial shortening and/or lengthening shall be expressed in percentage (%).

D.5.3.3.3.7 Test report

Refer to the information in the general test method, test report subclause (see D.5.2.3.1.7) with the following: the test article intended and measured axial shortening and/or lengthening shall be reported.

D.5.3.3.4 Bending fatigue and durability

D.5.3.3.4.1 Purpose

NOTE The information below is specific to this test and used in conjunction with D.5.2.3.1 which describes general fatigue and durability considerations.

The purpose of this test is to evaluate the long-term structural integrity of the stent when subjected to cyclic bending loading conditions appropriate for the device design and intended clinical use.

D.5.3.3.4.2 Materials

Refer to the materials listed in the general materials subclause (see D.5.2.3.1.2).

D.5.3.3.4.3 Sampling

Refer to the information in the general sampling subclause (see D.5.2.3.1.3).

D.5.3.3.4.4 Conditioning

Refer to the information in the general conditioning subclause (see D.5.2.3.1.4).