INTERNATIONAL STANDARD

ISO 25539-1

Second edition
2017-02

Cardiovascular implants — Endovascular devices —

Part 1: Endovascular prostheses

Implants cardiovasculaires — Dispositifs endovasculaires — Partie 1: Prothèses endovasculaires

Reference number
ISO 25539-1:2017(E)

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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 on 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 the following URL: www.iso. org/iso/foreword. html.

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

This second edition cancels and replaces the first edition (ISO 25539-1:2003), which has been technically revised.

It also incorporates the Amendment ISO 25539-1:2003/Amd1:2005.

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

Introduction

This document was prepared to provide minimum requirements for endovascular prostheses. The normative requirements are provided in the main body. 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 and a cross reference between the main body and these annexes are provided in additional informative annexes.

This document has been updated to reflect current knowledge regarding the testing and clinical use of endovascular prostheses, 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.

This document introduces methodology to identify appropriate testing and analyses for specific endovascular prosthesis, designated as the device evaluation strategy (DES). The requirement regarding the DES is in the main body, with informative guidance for the preparation of a DES table included in Annex A. Annex A also provides guidance for developing a DES for device design modifications and changes in 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.

New requirements also include the evaluation of leakage at a seal zone and dislodgement force of endovascular prosthesis from a balloon. Guidance for the development of appropriate tests to meet these requirements is included in Annex D.

The requirement for evaluating the strength of the connection(s) between the graft material and a discrete fixation system(s) has been clarified with respect to the applicability of this requirement, that is, this requirement is only applicable for prostheses with a fixation system that is discrete from any stent(s) intended to provide structural support within the prosthesis [e.g. suprarenal stent that is not continuous with the stent(s) in the prosthesis body].

The specific requirements to evaluate pushability, flexibility, torquability, trackability and deployment accuracy of an endovascular 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.

The requirement to evaluate stent-free surface area has been removed as this attribute is not relevant for endovascular prostheses, which includes covered stents.

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 included in Annex D.

The revisions to the titles of the annexes to this document are as follows.

Annex	ISO 25539-1:2003+A1:2005	ISO 25539-1:2017
A	Attributes of endovascular devices — Technical and clinical considerations	Relationship between testing requirements and device attributes and potential failure modes
B	Bench and analytical tests	Description of device and clinical effects of failure
C	Definitions of reportable clinical events	Bench and analytical tests
D	Test methods	Test methods
E	Sample equations as a supplement to the radial fatigue and durability test	There is no Annex E as this information was incorporated in Annex D

It is recognised by this ISO committee that many endovascular 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 version of this document. 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.

Cardiovascular implants — Endovascular devices —

Part 1: Endovascular prostheses

1 Scope

This document specifies requirements for the evaluation of endovascular systems (prostheses 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 an informative annex to this document. This document can be considered as a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants.

This document is applicable to endovascular systems used to treat aneurysms, stenoses or other vascular anomalies or pathologies (e.g. dissections, transections) or to create shunts between vessels [e.g. creation of transjugular intrahepatic portosystemic shunting (TIPS)]. Some of the requirements are specific to endovascular treatment of arterial aneurysms or stenoses. Although uses of endovascular systems other than treatment of arterial aneurysms or stenoses (e.g. dissections, transections, shunts) are within the scope of this document, the specific requirements and testing are not described. Similarly, specific prosthesis configurations (e.g. fenestrated, branched) are within the scope, but specific requirements and testing are not described for these devices.

This document is not applicable to vascular occluders, with the exception of contra-lateral iliac artery occluders when used as an integral part of aorto-uni-iliac endovascular prosthesis. Although contra-lateral iliac artery occluders when used as an integral part of aorto-uni-iliac endovascular prosthesis are within the scope of this document, specific requirements and testing are not described for these devices.

Balloons used to achieve adequate apposition of the prosthesis with the vessel wall or overlapping components are within the scope of this document, even if they are not integral to the endovascular system. This document provides requirements beyond the requirements of ISO 10555-4, specific to the use of balloons with endovascular prostheses.

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

The valve component of valved conduits constructed with an endovascular prosthesis component and the combination of the valved component and the endovascular prosthesis component are excluded from the scope of this document. This document can be helpful in identifying the appropriate evaluation of the endovascular prosthesis component of a valved conduit, but specific requirements and testing are not described for these devices.

NOTE 1 Cardiac valved conduits are within the scope of ISO 5840-1.

Pharmacological aspects of drug eluting or drug coated endovascular prostheses are not addressed in this document.

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

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

The requirements for, and the evaluation of, degradation and other time-dependant aspects of absorbable materials used in the construction of endovascular prostheses are not addressed in this document.

NOTE 3 Absorbable materials are within the scope of ISO/TS 17137 and ISO/TR 37137.

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 7198:2016, *Cardiovascular implants and extracorporeal systems — Vascular prostheses — Tubular vascular grafts and vascular patches*

ISO 10993-1, *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 14630:2012, *Non-active surgical implants — General requirements*

ISO 14937, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

ISO 14971, *Medical devices — Application of risk management to medical devices*

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 7198 and ISO 14630 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at https://www.iso.org/obp/

NOTE Additional descriptions of device and clinical effects of failure are included in Annex B.

3.1
adverse event
adverse 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
clinical effect of failure
specific clinical observations potentially associated with device failures

Note 1 to entry: The term device failure relates to the definition of a hazard as found in ISO 14971.

Note 2 to entry: Clinical effects of failure are described in Annex B.

3.3
delivery system
system or mechanism used to deliver the *endovascular prosthesis* (3.9) to the targeted position and then to deploy the prosthesis

Note 1 to entry: The delivery system is removed after implant deployment.

3.4
determine
quantitatively appraise or analyse

3.5
device effect of failure
consequence to the device potentially associated with device failures

Note 1 to entry: Device effects of failure are described in Annex B.

3.6
device evaluation strategy
DES
rationale for the testing selected to evaluate a specific *endovascular system* (3.10), based on the requirements of the device design and potential *failure modes* (3.13)

3.7
device evaluation strategy table
DES table
optional communication tool to present the *DES* (3.6) for a specific *endovascular system* (3.10)

3.8
endoleak
persistence of blood flow outside the lumen of an *endovascular prosthesis* (3.9), but within an aneurysm sac or vascular segment being treated by the graft

Note 1 to entry: Endoleaks in the presence of aneurysm are categorized as follows.

— Type I endoleak arising at or from a sealing zone, occurring at the proximal (Type Ia) or distal (Type Ib) attachment zone.

— Type II endoleak is caused by retrograde flow from patent branch arteries, for example, lumbar and intercostal arteries.

— Type III endoleak arises from an inadequate seal between modular graft components (Type IIIa) or from a defect in the *graft material* (3.15) (Type IIIb).

— Type IV endoleak is due to graft permeability, often identified by a generalized blush of contrast within the aneurysm sac.

3.9
endovascular prosthesis
endovascular graft
endovascular implant
vascular prosthesis (including modular components) which resides partially or completely within a blood vessel, or vascular conduit to form an internal bypass or shunt between sections of the vascular system, delivered and deployed using a *delivery system* (3.3)

3.10
endovascular system
system comprised of an *endovascular prosthesis* (3.9) and its *delivery system* (3.3)

3.11
evaluate
qualitatively appraise or analyse

3.12
factory anastomosis
factory manufactured seam-line in which two or more edges of *graft material* (3.15) are joined (e.g. sewn) together

Note 1 to entry: Bonds between stents or between the graft material and a stent or an attachment system are not covered under this definition.

3.13
failure mode
difficulty or failure of the *endovascular system* (3.10) that may be encountered (hazards) in pre-clinical *in vivo* or clinical use of an *endovascular system* (3.10) and could result in consequences (harm) to the subject

3.14
fixation system
system or feature of the *endovascular prosthesis* (3.9) that is designed to interface directly with the vessel wall in order to prevent migration

3.15
graft material
textile or non-textile, non-metallic material [e.g. polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), polyurethane] used to line or cover the mechanical support structures of the *endovascular prosthesis* (3.9) or to provide a vascular conduit for blood flow

4 General requirements for endovascular system

The following requirements shall apply to all endovascular systems.

4.1 Type of endovascular prosthesis

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

4.2 Materials and construction for endovascular system

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

4.3 Configuration and size designation for endovascular prosthesis

The configuration of endovascular prosthesis shall be designated by its geometry (e.g. straight, bifurcated, branched, fenestrated, tapered, flared).

The size of an endovascular system shall be designated by the outer diameter of the delivery system and the appropriate nominal relaxed diameters of each component of the endovascular prosthesis (e.g. main body, branches, extenders, cuffs) and the appropriate lengths.

4.4 Intended clinical use for endovascular system

The intended clinical use shall be designated by the disease state or lesion type to be treated (e.g. occlusive disease, stenosis, restenosis, aneurysm, dissection, transection) and one or more of the following implant locations:

a) ascending thoracic aortic;

b) aortic arch;

c) great vessels;

- left subclavian;
- left carotid;
- innominate (brachiocephalic);

d) descending thoracic aortic;

e) thoraco-abdominal aortic;

f) abdominal aortic and/or aorto-iliac;

- infrarenal;
- juxtarenal;
- pararenal and paravisceral;

g) visceral;

- renal;
- superior mesenteric;
- celiac;

h) peripheral;

- iliac;
- internal iliac;
- femoral;
- popliteal;
- tibial;
- carotid;

i) coronary;

j) arterio-venous shunt for vascular access;

k) transjugular intrahepatic shunt;

l) other vessels to be specified.

Anatomical indications (e.g. vessel diameter ranges for treatment of occlusive disease, range of landing zone diameters and lengths for the treatment of aneurysms, maximum angulation) shall be specified.

For branched or fenestrated devices, the additional vessels to be treated shall be specified.

For endovascular prostheses intended to be used in conjunction with adjunctive procedures (e.g. percutaneous transluminal angioplasty), the adjunctive procedure shall be specified.

If an endovascular prostheses may be used in a secondary procedure (e.g. treatment of in-stent restenosis, secondary repair of previously placed endovascular prosthesis with inadequate seal or fixation), the conditions of use shall be specified.

4.5 Balloon designation

Balloons integral to the endovascular system and balloons intended to achieve adequate apposition of the prosthesis shall be designated by the nominal diameter(s) as a function of the inflation pressure(s) or volume(s), the maximum recommended inflation pressure or volume and the rated burst pressure (RBP).

If a commercially available balloon is recommended for use in the instructions for use (IFU), the balloon shall be designated by the balloon type [e.g. percutaneous transluminal angioplasty (PTA), moulding, low-pressure aortic, compliant].

5 Intended performance

The requirements of ISO 14630:2012, Clause 4 shall apply.

6 Design attributes

6.1 General

The requirements of ISO 14630:2012, Clause 5 shall apply. General design attributes for endovascular systems are listed in Tables A.3 and A.4 with reference to the nonclinical testing necessary for the evaluation of the design. It is recognised that not all tests identified in a category will be necessary or practical for any given endovascular prosthesis and/or system. The rationale for the selection of tests shall be documented.

6.2 Endovascular system

In addition to the general requirements, the design attributes of the endovascular 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 endovascular prosthesis;

c) ability to safely withdraw the delivery system;

d) ability to minimize blood loss (haemostasis).

6.3 Endovascular prosthesis

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

a) ability of the endovascular prosthesis to ensure effective fixation within the vasculature;

b) ability of the endovascular prosthesis to maintain adequate integrity;

c) ability of the endovascular prosthesis to isolate the lesion as appropriate to its intended use (e.g. provide seal between the endovascular prosthesis and aneurysm, prevent blood from flowing through the implant wall);

Changes in wall permeability after implantation shall be considered when establishing an appropriate *in vitro* specification for permeability.

d) appropriate interaction between endovascular prosthesis modular components;

e) compatibility of the endovascular prosthesis dimensions for use in specified vessel diameters;

f) ability of the endovascular prosthesis to maintain adequate blood flow through the lumen (patency);

g) ability to safely use magnetic resonance imaging (MRI) on a patient with an implanted endovascular prosthesis.

6.4 Endovascular system and endovascular prosthesis

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

a) visibility of the endovascular system, delivery system and endovascular prosthesis under fluoroscopy or other technologies;

b) compliance of the delivery system and endovascular prosthesis with the requirements of ISO 10993-1 and other appropriate parts of the ISO 10993- series;

c) sterility of the endovascular system and endovascular prosthesis.

7 Materials

The requirements of ISO 14630:2012, Clause 6 shall apply. Additional testing specific to certain materials 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.

8 Design evaluation

8.1 General

The requirements of ISO 14630:2012, Clause 7 shall 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 an endovascular system.

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

— device description (e.g. physical description, figures, materials of construction), what the device key design features are intended to do, how the key design features accomplish the intended objective;

— intended clinical use (see 4.4);

— conditions of use/intended *in vivo* environment;

— minimum design life of the device.

A device evaluation strategy (DES) shall be created. A DES provides the rationale for the testing selected to evaluate the endovascular system based on the requirements of the device design and potential failure modes. DES may be communicated in a table (DES table) with column headings as presented and explained in Table A.1. Tables A.3 and A.4 may serve as the foundation for DES applicable to specific endovascular prosthesis and would be expanded upon as appropriate to address the unique aspects of the device. Alternative methods for presenting DES may be used (e.g. a non-tabular presentation of the rationale for the testing based on the potential risks and benefits of the endovascular system for the intended clinical use).

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

NOTE 1 All testing might not be appropriate for all endovascular system designs or intended clinical uses.

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 endovascular system shall be performed. The device evaluation strategy may be outlined in a table with column headings as presented in Table A.5. Appropriate testing shall be conducted as deemed necessary, considering the potential failure modes associated with 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. migration resistance, seal, kink resistance, durability, proper positioning, configuration or 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. 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). Justification for the selection of tests shall be provided.

NOTE 2 ASTM F2914 provides guidance for the determination of appropriate tests for the evaluation of shelf-life.

8.2 Sampling

A sampling plan should be used that 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 endovascular 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 or overlapping prostheses (e.g. separation force for overlapping endovascular prostheses), or if the attribute under test could be significantly affected by the overlap (e.g. ability to resist kinking), the test articles should include overlapped 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. A rationale should be provided for sample selection.

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

The need for testing of more than one area in endovascular prosthesis to ensure adequate characterization for some parameters (e.g. proximal and distal diameters in a tapered prosthesis,

wall thickness in devices with non-uniform wall thickness) should be considered in establishing the sampling plan.

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

8.3 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 that can affect the test results. Examples of conditioning are preparation of the endovascular system, loading of the prosthesis inside the delivery catheter, passage through simulated tortuous vasculature, warming of the system to body temperature and deployment of the prosthesis.

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) 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 the following:

   — 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 cross references to the test summary and full test report.

c) Individual test summaries should include the following:

   — a brief summary of the purpose, methods, and results;

   — the significance of the test results:

      — for tests with acceptance criteria, justification for the criteria;

      — 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, 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;

— conclusions: state conclusions, based on comparing results to acceptance criteria or provide an explanation of the relevance of the results for characterization tests and, if appropriate, include a discussion on the potential clinical significance of the results.

8.5 Bench and analytical tests

Testing of the endovascular system, delivery system and endovascular prosthesis 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.

8.5.1 Endovascular system and delivery system

The ability of the endovascular 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 assessed.

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 Table A.3.

Testing shall include the items listed in 8.5.1.1 through 8.5.1.11, as appropriate to the design of the endovascular system.

8.5.1.1 Balloon testing

The following requirements apply to balloons integral to the endovascular system and accessory balloons used to achieve adequate apposition of the prosthesis.

If the IFU for the endovascular prosthesis requires the use of a commercially available balloon, simulated use testing as required by 8.5.1.5 shall include use of the specified balloon or a balloon with characteristics representative of the type of balloon specified in the IFU. The balloon testing as required by 8.5.1.1 is not required for the commercially available balloon.

8.5.1.1.1 Balloon burst pressure for non-compliant balloons

Determine the mean and rated burst pressure (RBP) of the balloon when inside of the endovascular prosthesis.

8.5.1.1.2 Balloon deflation times

Determine the time required to completely deflate the balloon when inside of the endovascular prosthesis.

8.5.1.1.3 Balloon rated fatigue

Determine the ability of the balloon, when inside of the endovascular prosthesis, to withstand repeated inflation cycles to the maximum recommended pressure or volume, taking into consideration the number of inflation cycles expected clinically.

8.5.1.1.4 Balloon volume to burst for compliant balloons

Determine the volume required to burst a compliant balloon when inside of the endovascular prosthesis.

8.5.1.2 Dimensional verification of the endovascular system

Determine the endovascular system dimensions, including the useable length, profile and all other appropriate dimensions, for verification to design specifications.

8.5.1.3 Dislodgement force (pre-mounted, balloon-expandable endovascular prosthesis)

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

8.5.1.4 Force to deploy for self-expanding endovascular prostheses

Determine the force to deploy the endovascular prosthesis under simulated anatomical conditions. All applicable steps of the deployment process should be evaluated.

This force may be used to establish relevant bond strength acceptance criteria.

8.5.1.5 Simulated use

Evaluate the ability to access, deploy and withdraw the endovascular system, including pushability, flexibility, torquability, trackability and deployment accuracy, using an anatomical model(s) that is (are) representative of the anatomical variation in the intended patient population. Evaluate the compatibility of the endovascular system with accessory devices. Evaluate the conformability of the deployed endovascular prosthesis to the vessel wall, positioning (including orientation, if applicable), and absence of anomalies (e.g. kinks, twists, component separation, non-uniform expansion, prosthesis damage).

If visible particle generation is observed during access, deployment and withdrawal of the endovascular system, this observation should be noted. The relevance of any observations should be explained in the context of the intended clinical use.

8.5.1.6 Tensile bond strength

Determine the 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].

8.5.1.7 Torsional bond strength

Determine the torque required to cause failure of the joints and/or fixed connections in the appropriate segments of the delivery system (i.e. joints and/or fixed connections 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 determination.

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

8.5.1.8 Haemostasis

Evaluate the ability of any haemostatic seal or valve in the delivery system to minimize leakage of blood.

8.5.1.9 Biocompatibility

The biocompatibility of the delivery system and the endovascular prosthesis shall be ensured in accordance with ISO 10993-1 and appropriate parts of the ISO 10993- series.

8.5.1.10 Sterilization assurance

Sterilization shall be ensured in accordance with appropriate International Standards.

8.5.1.11 Visibility

Evaluate the ability to visualize the endovascular system and endovascular prosthesis using the imaging techniques specified in the instructions for use (IFU).

8.5.2 Endovascular prosthesis

The ability of the implant 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.4.

Testing shall include the items listed in 8.5.2.1 through 8.5.2.9, as appropriate to the design of the endovascular prosthesis. 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.

8.5.2.1 Corrosion

Evaluate the susceptibility of the metallic materials of the endovascular prosthesis to corrosion.

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 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.

8.5.2.3 Fatigue and durability — *in vitro* testing

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

Potential integrity failures to be assessed might include fractures, abrasion, perforation, suture breaks, bonding failures, suture hole elongation, weave separation and delamination.

In vitro fatigue testing of the prosthesis or appropriately justified test article shall be performed to demonstrate a minimum design life of 10 years. For pulsatile-related 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 an endovascular prosthesis to a prosthesis 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, active fixation) 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 (i.e. loading caused by the cardiac cycle) results in radial dilatation and can also produce non-radial (i.e. bending, torsional and axial) deformation. Non-pulsatile loading (e.g. loading from respiration, walking) can result in non-radial deformation. Examples of clinical uses with their associated modes of loading (e.g. bending, axial, torsion, radial) include the following:

— arterial endovascular prostheses will generally be subject to radial loading;

— non-aortic endovascular prostheses could also be subject to axial, bending and torsion;

— thoracic aortic endovascular prostheses could also be subject to bending.

8.5.2.3.2 Radial fatigue and durability

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

8.5.2.3.3 Active fixation fatigue and durability

Evaluate the long-term structural integrity of the securement of the active fixation components (e.g. barbs, hooks, pins) to the attachment system (e.g. proximal stent) and the securement of the attachment system to the endovascular prosthesis body when subjected to cyclic loading conditions, if applicable.

8.5.2.3.4 Axial fatigue and durability

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

8.5.2.3.5 Bending fatigue and durability

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

8.5.2.3.6 Torsional fatigue and durability

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

8.5.2.4 Fixation and seal

Determine the leakage at the seal zone and the separation force for overlapping endovascular prostheses. Also, evaluate the migration resistance of the endovascular prosthesis.

Additional testing may be appropriate to address potential effects of failure that can be related to inadequate fixation effectiveness such as radial force, recoil and strength of the connection(s) between

the graft material and a discrete fixation system(s) which are listed under 8.5.2.5, 8.5.2.7 and 8.5.2.8, respectively. In addition, testing to address the maintenance of fixation effectiveness is addressed under 8.5.2.2 and 8.5.2.3.

8.5.2.4.1 Leakage at seal zone

This test applies to a device design modification that may affect the seal zone(s).

Determine the leakage between the seal zone(s) of the endovascular prosthesis and a mock artery and compare the results to those for the unmodified device. This requirement can alternatively be met through evaluation of Type I endoleaks in a clinical study.

The evaluation of seal zone leakage is not necessary for endovascular prostheses intended for clinical uses for which seal zone leakage is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).

8.5.2.4.2 Migration resistance

Evaluate the ability of the endovascular prosthesis to resist migration when subjected to a force or pressure. The evaluation of migration resistance is not necessary for endovascular prostheses intended for clinical uses for which migration is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).

8.5.2.4.3 Separation force for overlapping endovascular prostheses

Determine the force required to separate overlapping endovascular prostheses or modular components (e.g. main body, cuffs, extenders) in the deployed state. The evaluation of separation force is not necessary for endovascular prostheses intended for clinical uses for which component separation is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).

8.5.2.5 Patency-related tests

Crush resistance, local compression and radial force characterize different patency-related attributes of the endovascular prosthesis and are applicable for specific device types and implant locations as described in Table 1. Resistance to kinking (flexibility) is applicable to all endovascular prostheses.

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

Test	Purpose	Rationale for applicability			
		Non-aortic implant locations		Aortic implant locations	
		Balloon-expandable endovascular prostheses	Self-expanding endovascular prostheses	Balloon-expandable endovascular prostheses	Self-expanding endovascular prostheses
Compression resistance to perpendicularly applied load (self-expanding, non-aortic endovascular prostheses)	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 prosthesis.	Not applicable because this test does not evaluate permanent deformation relevant to balloon-expandable prostheses.	**Applicable** because a non-aortic self-expanding prosthesis might be subjected to compressive forces that can affect patency.	Not applicable because the aorta is not typically subjected to perpendicularly applied loads.	Not applicable because the aorta is not typically subjected to perpendicularly applied loads.
Crush resistance with perpendicularly applied load (balloon-expandable, non-aortic endovascular prostheses)	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 prosthesis.	**Applicable** because a non-aortic balloon-expandable prosthesis may be permanently deformed by an external load.	Not applicable because self-expanding devices do not typically undergo permanent deformation.	Not applicable because the aorta is not typically subjected to perpendicularly applied loads.	Not applicable because the aorta is not typically subjected to perpendicularly applied loads.
Crush resistance with radially applied load (balloon-expandable endovascular prostheses)	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 non-aortic balloon-expandable prosthesis may be permanently deformed by a radially applied load.	Not applicable because self-expanding devices do not typically undergo permanent deformation.	**Applicable** because an aortic balloon-expandable prosthesis may be permanently deformed by a radially applied load.	Not applicable because self-expanding devices do not typically undergo permanent deformation.
Radial force (self-expanding, endovascular prostheses)	The purpose of this test is to determine the outward force as a function of the diameter of the endovascular prosthesis.	Not applicable because balloon-expandable devices can exhibit permanent deformation which is not evaluated by this test.	**Applicable** because a non-aortic self-expanding prosthesis exerts a radial outward force against the vessel wall.	Not applicable because balloon-expandable devices can exhibit permanent deformation which is not evaluated by this test.	**Applicable** because an aortic self-expanding prosthesis exerts a radial outward force against the vessel wall.

8.5.2.5.1 Compression resistance to perpendicularly applied load (self-expanding, non-aortic endovascular prostheses)

Determine the force at which a pre-specified displacement occurs under a load applied perpendicular to the longitudinal axis of the prosthesis.

8.5.2.5.2 Crush resistance with perpendicularly applied load (balloon-expandable, non-aortic endovascular prostheses)

Determine the force at which a pre-specified amount of permanent deformation occurs under a load applied perpendicular to the longitudinal axis of the prosthesis.

8.5.2.5.3 Crush resistance with radially applied load (balloon-expandable endovascular prostheses)

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

8.5.2.5.4 Radial force (self-expanding endovascular prostheses)

Determine the outward force as a function of the diameter of the endovascular prosthesis.

8.5.2.5.5 Resistance to kinking (flexibility)

Determine the minimum radius that the endovascular prosthesis can accommodate without kinking.

8.5.2.6 Permeability

Determine the porosity, water permeability and/or water entry pressure, as appropriate to the endovascular prosthesis. The selection of appropriate tests from those listed below shall be justified based on the graft material of construction. Integral water leakage is applicable to all endovascular prostheses.

8.5.2.6.1 Integral water leakage

Evaluate the water leakage between modular components and through holes in the graft material resulting from the construction of the endovascular prosthesis (e.g. holes created by suturing stent structures to the graft material).

8.5.2.6.2 Porosity (non-textile materials)

Determine the porosity of the graft material for an endovascular prosthesis constructed of non-textile materials.

8.5.2.6.3 Water entry pressure (non-textile materials)

Determine the pressure required to force water through the graft material of an endovascular prosthesis constructed of non-textile materials.

8.5.2.6.4 Water permeability (textile materials)

Determine the water flow rate through the graft material of an endovascular prosthesis constructed with a water-permeable graft material (e.g. woven graft material).

8.5.2.7 Sizing-related testing

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

8.5.2.7.1 Dimensional verification of the endovascular prosthesis

Determine the graft material wall thickness(es) and the endovascular prosthesis dimensions in the deployed state, including the length(s), outer diameter(s) and all other appropriate dimensions, for verification to design specifications.

8.5.2.7.2 Implant diameter to balloon inflation pressure (balloon-expandable endovascular prostheses)

Determine the relationship between the prosthesis diameter and the balloon inflation pressure for balloon-expandable endovascular prostheses.

8.5.2.7.3 Implant length to diameter relationship (endovascular prostheses that have clinically relevant length changes with diameter changes)

Determine the relationship between the length and diameter for endovascular prostheses that have clinically relevant length changes with diameter changes.

8.5.2.7.4 Recoil (balloon-expandable endovascular prostheses)

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

8.5.2.8 Strength

Determine the burst strength, factory seam strength, longitudinal tensile strength, strength after repeated puncture and strength of the connection(s) between the graft material and a discrete fixation system(s), as appropriate to the endovascular prosthesis. The selection of appropriate tests from those listed below shall be justified based on the design of the endovascular prosthesis.

8.5.2.8.1 Burst strength

Determine the pressurized burst strength of the graft material or alternatively, the burst strength of the entire endovascular prosthesis if processing may reduce the strength of the graft material.

8.5.2.8.2 Factory seam strength (endovascular prostheses with seams in the graft material)

Determine the tensile strength of any factory manufactured seams in the graft material. This requirement is not intended to apply to any connections between stents or between the graft material and a stent or an attachment system (see 8.5.2.8.5).

8.5.2.8.3 Longitudinal tensile strength

Determine the longitudinal tensile strength of the graft material.

8.5.2.8.4 Strength after repeated puncture (endovascular prostheses for vascular access)

Determine the strength of the endovascular prosthesis following repeated dialysis-needle punctures for a prosthesis that will be cannulated to provide blood access for haemodialysis.

8.5.2.8.5 Strength of the connection(s) between the graft material and a discrete fixation system(s)

Determine the strength of the connection(s) between the graft material and the fixation system(s). This requirement applies to prostheses with a fixation system that is discrete from any stent(s) intended to provide structural support within the prosthesis (e.g. suprarenal stent that is not continuous with the stent(s) in the prosthesis body).

This requirement is to determine the securement of a fixation system (e.g. suprarenal stent) to the endovascular prosthesis body and not to evaluate the securement of an active fixation component (e.g. barb, hook, pin) to the fixation system or graft material. As such, the location or presence of an active fixation component is not relevant for this requirement.

NOTE The structural integrity of the securement of an active fixation component (e.g. barb, hook, pin) to the fixation system is addressed in 8.5.2.3.3.

8.5.2.9 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 magnetically induced displacement force and torque and RF induced heating of the prosthesis. 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 prosthesis. 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 prosthesis. For example, although image artefact associated with an abdominal prosthesis 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, and

— ASTM F2119.

8.6 Preclinical *in vivo* evaluation

8.6.1 Purpose

The purpose of preclinical *in vivo* testing is to evaluate the deployment of the endovascular prosthesis, the biological response of the host to the prosthesis and the effect of the implant environment on the prosthesis. 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.

The principles of 8.6 may be applied for the preclinical *in vivo* evaluation of particular configurations of prostheses (e.g. fenestrated, branched) and vascular uses other than the treatment of arterial stenoses and aneurysms. Additional specific aims, endpoints and reporting requirements might be needed to define an appropriate study.

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 endovascular prosthesis;

c) evaluate the accuracy of deployment;

d) evaluate the compatibility of accessory devices with the endovascular system, including balloons used post-deployment;

e) evaluate the ability to withdraw the delivery system;

f) evaluate the functional haemostasis of the delivery system and sheath introducer;

g) evaluate the position, structural and material integrity and patency of the endovascular prosthesis acutely and at explant;

h) evaluate histology and pathology of explants and pertinent tissues/organs;

i) record failure modes, device and clinical effects of failure (see Annex B for potential failure modes and effects of failure) and adverse events.

8.6.3 Protocol considerations

Each type of prosthesis shall be tested by implantation at the intended, or an analogous, vascular site in a reasonable number of animals for an adequate duration of time 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. 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.

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, sex, 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.

Appropriate quality management practices and animal welfare protection measures should be followed in the execution of an animal study.

8.6.4 Data acquisition

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

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) medication (e.g. prophylactic antibiotics);

c) operative data:

1) date of procedure;

2) name of person(s) performing procedure;

3) prosthesis identification;

4) *in situ* length of prosthesis;

5) target vessel and prosthesis diameters;

6) location and length of overlap for overlapping devices;

7) use of systemic antiplatelet/anticoagulant therapy;

8) assessment of the ability to access the target vessel location (e.g. pushability, flexibility, torquability, trackability);

9) assessment of the ease and ability to accurately deploy the prosthesis;

10) assessment of the ability to visualize the delivery system and the implant;

11) assessment of the ability to withdraw the delivery system;

12) assessment of the compatibility with accessory devices (e.g. balloons used during or after deployment);

13) assessment of blood loss (e.g. amount and location);

14) assessment of position, conformability, patency and absence of abnormalities (e.g. kinks, twists, component separation, non-uniform expansion and prosthesis damage) of the implant;

15) observed device and clinical effects of failure and adverse perioperative events, including severity, management and outcome;

16) any significant deviation from the proposed deployment instructions or protocol;

d) post-operative and follow-up data:

1) medications, including those that affect coagulation;

2) assessment of structural integrity, patency and position of the prosthesis, including the method and date of visualization;

3) observed device and clinical effects of failure and adverse events, including date of occurrence, severity, management and outcome;

4) any significant deviation from the protocol;

e) termination data:

1) date of sacrifice;

2) name of person(s) performing procedures and assessments;

3) assessment of structural integrity, patency and position of prosthesis, including method of visualization;

4) gross alteration in the dimensional and physical properties of the prosthesis;

5) histological and pathological 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, if applicable;

   4) implantation periods;

   5) methods of assessment;

   6) intervals of observation;

   7) sample size (i.e. number of animals and implants);

c) summary of results:

   1) animal accountability, including rationale for exclusion of data from the primary analysis;

   2) number of animals for which there was successful implantation of the prosthesis;

   3) operator assessment of ease of deployment, visualization and handling;

   4) discussion of appropriateness of sizing and potential impact on study results;

   5) summary of any changes in position, structural and material integrity and patency of the prosthesis;

   6) summary of device and clinical effects of failure and adverse events;

   7) summary of early deaths or sacrifices for cause;

   8) significant and/or relevant deviations from protocol;

   9) summary of pathology and histology of explants and appropriate tissues/organs, including representative gross photographs and micrographs;

   10) comparison of outcomes for test and control groups, if applicable;

   11) conclusions from study;

   12) 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 an endovascular system. This evaluation is not intended to demonstrate the long-term performance of the prosthesis. An investigation should be carried out for each new prosthesis or new clinical application of a prosthesis 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. Additional prosthesis sizes outside the previously evaluated range might require clinical evaluation.

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.

The principles of 8.7 may be applied for the clinical evaluation of particular configurations of prostheses (e.g. fenestrated, branched) and vascular uses other than the treatment of arterial stenoses and aneurysms. Additional specific aims, endpoints, and reporting requirements might be needed to define an appropriate study.

8.7.2 Specific aims

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

a) evaluate the effectiveness of the endovascular system, such as the following:

   1) ability to access the target location with the delivery system;

   2) accuracy of deployment;

   3) ability to withdraw the delivery system;

   4) position, structural and material integrity and functionality of the prosthesis acutely and over time;

   5) lesion characteristics (e.g. aneurysm size, restenosis, false lumen perfusion) over time;

   6) device effects of failure (see Annex B for potential effects of failure);

b) evaluate the safety of the endovascular system, such as the following:

   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. technical success in absence of serious device related events) or combined safety and effectiveness endpoints (e.g. 30-day mortality for the treatment of dissections) to be measured. Definitions of success and failure for each endpoint and the duration of follow-up needed to assess each endpoint shall be specified. A definition for the study success shall also be specified (e.g. meeting both the safety and effectiveness primary endpoints).

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

The clinical investigation shall be continued for a minimum of 12 mos for each patient unless a justification for a different study duration is provided. Patient follow-up intervals shall include a minimum of a baseline assessment at discharge and an assessment 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 endpoint analyses, shall be recorded and reported. The final report may be

completed when the required number of patients to test the hypotheses has reached the specified study duration. The report shall include current follow-up data on all patients. Longer-term patient follow-up (e.g. 3 years to 5 years after the last prosthesis 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 the following terms:

— randomized, multi-arm, "unblinded" study with a concurrent control using an alternative or no treatment;

— non-randomized study with concurrent control;

— single-arm study with patient serving as own control (include designed single-arm crossover);

— single-arm study with historical control using patient-level data;

— single-arm study with literature control;

— single-arm study with performance goals.

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 implant 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 enrolment).

Definitions, primary and secondary clinical endpoints, measurement methods and data analysis shall be specified in the clinical protocol. Secondary endpoints might include the following:

— individual components that make up any composite primary endpoints;

— technical success [e.g. successful placement of all endovascular graft components at the intended implantation site(s) with patency and an absence of significant device deformations, e.g. kinks, stent eversion, twists];

— procedural success (e.g. technical success in absence of serious device-related adverse events at 30 d);

— device and clinical effects of failure;

— secondary endovascular procedures;

— conversions to open surgical repair;

— indication-related mortality (e.g. aneurysm-related mortality);

— longer-term outcomes (e.g. 12-month safety data if the primary safety endpoint is at 30 d).

8.7.4 Data acquisition

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

a) identification and demographic data:

   1) patient identification;

   2) indication for treatment (e.g. malperfusion, rapidly expanding aneurysm, critical limb ischaemia) and associated medical diagnosis (e.g. aneurysm, dissection, occlusion, transection);

3) demographics:

   i) date of birth;

   ii) sex;

   iii) weight;

   iv) height;

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

4) name of investigator;

5) name of institution;

b) pre-operative data:

1) risk factors, such as hypertension, diabetes, coronary artery 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. carotid-subclavian bypass, aortic vessel debranching), 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, neck lengths, extent of dissection, location of primary entry tear, tortuosity, angle of seal zones);

c) operative data:

1) name of implanting physician;

2) date of procedure;

3) identification data for the endovascular prosthesis(es) including model number, implant traceability, size and configuration;

4) urgency of intervention (i.e. urgent, emergent or elective);

5) information regarding the procedure (e.g. adjunctive vascular procedures performed, type of anaesthesia, total fluoroscopy time, coverage of main branch vessels);

6) relevant medications (e.g. heparin, other anticoagulants);

7) assessment of technical success;

8) position of prosthesis (e.g. neck length covered by prosthesis for treatment of aneurysms, distance from anatomical landmarks);

9) assessment of prosthesis effectiveness (e.g. endoleaks, including type, location, need for intervention; residual stenosis; patency);

10) plan for additional procedures to complete the repair (e.g. staged procedure);

For staged procedures, consistent information should be captured for each intervention at the time of each procedure.

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

12) date of hospital discharge;

d) follow-up:

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

2) date of follow-up visit;

3) clinical and imaging evaluation:

i) clinical assessment;

ii) objective assessment of prosthesis positioning, integrity and effectiveness and method of assessment;

iii) objective assessment of targeted lesion characteristics (e.g. aneurysm size, false lumen thrombosis, patency, branch vessel patency, percentage of diameter stenosis) and method of assessment;

4) relevant medications, such as anticoagulants or antiplatelets;

5) record device and clinical effects of failure and adverse events [see item 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 prosthesis involvement;

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

f) secondary procedures associated with the index procedure:

1) date;

2) reason for intervention;

3) type of intervention;

4) outcome of intervention;

g) death:

1) date;

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

3) cause of death;

4) whether or not the death was related to the prosthesis or procedure;

h) explant of prosthesis:

1) date;

2) whether the subject is living or deceased;

3) reason for explant;

4) associated device effects of failure, if applicable;

5) relevant observations (e.g. device integrity, device positioning, tissue incorporation, vascular tissue erosion);

i) 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 clinical 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 endpoints, hypotheses and definitions of success;

3) definition of study success;

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

5) follow-up intervals;

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

7) data analysis plan;

8) 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 endpoint analyses;

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

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

g) significant and/or relevant deviations from protocol;

h) results:

1) technical success;

2) procedural success;

3) safety:

i) primary and secondary endpoint 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 endpoint outcomes;

ii) summary of secondary interventions;

5) summary of explant analyses;

6) 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

Endovascular 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 apply.

11 Sterilization

11.1 Products supplied sterile

Endovascular systems shall be labelled "Sterile", comply with national or regional standards and have a sterility assurance level (SAL) of 10^{-6}. Sterilization processes shall be validated and routinely controlled.

a) For endovascular systems that are to be sterilized by ethylene oxide, ISO 11135 applies.

b) For endovascular systems that are to be sterilized by radiation, ISO 11137 (all parts) applies.

c) For single-use endovascular systems incorporating animal tissue that are to be sterilized using liquid chemical sterilants, ISO 14160 applies.

d) For endovascular systems that are to be sterilized by other sterilization processes, ISO 14937 applies.

11.2 Sterilization residuals

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

12 Packaging

12.1 Protection from damage in storage and transport

12.1.1 General

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

12.1.2 Unit container

Each endovascular system shall be packaged in a unit container providing a sterile barrier. 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, may 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

The unit container shall be designed to maintain the sterility of the endovascular system under nominal 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 endovascular system shall be accompanied by a label(s) on an appropriate container(s). At least the following information shall be provided on the label(s):

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

b) product name;

c) the material of construction and type of construction;

d) the configuration (see 4.3). A symbol may be substituted for a written description of the prosthesis;

e) the nominal length(s);

f) the nominal diameter(s);

g) the words “STERILE — DO NOT RESTERILIZE — SINGLE USE ONLY”, or equivalent phrase or symbols, in prominent form;

h) method of sterilization;

i) sterile lot number;

j) date of sterilization and/or the expiry/expiration date;

k) manufacturer's batch or lot number;

l) a warning against the use of the endovascular system if the package is open or damaged;

m) manufacturer's recommendations for storage, when applicable.

NOTE If the manufacturer's batch or lot number [see item k)] and the sterile lot number [see item i)] can be traced to the same information, only one number needs to be given.

12.2.2 Record label

Each endovascular system should be supplied with transferable record labels suitable for attachment to the records of the patient receiving the prosthesis. The record label shall 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 Instructions for use

12.3.1 General

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

12.3.2 Information and instructions for use for endovascular systems

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

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

b) product name;

c) device description and materials of construction;

d) indications for use;

e) contraindications, cautions and warnings;

f) potential adverse events;

g) data from clinical studies, if applicable;

h) recommendations for endovascular prosthesis sizing;

i) recommended methods for the preparation of the endovascular system and implantation techniques;

j) the statement "STERILE — DO NOT RESTERILIZE — SINGLE USE ONLY" in prominent form;

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

l) recommendations for storage, if applicable;

m) recommendations for visualization;

n) MRI safety information;

o) revision date.

Annex A
(informative)

Relationship between testing requirements and device attributes and potential failure modes

A.1 General

Tables A.3 and A.4 provide the rationale for the requirements specified in this document for bench tests and analyses to assess device performance. The table headings are described in Table A.1. Clause A.2 also provides guidance on the identification of appropriate testing to evaluate a specific device design. Clause A.3, with Tables A.5 to A.7, provides guidance on the identification of appropriate testing to evaluate design modifications and changes in intended use.

Annex B provides a description of the potential effects of failure identified in Annex A.

Annex C provides a list of the bench tests and analyses, with a description of the purpose of each test, the associated device-related and procedure-related functions identified in Annex A, and reference to applicable design evaluation sections in this document (Clause 8) and the applicable test methods in Annex D.

Annex D provides information to consider in developing appropriate bench test and analytical methods.

A.2 Identification of appropriate testing

A device evaluation strategy (DES) provides the rationale for the evaluation plan for a specific device design. Identification of the appropriate testing involves describing each device-related and procedure-related function needed to achieve the desired performance, the associated device design features, the potential specific failure modes if the function is not attained, how the failures could affect the device and patients (i.e. the effects of failure) and finally, the testing needed to assess the device attribute or failure mode. A DES table may have column headings as presented and explained in Table A.1. The most critical functions and failure modes that represent the highest risk to patients should be highlighted in the DES table to provide perspective on the appropriate level of mitigation activities.

Tables A.3 and A.4 provide the rationale for the requirements specified in this document, including basic information that is applicable to most endovascular prostheses. The device design column is not included in Tables A.3 and A.4 because these tables provide general information and not design-specific information.

The columns for a device-specific DES are outlined in Table A.1, however, additional columns may be added. The information provided in Tables A.3 and A.4 may be of use in populating a device-specific DES table with these column headers. These tables may be modified to remove information that is not applicable for the device being evaluated and to add information specific to the unique design or intended use of the device. For example, rows that address balloon testing should be removed if there is no balloon used in the delivery of the device. It may be appropriate to include subcategories of potential device effects of failure applicable to the device design (e.g. subcategories for "delivery system damage" to identify the potential types of damage to specific components of the delivery system). The nonclinical testing column may include bench tests, analyses and information on preclinical *in vivo* evaluations of the device as related to the evaluation of a particular function or potential failure mode.

Regarding potential device effects of failure, further categorization is included in Tables A.3 and A.4 to acknowledge that one effect might lead to a subsequent effect of failure. For example, attachment system disconnection might lead to migration. For this example, attachment system disconnection

would be listed under “device effects of failure” and migration would be listed under “subsequent device effects of failure”.

Regarding potential clinical effects of failure, commonly listed groups of clinical effects have been assigned abbreviations as described in Table A.2. These abbreviations are used throughout this document to minimize redundancy. “A non-specific clinical event or use of additional devices or procedures”, designated as ACE4 in Table A.2, is applicable for all potential failure modes, but is not repeated to decrease redundancy. Although they are known potential clinical effects, “Death” and “Surgical Conversion” are not listed in the tables because conversion and death are correlated to 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 — Table headings and explanations for Tables A.3 and A.4 and for a device-specific DES[a]

Device/Procedure related function(s)	Device design information (applicable for a device-specific DES table)[a]	Potential failure mode(s)	Potential effect(s) of failure			Nonclinical device testing[b]
			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. NOTE Functions should be attributes of the device or procedure and therefore, should be stated in the positive.	The key design feature characteristics intended to provide the function or to address or mitigate the potential failure mode. Optional: provide relevant information about 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 relevant information would be the incorporation of the design characteristic of controlled release of the proximal attachment system to avoid improper positioning, configuration, or orientation, as this has been successful in other devices.*	The specific failures that might occur and could result in consequences (effects) to the device or patient if the function is not attained. NOTE 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.

[a] The device design column should be included in a device-specific DES table. This column is not included in Tables A.3 and A.4 because these tables provide general information and not design-specific information.

[b] This column may also include information on any preclinical *in vivo* evaluations used to evaluate a particular function or failure mode for a device-specific DES table.

Table A.2 — Legend for grouped associated clinical effects of failure

ACE1 Migration	ACE2 Prosthesis component separation	ACE3 Loss of patency	ACE4 Non-specific consequences
— Aneurysm enlargement — Aneurysm rupture — Aortic enlargement — Branch vessel loss of patency — False lumen patency — False lumen perfusion — Ischaemia — Lumen obstruction — Type I endoleak	— Aneurysm enlargement — Aneurysm rupture — Branch vessel loss of patency — Ischaemia — Lumen obstruction — Type IIIa endoleak	— Amputation — Ischaemia — Lumen obstruction — Prosthesis occlusion — Restenosis — Thrombosis	A non-specific clinical event or use of additional devices or procedures

Table A.3 — Device evaluation strategy for the endovascular 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	Endovascular system is incompatible with accessory devices	— Access failure — Accessory device failure — Delivery system damage — Prosthesis damage	None	— Access vessel injury — Failure to complete device implantation	— Dimensional verification — Simulated use
	Inability to advance endovascular system to target site	— Access failure — Delivery system damage — Prosthesis damage	None	— Access vessel injury — Access vessel rupture — Failure to complete device implantation — Vascular injury–Delivery system related	— Simulated use — Torsional bond strength
	Prosthesis dislodgement from the delivery system	— Prosthesis dislodgement from the delivery system	None	— Failure to complete device implantation — Foreign body embolization — Ischaemia	— Dislodgement force — Simulated use
Ability to deploy	Inability to activate deployment mechanism or procedure	— Balloon-related deployment failure — Deployment system failure — Inability to deploy	None	— Failure to complete device implantation	— Force to deploy — 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)		
	Improper positioning, configuration, or orientation	— Inaccurate deployment — Lack of conformance to the vessel wall (e.g. bird beaking) — Maldeployment — Misaligned deployment	None	ACE3 — Aneurysm enlargement — Aneurysm rupture — Aortic enlargement — Branch vessel blockage — Branch vessel coverage — Dissection creation or extension — False lumen patency — False lumen perfusion — Type I endoleak — Vascular injury – endovascular prosthesis related	— Implant length to diameter relationship — Simulated use
	Excessive balloon inflation	— Balloon rupture	None	— Branch vessel thrombosis — Dissection creation or extension — Foreign body embolization (balloon fragments) — Restenosis — Thrombosis — Vascular injury–Delivery system — Vessel rupture	— Balloon pressure for non-compliant balloons — Balloon volume to burst for compliant balloons
Ability to withdraw	Incomplete balloon deflation	— Prosthesis dislodgement	— Migration	ACE1 — Access vessel injury — Access vessel rupture — Vascular injury – delivery system related	— Balloon deflation time — Simulated use
	Damage of implant components by other components (e.g. delivery system snagging on the prosthesis)	— Prosthesis damage — Prosthesis dislodgement	— Migration	— ACE1 — Foreign body embolization	— Dimensional verification — 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)		
Atraumatic introduction, tracking and withdrawal	Emboli generation	None	None	— Embolism — Ischaemia	— None
	Particulate generation	None	None	— Adverse biological response — Ischaemia	— Simulated use
	Trauma to vasculature	None	None	— Access vessel injury — Access vessel rupture — Unintentional dissection septum perforation — Vascular injury–Delivery system related	— Dimensional verification — Simulated use
Delivery system integrity	Separation of delivery system components (e.g. bond failures, complete tip separation)	— Delivery system damage	— Deployment system failure	— Failure to complete device implantation — Foreign body embolization — Vascular injury – delivery system related	— Simulated use — Tensile bond strength — Torsional bond strength
	Tubing material failure	— Delivery system damage	— Deployment system failure	— Failure to complete device implantation — Foreign body embolization — Vascular injury–Delivery system related	— Simulated use — Tensile bond strength — Torsional bond strength
	Loss of balloon integrity	— Balloon-related deployment failure — Balloon rupture	None	— Failure to complete device implantation — Foreign body embolization	— Balloon rated fatigue — Balloon burst pressure for non-compliant balloons — Balloon volume to burst for compliant balloons
	Other loss of delivery system integrity	— Delivery system damage	— Deployment system failure	— Failure to complete device implantation	— As appropriate to the design of the device
Haemostasis	Inadequate haemostasis	None	None	— Blood loss	— Dimensional verification — Haemostasis
Sterility	Non-sterile product	None	None	— Insertion site infection — Prosthesis infection	— Sterilization assurance

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)		
Biocompatibility	Non-biocompatible	None	None	— Adverse biological response	— Biocompatibility
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 prosthesis	None	None	— Inability to monitor the prosthesis over time	

Table A.4 — Device evaluation strategy for endovascular prosthesis

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)		
Fixation effectiveness	Excessive radial force	None	None	— Dissection creation or extension — Erosion leading to fistula formation — Vascular injury–endovascular prosthesis related	— Radial force (self-expanding)
	Inadequate fixation	— Migration — Prosthesis component separation	None	ACE1 ACE2	— Migration resistance — Radial force (self-expanding) — Recoil (balloon-expandable) — Separation force for overlapping prostheses — Strength of the connection(s) between the graft material and a discrete fixation system(s)
Prosthesis integrity	Structural failure of graft material *(includes loss of integrity due to any cause, such as wear between modular components)*	— Delamination	— Graft dilatation or rupture	— Aneurysm enlargement — Aneurysm rupture — Aortic enlargement — Type IIIb endoleak	— Fatigue and durability
		— Graft dilatation or rupture	None	— Aneurysm enlargement — Aneurysm rupture — Aortic enlargement	— Burst strength — Longitudinal tensile strength
		— Graft material holes	None	— Type IIIb endoleak	— Fatigue and durability

Table A.4 *(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)		
	Structural failure of mechanical support structures or fixation systems *(includes loss of integrity due to any cause, such as wear between modular components, fatigue)*	— Active fixation element (hook/barb) fracture	— Lack of conformance to the vessel wall — Migration	ACE1	— Active fixation fatigue and durability — Computational analyses
		— Support structure fracture	— Graft material holes — Lack of conformance to the vessel wall — Migration — Prosthesis component separation	ACE1 ACE2 — Foreign body embolization — Type IIIb endoleak — Vascular injury – endovascular prosthesis related	— Computational analyses — Fatigue and durability — Simulated use
		— Metallic bond fracture	— Attachment system disconnection — Graft material holes — Migration — Support structure separation	ACE 1 — Foreign body embolization — Type IIIb endoleak	— Computational analyses — Fatigue and durability — Simulated use — Strength of the connection(s) or bond(s) between the graft material and the stent(s) or attachment system(s)

Table A.4 *(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)		
	Loss of attachment between parts of the endovascular prosthesis (e.g. between graft material and mechanical support structure, between stent rings)	— Attachment system disconnection	— Migration	ACE1	— Computational analyses — Fatigue and durability — Simulated use — Strength of the connection(s) or bond(s) between the graft material and the stent(s) or attachment system(s)
		— Separation of covering from stent	— Graft material holes	— Type IIIb endoleak	— Fatigue and durability — Simulated use — Strength of the connection(s) or bond(s) between the graft material and the stent(s) or attachment system(s)
		— Suture breaks — Graft material tear at seams	— Attachment system disconnection — Graft material holes — Migration — Support structure separation	ACE1 — Type IIIb endoleak	— Factory seam strength — Fatigue and durability — Simulated use — Strength of the connection(s) or bond(s) between the graft material and the stent(s) or attachment system(s)
		— Leakage at factory seam	None	— Aneurysm enlargement — Aneurysm rupture — Aortic enlargement — Aortic rupture — Type IIIb endoleak	— Integral water leakage
	Structural failure of graft material after repeated puncture for vascular access grafts	— Delamination — Graft dilatation or rupture	None	— Blood loss	— Strength after repeated puncture for vascular access

Table A.4 *(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)		
	Corrosion	— Active fixation element (hook/barb) fracture — Metallic bond fracture — Support structure fracture	— Lack of conformance to the vessel wall — Prosthesis component separation — Migration	ACE1 ACE2 — Adverse biological response — Foreign body embolization — Vascular injury–endovascular prosthesis related	— Corrosion
Adequate Seal	Inadequate exclusion of the lesion	— Lack of conformance to the vessel wall (e.g. bird beaking)	None	— False lumen patency — False lumen perfusion — Type I endoleak	— Leakage at seal zone — Simulated use
Appropriate permeability	Inadequate biological incorporation due to insufficient permeability	None	None	ACE1 — Prosthesis infection — Thrombosis	— Porosity, water permeability, integral water leakage and water entry pressure, as appropriate
	Excessive permeability or leakage	— Leaking through graft material — Leaking through holes in graft wall	None	— Aneurysm enlargement — Aneurysm rupture — Aortic enlargement — Aortic rupture — Type IV endoleak	— Porosity, water permeability, integral water leakage and water entry pressure, as appropriate
Modularity and intended overlap	Dimensional mismatch between implant components	— Prosthesis component separation — Poor apposition between components	None	ACE2	— Dimensional verification
	Inaccurate positioning or orientation	— Branch vessel prosthesis compression or kink — Prosthesis component separation	None	ACE2 — Branch vessel blockage — Branch vessel coverage	— Simulated use — Visibility
	Separation between implant components simulated	— Prosthesis component separation	None	ACE2	— Migration resistance — Radial force — Separation force for overlapping prostheses — Simulated use
	Angulation or kink between implant components	— Branch vessel prosthesis compression or kink — Prosthesis kink	None	ACE3 — Branch vessel blockage — Branch vessel coverage	— Resistance to kinking — Simulated use

Table A.4 *(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)		
	Damage to, obstruction of, or movement of implant component by other implant component	— Branch vessel prosthesis compression or kink — Prosthesis component separation — Graft material holes — Migration — Stent or attachment system fracture	None	ACE1 ACE2 — Branch vessel blockage — Branch vessel coverage — Vascular injury–endovascular prosthesis related	— Fatigue and durability — Simulated use
Appropriate sizing recommendations	Excessive oversizing	— Lack of conformance to the vessel wall (e.g. bird beaking) — Prosthesis compression or collapse — Graft material infolding	— Prosthesis kink	ACE3 — Dissection creation or extension — False lumen patency — False lumen perfusion — Thrombosis — Type I endoleak — Vascular injury–endovascular prosthesis related — White thrombus formation	— Computational analyses — Dimensional verification — Fatigue and durability — Implant diameter to balloon inflation pressure — Implant length to diameter relationship — Radial force — Recoil — Simulated use
	Undersizing	— Prosthesis component separation — Incomplete apposition to vessel wall — Migration	— Prosthesis kink	ACE1 ACE2	— Dimensional verification — Implant diameter to balloon inflation pressure — Implant length to diameter relationship — Radial force — Recoil — Migration resistance — Simulated use

Table A.4 *(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)		
Patency	Kinking	— Prosthesis kink	None	ACE3 — Embolism — White thrombus formation For TIPS: — Recurrence of portal hypertension	— Resistance to kinking — Simulated use
	Improper positioning, configuration or orientation	— Lack of conformance to the vessel wall (e.g. bird beaking) — Maldeployment — Misaligned deployment	None		— Simulated use
	Graft material in-folding	— Graft material in-folding	None		— Simulated use
	Prosthesis compression or collapse	— Prosthesis compression or collapse	— Support structure fracture		— Crush resistance, compression resistance, radial force, as appropriate — Simulated use
	Thrombosis due to material-related factors	— None	None	— Amputation — Ischaemia — Limb loss — Prosthesis occlusion — Restenosis — Thrombosis	— Biocompatibility
	Branch vessel prosthesis compression or kink	— Branch vessel prosthesis compression or kink	None	— Branch vessel blockage — Branch vessel coverage — Embolism — Ischaemia	— Crush resistance, compression resistance, radial force, as appropriate — Resistance to kinking — Simulated use
Magnetic resonance imaging (MRI) safety	Heating	None	None	— Vascular injury–MR related	— MR safety
	Lack of quality MRI imaging	None	None	— Inability to monitor prosthesis over time with MR imaging — Inadequate MR imaging	
	Movement of implant	— Migration — Prosthesis component separation	None	ACE1 ACE2 — Dissection creation or extension — MR related	

A.3 Identification of appropriate testing for device design modifications and changes in intended use

Identification of the appropriate testing for device design modifications and changes in intended use involves identifying the device-related and procedure-related functions that may be affected by each modification and developing a device evaluation strategy focusing on these functions. This may be

presented in tabular format, first addressing any design differences and differences in the intended *in vivo* environment, followed by a DES table that addresses the device-related and procedure-related attributes identified in the comparison tables. Examples of these tables are provided in Tables A.5 to A.7.

The tables (e.g. Tables A.5 to A.7) should be complemented by text to explain why other attributes would not likely be affected by the changes in the device and/or the indications for use.

The testing to be completed on the modified device or for the new intended use and the testing to be leveraged should also be summarized. This is best presented in tabular format, amending the table in Annex C to include a column with the rationale for not repeating testing.

Table A.5 — 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**
		(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 reduce crossing profile, improve conformability, improve deployment accuracy and incorporate visceral branching.*	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 graft material, stent material, stent geometry, active fixation system and addition of a branch.*	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 graft material include graft material processing, graft weave, graft wall thickness and permeability.*	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.

Table A.6 — Indication for use comparison of a previously evaluated device and the study device[a]

Differences in the *in vivo* environment	Comparison of *in vivo* parameters		Potentially affected device/procedure-related functions
	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 in the *in vivo* parameter.

[a] For example, an indication for use change from abdominal aortic aneurysms to thoraco-abdominal aneurysms or a change of the minimum proximal landing zone length requirement from 15 mm to 10 mm.

Table A.7 — Device evaluation strategy for device design modifications and/or changes in intended use

Device or procedure-related function that could potentially be impacted by the differences	Potential failure modes	Relative potential effects of failure		Device design information	Value of information from previously evaluated device	Nonclinical device testing
		Potential device effects of failure	Potential clinical effects of failure			
List each device-related and procedure-related function or feature that could be affected by the difference(s), as identified in Table A.5 and/or A.6.	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.	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.	Discuss the relevant information considered in the design of the device to explain why the function will be maintained or improved.	Provide an explanation regarding how information obtained from the assessment of the previously evaluated device is informative. *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).*	Identify the bench tests and analyses appropriate to evaluate the function and the potential failure mode(s), taking into consideration the information available from the previously evaluated device.

Annex B
(informative)

Description of clinical and device effects of failure

Table B.1 — Description 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 lack of viability caused by ischaemia.
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 total aortic diameter greater than documented measurement error as compared to the first post-implant CT measure using orthogonal (i.e. perpendicular to the centerline) measurements after treatment of a dissection.
Blood loss	Any blood loss requiring intervention (i.e. transfusion, medical therapy, surgical repair).
Branch vessel loss of patency	Reduction of blood flow in a branch vessel.
Branch vessel blockage	Complete occlusion of a branch vessel prosthesis caused by prosthesis kinking or compression.
Branch vessel coverage	Clinically significant, unplanned exclusion of a major branch vessel by the endovascular prosthesis.
Branch vessel thrombosis	Haemodynamically significant thrombus formation within the lumen of a branch vessel endovascular prosthesis.
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 endovascular procedure.
Post-procedural dissection	Creation or extension of a dissection due to the creation of a new entry tears at the margins of the endovascular prosthesis post procedure.
Embolism	Migration of intraluminal debris (e.g. thrombus, atheromas material) in the presence of clinical sequelae.
Endoleak	Persistence of blood flow abluminal to the endovascular prosthesis.
Type I	An endoleak arising at or from a sealing zone (proximal or distal).
Type Ia	A Type I endoleak originating from the proximal fixation zone of the endovascular prosthesis.
Type Ib	A Type I endoleak originating from the distal fixation zone of the endovascular prosthesis.
Type II	A Type II endoleak is caused by retrograde flow from patent branch arteries, for example, lumbar and intercostal arteries.
Type III	An endoleak arising from a defect in the graft material or from an inadequate seal between modular graft components
Type IIIa	A Type III endoleak originating from an inadequate seal between modular components.

Table B.1 *(continued)*

Event	Description
Type IIIb	A Type III endoleak originating from a defect in the graft material.
Type IV	An endoleak through the graft wall due to graft permeability.
False lumen patency	Persistence of blood flow into the false lumen after endovascular 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.
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 endovascular 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 endovascular stent-graft, 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 endovascular stent-graft, through fenestrations in the dissection septum, secondary aortic tears or re-entry points into the aortic false lumen.
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).
Failure to complete device implantation	Inability to implant an endovascular graft due to an inability to access the intended implantation site or to deploy the prosthesis.
Foreign body embolization	Intraluminal migration of a piece or pieces of the endovascular system (e.g. balloon fragments, pieces of a delivery system, fragments of the endovascular prosthesis).
Inability to monitor prosthesis over time	Inability to monitor device integrity and position over time due to an inability to visualize the device.
Inadequate MR imaging	Inability to obtain quality MR imaging due to distortion or imaging artefact caused by the endovascular prosthesis.
Insertion site infection	Development of an insertion site infection.
Ischaemia	Oxygen supply decrease due to inadequate blood supply.
Lumen obstruction	Blockage of the lumen of an endovascular prosthesis by physical (e.g. kink, twist, collapse, graft material infolding), rather than physiological, means.
Prosthesis infection	Development of a prosthesis infection.
Prosthesis occlusion	Complete blockage of the lumen of an endovascular prosthesis.
Recurrence of portal hypertension	Recurrent high blood pressure in the portal venous system.
Restenosis	Significant reduction in diameter when compared to the reference diameter.
Thrombosis	Haemodynamically significant thrombus formation within the lumen of the endovascular prosthesis.
Vascular trauma	Injuries to vessels as a result of an endovascular procedure,
Access vessel injury	Injury to a vessel at the access site during the endovascular procedure which may result in hematoma or false aneurysm formation.
Access vessel rupture	Rupture of an access vessel, including disruption of the vessel during insertion or removal of the delivery system.

Table B.1 *(continued)*

Event	Description
Erosion leading to fistula formation	Creation of a fistula caused by erosion of the endovascular prosthesis through the blood vessel and an adjoining structure. The type of fistula should be specified.
Unintentional dissection septum perforation	Creation of a new entry tear caused by erosion of, or penetration by, the endovascular prosthesis through the dissection septum,
Vascular injury–delivery system related	Blunt traumatic injury to a vessel during an endovascular procedure, including dissection and perforation or injury to a vessel due to a delivery system or balloon failure, including vessel wall injury that may lead to stenosis or restenosis,
Vascular injury–endovascular prosthesis related	Injury to a vessel related to the presence of the endovascular prosthesis over time, including vessel perforation and rupture.
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.
White thrombus formation	Platelet aggregation as a consequence of high shear stress (e.g. caused by graft infolding in limbs).

Table B.2 — Description of device effects of failure

Event	Description
Access failure	Failure to reach the intended site with the endovascular 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, moulding, or touch-up of an endovascular prosthesis.
Attachment system disconnection	Loss of securement of the attachment system to the endovascular prosthesis.
Branch vessel prosthesis compression or kink	Significant reduction in luminal diameter due to compression or kink. Contributing factors may include migration of the main body component and aortic remodelling.
Delamination	Separation of layers of the graft material used in the construction of an endovascular prosthesis.
Delivery system damage	Damage incurred to the delivery system (e.g. kink, bond failures, complete tip separation).
Deployment failure	Inability to deploy the endovascular prosthesis per the instructions for use.
Balloon-related deployment failure	Inability to fully deploy the endovascular prosthesis due to balloon failure.
Deployment system failure	Inability to deploy the prosthesis at the intended site due to mechanical failure.
Inability to deploy	Inability to deploy the prosthesis at the intended site due to patient anatomy.
Graft dilatation or rupture	Clinically significant graft dilatation or any graft rupture.
Graft material holes	Holes in the graft material due to suture pull out, suture hole elongation, suture breaks or wear.
Graft material infolding	Clinically significant infolding of the graft material.
Inaccurate deployment	Improper positioning, configuration or orientation of the endovascular prosthesis during deployment.

Table B.2 *(continued)*

Event	Description
Lack of conformance to the vessel wall	Incomplete or a loss of apposition of the endovascular prosthesis to the vessel wall (e.g. bird beaking).
Maldeployment	Asymmetric deployment of the proximal end of a prosthesis (e.g. stent inversion) in angulated anatomy that could not be corrected prior to completion of the procedure.
Metallic bond fracture	Fracture or breakage of metallic bonds (e.g. welds) between support structure components.
Migration	Significant longitudinal movement of an endovascular prosthesis relative to anatomical landmarks that were determined prior to discharge (e.g. requires intervention, ≥1 cm).
Misaligned deployment	Asymmetric deployment of the proximal end of a prosthesis (e.g. stent inversion) in angulated anatomy that may be corrected prior to completion of the procedure.
Poor apposition between components	Incomplete apposition between two or more endovascular prostheses or components of a modular system.
Prosthesis component separation	Movement of one or more endovascular components resulting in an inadequate seal between the components.
Prosthesis compression or collapse	Significant reduction in luminal diameter due to compression or collapse. Contributing factors may include excessive oversizing, lack of conformance of the prosthesis to the vessel wall and local compression.
Prosthesis damage	Damage to the prosthesis incurred during access or withdrawal.
Prosthesis dislodgement	Movement of the prosthesis from its intended implantation site during withdrawal of the delivery system.
Prosthesis dislodgement from the delivery system	Inability to deliver and position an endovascular prosthesis at the intended site due to prosthesis dislodgement from the delivery system.
Prosthesis kink	Kinking of the endovascular prosthesis resulting in a significant reduction in blood flow.
Separation of covering from stent	Disconnection between graft material and structural components of the endovascular prosthesis.
Support structure fracture	Fracture or breakage of the support structure or stent.
Support structure separation	Separation between structural components due to suture or metallic bond breaks.
Suture breaks	Breakage of sutures that are intended to connect a graft material to the support structure of the endovascular prosthesis or sutures that are intended to connect structural components together.

Annex C
(informative)

Bench and analytical tests

Table C.1 — Bench and analytical tests

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Active fixation fatigue and durability	The purpose of this test is to evaluate the long-term structural integrity of the securement of the active fixation components (e.g. barbs, hooks, pins) to the attachment system (e.g. proximal stent), and the securement of the attachment system to the endovascular prosthesis body when subjected to cyclic loading conditions.	Prosthesis integrity	8.5.2.3.3	D.5.2.3.3
Axial fatigue and durability	The purpose of this test is to evaluate the long-term structural integrity of the endovascular prosthesis when subjected to cyclic axial loading conditions.	Prosthesis integrity Appropriate sizing recommendations	8.5.2.3.4	D.5.2.3.4
Balloon burst pressure for non-compliant balloons	The purpose of this test is to determine the mean and rated burst pressure (RBP) of the balloon when inside of the endovascular prosthesis.	Ability to deploy Delivery system integrity	8.5.1.1.1	D.5.1.1.1
Balloon deflation time	The purpose of this test is to determine the time required to completely deflate the balloon when inside of the endovascular prosthesis.	Ability to withdraw	8.5.1.1.2	D.5.1.1.2
Balloon rated fatigue	The purpose of this test is to determine the ability of the balloon, when inside of the endovascular prosthesis, to withstand repeated inflation cycles to the maximum recommended pressure or volume, taking into consideration the number of inflation cycles expected clinically.	Delivery system integrity	8.5.1.1.3	D.5.1.1.3
Balloon volume to burst for compliant balloons	The purpose of this test is to determine the volume required to burst a compliant balloon when inside of the endovascular prosthesis.	Ability to deploy Delivery system integrity	8.5.1.1.4	D.5.1.1.4
Bending fatigue and durability	The purpose of this test is to evaluate the long-term structural integrity of the endovascular prosthesis when subjected to cyclic bending loading conditions.	Prosthesis integrity Appropriate sizing recommendations	8.5.2.3.5	D.5.2.3.5
Biocompatibility	The purpose of biocompatibility tests are included in the ISO 10993- series.	Patency Biocompatibility	8.5.1.9	See ISO 10993- series

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Burst strength	The purpose of this test is to determine the pressurized burst strength of the graft material, or alternatively, the burst strength of the entire endovascular prosthesis if processing may reduce the strength of the graft material.	Prosthesis integrity	8.5.2.8.1	D.5.2.8.1
Compression resistance to perpendicularly applied load (self-expanding, non-aortic endovascular prostheses)	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 prosthesis.	Patency	8.5.2.5.1	D.5.2.5.1
Corrosion	The purpose of this assessment is to evaluate the susceptibility of the metallic materials of the endovascular prosthesis to corrosion.	Prosthesis integrity	8.5.2.1	D.5.2.1
Crush resistance with perpendicularly applied load (balloon-expandable, non-aortic endovascular prostheses)	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 prosthesis.	Patency	8.5.2.5.2	D.5.2.5.2
Crush resistance with radially applied load (balloon-expandable endovascular prostheses)	The purpose of this test is to determine the radially applied load at which a pre-specified amount of permanent deformation occurs.	Patency	8.5.2.5.3	D.5.2.5.3
Dimensional verification of the endovascular prosthesis	The purpose of this test is for verification to design specifications, to determine the graft material wall thickness(es) and the endovascular prosthesis dimensions in the deployed state, including the length(s), outer diameter(s) and all other appropriate dimensions.	Modularity and intended overlap Appropriate sizing recommendations	8.5.2.7.1	D.5.2.7.1
Dimensional verification of the endovascular system	The purpose of this test is to determine the endovascular system dimensions, for verification to design specifications, including the useable length, profile and all other appropriate dimensions.	Ability to access Atraumatic introduction, tracking and withdrawal Haemostasis	8.5.1.2	D.5.1.2

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Dislodgement force (pre-mounted, balloon-expandable endovascular prostheses)	The purpose of the test is to determine the force required to displace the pre-mounted endovascular prosthesis from its position on the non-expanded balloon.	Ability to access	8.5.1.3	D.5.1.3
Factory seam strength (endovascular grafts with seams in the graft material)	The purpose of this test is to determine the tensile strength of any factory manufactured seams in the graft material. This requirement is not intended to apply to any connections between stents or between the graft material and a stent or an attachment system.	Prosthesis integrity	8.5.2.8.2	D.5.2.8.2
Fatigue and durability-computational analyses	The purpose of the computational analyses is to determine the magnitude and location of the maximum stresses and/or strains and fatigue safety factors 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.	Prosthesis integrity Appropriate sizing recommendations	8.5.2.2	D.5.2.2
Fatigue and durability–*in vitro* testing (See the specific Fatigue and Durability tests for the associated specific purposes.)	Evaluate the long-term structural integrity of the endovascular prosthesis under cyclic loading conditions that represent the *in vivo* environment. This can require several different test configurations.	Prosthesis integrity Appropriate sizing recommendations	8.5.2.3	D.5.2.3
Force to deploy	The purpose of this test is to determine the force to deploy the endovascular prosthesis under simulated anatomical conditions. All applicable steps of the deployment process should be evaluated.	Ability to deploy	8.5.1.4	D.5.1.4
Haemostasis	The purpose of this test is to evaluate the ability of any hemostatic seal or valve in the delivery system to minimize leakage of blood.	Haemostasis	8.5.1.8	D.5.1.8

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Implant diameter to balloon inflation pressure (balloon-expandable endovascular prostheses)	The purpose of this test is to determine the relationship between the prosthesis diameter and the balloon inflation pressure for balloon-expandable endovascular prostheses.	Appropriate sizing recommendations	8.5.2.7.2	D.5.2.7.2
Implant length to diameter relationship (endovascular prostheses that have clinically relevant length changes with diameter changes)	The purpose of this test is to determine the relationship between the length and diameter for endovascular prostheses that have clinically relevant length changes with diameter changes.	Ability to deploy Appropriate sizing recommendations	8.5.2.7.3	D.5.2.7.3
Integral water leakage	The purpose of this test is to evaluate the water leakage between modular components and through holes in the graft material resulting from the construction of the endovascular prosthesis (e.g. holes created by suturing stent structures to the graft material).	Appropriate permeability	8.5.2.6.1	D.5.2.6.1
Leakage at seal zone	This test applies to a device design modification that may affect the seal zone(s). Determine the leakage between the seal zone(s) of the endovascular prosthesis and a mock artery and compare the results to those for the unmodified device. This requirement can alternatively be met through evaluation of Type I endoleaks in a clinical study. The evaluation of seal zone leakage is not necessary for endovascular prostheses intended for clinical uses for which seal zone leakage is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).	Adequate seal Appropriate permeability	8.5.2.4.1	D.5.2.4.1
Longitudinal tensile strength	The purpose of this test is to determine the longitudinal tensile strength of the graft material.	Prosthesis integrity	8.5.2.8.3	D.5.2.8.3

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Magnetic Resonance Imaging (MRI) safety	The purpose of MRI safety testing is to evaluate the potential for 1) magnetically induced displacement force and torque; and 2) RF induced heating of the prosthesis and to determine the appropriate MR safety term (i.e. MR Safe, MR Conditional, or MR Unsafe) as defined in ASTM F2503.	Magnetic resonance imaging (MRI) safety	8.5.2.9	See ASTM F2503, ASTM F2052, ASTM F2119, ASTM F2182, ASTM F2213
Migration resistance	The purpose of this test is to evaluate the ability of the endovascular prosthesis to resist migration when subjected to force or pressure. The evaluation of migration resistance is not necessary for endovascular prostheses intended for clinical uses for which migration is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).	Fixation effectiveness Appropriate sizing recommendations Modularity and intended overlap	8.5.2.4.2	D.5.2.4.2
Porosity (non-textile materials)	The purpose of this test is to determine the porosity of the endovascular prostheses constructed of non-textile materials.	Appropriate permeability	8.5.2.6.2	D.5.2.6.2
Radial fatigue and durability	The purpose of this test is to evaluate the long-term structural integrity of the endovascular prosthesis when subjected to cyclic radial loading conditions.	Prosthesis integrity Appropriate sizing recommendations	8.5.2.3.2	D.5.2.3.2
Radial force (self-expanding endovascular prostheses)	The purpose of this test is to determine the outward force as a function of the diameter of the endovascular prostheses.	Fixation effectiveness Modularity and intended overlap Appropriate sizing recommendations Patency	8.5.2.5.4	D.5.2.5.4
Recoil (balloon-expandable endovascular prostheses)	The purpose of this test is to determine the amount of elastic recoil (percent of the diameter reduction), after the deployment of a balloon-expandable prosthesis.	Fixation effectiveness Appropriate sizing recommendations	8.5.2.7.4	D.5.2.7.4
Resistance to kinking (flexibility)	The purpose of this test is to determine the minimum radius that the endovascular prosthesis can accommodate without kinking.	Modularity and intended overlap Patency	8.5.2.5.5	D.5.2.5.5

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Separation force for overlapping endovascular prostheses	Determine the force required to separate overlapping endovascular prostheses or modular components (e.g. main body, cuffs, extenders) in the deployed state. The evaluation of separation force is not necessary for endovascular prostheses intended for clinical uses for which component separation is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).	Fixation effectiveness Modularity and intended overlap	8.5.2.4.3	D.5.2.4.3
Simulated use	The purpose of this test is to evaluate the ability to access, deploy and withdraw the endovascular system, including pushability, flexibility, torquability, trackability and 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 endovascular system with accessory devices and to evaluate the occurrence of visible particle generation associated with access, deployment and withdrawal of the endovascular system. Additionally, this test is intended to evaluate the conformability of the deployed prosthesis to the vessel wall, positioning (including orientation, if applicable) and absence of anomalies (e.g. kinks, twists, component separation, non-uniform expansion, prosthesis damage).	Ability to access Ability to deploy Ability to withdraw Atraumatic introduction, tracking and withdrawal Delivery system integrity Prosthesis integrity Adequate seal Modularity and intended overlap Appropriate sizing recommendations Patency	8.5.1.5	D.5.1.5
Sterilization assurance	Sterilization shall be ensured in accordance with appropriate International Standards.	Sterility	8.5.1.10	See appropriate International Standards
Strength after repeated puncture (endovascular prostheses for vascular access)	The purpose of this test is to determine the strength of the endovascular prostheses following repeated dialysis-needle punctures for a prosthesis that will be cannulated to provide blood access for haemodialysis.	Prosthesis integrity	8.5.2.8.4	D.5.2.8.4

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Strength of the connection(s) between the graft material and a discrete fixation system(s)	The purpose of this test is to determine the strength of the connection(s) between the graft material and the fixation system(s). This test applies to prostheses with a fixation system that is discrete from any stent(s) intended to provide structural support within the prosthesis (e.g. suprarenal stent that is not continuous with the stent(s) in the prosthesis body). Additionally, the purpose of this test is to determine the securement of a fixation system (e.g. suprarenal stent) to the endovascular prosthesis body and not to evaluate the securement of an active fixation component (e.g. barb, hook, pin) to the fixation system or graft material. As such, the location or presence of an active fixation component is not relevant for this test.	Prosthesis integrity	8.5.2.8.5	D.5.2.8.5
Tensile bond strength	The purpose of this test is to determine the bond strength of the joints and/or fixed connections of the delivery system and to evaluate the strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing), either separately or concurrently.	Delivery system integrity	8.5.1.6	D.5.1.6
Torsional bond strength	The purpose of this test is to determine the torque required to cause failure of the joints and/or fixed connections in the appropriate segments of the delivery system (i.e. joints and/or fixed connections that are subjected to torsion during clinical use) and to evaluate the torsional strength of the segments adjacent to the bonds of the delivery system (e.g. sheath, tubing), either separately or concurrently.	Ability to access Delivery system integrity	8.5.1.7	D.5.1.7
Torsional fatigue and durability	The purpose of this test is to evaluate the long-term structural integrity of the endovascular prosthesis when subjected to cyclic torsional loading conditions.	Prosthesis Integrity Appropriate sizing recommendations	8.5.2.3.6	D.5.2.3.6

Table C.1 *(continued)*

Tests	Purpose of test	Device/Procedure related function(s)	Design evaluation section	Test method guidance
Visibility	The purpose of this test is to evaluate the ability to visualize the endovascular system and endovascular prosthesis using the imaging techniques specified in the instructions for use (IFU).	Modularity and intended overlap Visualization	8.5.1.11	D.5.1.9
Water entry pressure (non-textile materials)	The purpose of this test is to determine the pressure required to force water through a non-textile graft material of an endovascular prosthesis.	Appropriate permeability	8.5.2.6.3	D.5.2.6.3
Water permeability (textile materials)	The purpose of this test is to determine the water flow rate through the graft material of an endovascular prostheses constructed with a water-permeable graft material (e.g. woven graft material).	Appropriate permeability	8.5.2.6.4	D.5.2.6.4

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 endovascular system. Guidance for reporting the test results is also provided. It is recognised that not all the tests described in this annex are applicable to all system designs. It is also recognised that testing intended to ensure that the device meets specifications during manufacture may be conducted in a manner other than those outlined in this annex.

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 enhance consistency in the testing of devices, use of 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 recognised 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 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 endovascular 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 precision and accuracy, and be calibrated or verified against traceable measurement standards, as appropriate. The precision and accuracy should be adequate to determine the measured value relative to the acceptance criteria.

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

D.2 Sampling

A sampling plan should be used that 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 endovascular 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 or overlapping prostheses (e.g. separation force for overlapping endovascular prostheses), or if the attribute under test could be significantly affected by the overlap (e.g. ability to resist kinking), the test articles should include overlapped 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. A rationale should be provided for sample selection.

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

The need for testing of more than one area in an endovascular prosthesis to ensure adequate characterization for some parameters (e.g. proximal and distal diameters in a tapered prosthesis, wall thickness in devices with non-uniform wall thickness) 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.

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 that can affect the test results. Examples of conditioning are preparation of the endovascular system, loading of the prosthesis inside the delivery catheter, passage through simulated tortuous vasculature, warming of the system to body temperature and deployment of the prosthesis.

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: 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 the following:

   — 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 cross references to the test summary and full test report.

c) Individual test summaries should include the following:

   — 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: 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;

— conclusions: state conclusions, based on comparing results to acceptance criteria or provide an explanation of the relevance of the results for characterization tests and, if appropriate, include a discussion on the potential clinical significance of the results.

D.5 Test method development guidance

This clause lists guidelines for tests where appropriate. An index of test methods is given in Table D.1.

Table D.1 — Index of test methods

Design evaluation section	Tests	Annex D subclause
8.5.1	Endovascular system	D.5.1
8.5.1.1	Balloon testing	D.5.1.1
8.5.1.1.1	Balloon burst pressure for non-compliant balloons	D.5.1.1.1
8.5.1.1.2	Balloon deflation times	D.5.1.1.2
8.5.1.1.3	Balloon rated fatigue	D.5.1.1.3
8.5.1.1.4	Balloon volume to burst for compliant balloons	D.5.1.1.4
8.5.1.2	Dimensional verification of the endovascular system	D.5.1.2
8.5.1.3	Dislodgement force (pre-mounted, balloon-expandable endovascular prostheses)	D.5.1.3
8.5.1.4	Force to deploy	D.5.1.4
8.5.1.5	Simulated Use	D.5.1.5
8.5.1.6	Tensile bond strength	D.5.1.6
8.5.1.7	Torsional bond strength	D.5.1.7
8.5.1.8	Haemostasis	D.5.1.8
8.5.1.9	Biocompatibility	See ISO 10993-1 and other appropriate parts
8.5.1.10	Sterilization assurance	See appropriate International Standards
8.5.1.11	Visibility	D.5.1.9
8.5.2	Endovascular prosthesis	D.5.2

Table D.1 *(continued)*

Design evaluation section	Tests	Annex D subclause
8.5.2.1	Corrosion	D.5.2.1
8.5.2.2	Fatigue and durability — Computational analyses	D.5.2.2
8.5.2.3	Fatigue and durability — *in vitro* testing	D.5.2.3
8.5.2.3.1	General	D.5.2.3.1
8.5.2.3.2	Radial fatigue and durability	D.5.2.3.2
8.5.2.3.3	Active fixation fatigue and durability	D.5.2.3.3
8.5.2.3.4	Axial fatigue and durability	D.5.2.3.4
8.5.2.3.5	Bending fatigue and durability	D.5.2.3.5
8.5.2.3.6	Torsional fatigue and durability	D.5.2.3.6
8.5.2.4	Fixation and Seal	D.5.2.4
8.5.2.4.1	Leakage at seal zone	D.5.2.4.1
8.5.2.4.2	Migration resistance	D.5.2.4.2
8.5.2.4.3	Separation force for overlapping endovascular prostheses	D.5.2.4.3
8.5.2.5	Patency-related tests	D.5.2.5
8.5.2.5.1	Compression resistance to perpendicularly applied load (self-expanding, non-aortic endovascular prostheses)	D.5.2.5.1
8.5.2.5.2	Crush resistance with perpendicularly applied load (balloon-expandable, non-aortic endovascular prostheses)	D.5.2.5.2
8.5.2.5.3	Crush resistance with radially applied load (balloon-expandable endovascular prostheses)	D.5.2.5.3
8.5.2.5.4	Radial force (self-expanding endovascular prostheses)	D.5.2.5.4
8.5.2.5.5	Resistance to kinking (flexibility)	D.5.2.5.5
8.5.2.6	Permeability	D.5.2.6
8.5.2.6.1	Integral water leakage	D.5.2.6.1
8.5.2.6.2	Porosity (non-textile materials)	D.5.2.6.2
8.5.2.6.3	Water entry pressure (non-textile materials)	D5.2.6.3
8.5.2.6.4	Water permeability (textile materials)	D5.2.6.4
8.5.2.7	Sizing-related testing	D.5.2.7
8.5.2.7.1	Dimensional verification of the endovascular prosthesis	D.5.2.7.1
8.5.2.7.2	Implant diameter to balloon inflation pressure (balloon-expandable endovascular prostheses)	D.5.2.7.2
8.5.2.7.3	Implant length to diameter relationship (endovascular prostheses that have clinically relevant length changes with diameter changes)	D.5.2.7.3
8.5.2.7.4	Recoil (balloon-expandable endovascular prostheses)	D.5.2.7.4
8.5.2.8	Strength	D.5.2.8
8.5.2.8.1	Burst strength	D.5.2.8.1
8.5.2.8.2	Factory anastomotic strength (endovascular grafts with seams in the graft material)	D.5.2.8.2
8.5.2.8.3	Longitudinal tensile strength	D.5.2.8.3

Table D.1 *(continued)*

Design evaluation section	Tests	Annex D subclause
8.5.2.8.4	Strength after repeated puncture (endovascular prostheses for vascular access)	D.5.2.8.4
8.5.2.8.5	Strength of the connection(s) or bond(s) between the graft material and the stent(s) or attachment system(s)	D.5.2.8.5
8.5.2.9	Magnetic Resonance Imaging (MRI) safety	See appropriate International Standards

D.5.1 Endovascular system

This subclause describes testing that includes the endovascular system, the delivery system without the endovascular prosthesis and balloons integral to the endovascular system and accessory balloons used to achieve adequate apposition of the prosthesis.

D.5.1.1 Balloon testing

The following tests apply to balloons integral to the endovascular system and accessory balloons used to achieve adequate apposition of the prosthesis.

D.5.1.1.1 Balloon burst pressure for non-compliant balloons

D.5.1.1.1.1 Purpose

The purpose of this test is to determine the mean and rated burst pressure (RBP) of the balloon when inside of the endovascular prosthesis.

D.5.1.1.1.2 Materials

The following materials apply:

— endovascular system for devices with balloons integral to the system or endovascular prosthesis and balloon catheter for balloons that are not integral to the system;

— recommended guide wire 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 drop monitor, flow rate monitor);

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

— timer with an accuracy of ±1 s.

D.5.1.1.1.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.1.1.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.1.1.5 Test method

Develop a test method based on the following steps:

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

   For self-expanding endovascular prostheses, submerge a deployed endovascular prosthesis in the water bath, insert the guide wire and advance the balloon over the guide wire into the endovascular prosthesis.

   An endovascular system may be used to deploy the endovascular prosthesis in the water bath.

b) Initiate inflation of the balloon, bringing the balloon to the nominal inflation pressure.

c) Incrementally increase the pressure and hold the pressure for a minimum of 10 s after each increment.

d) Monitor the system after each incremental increase for any persistent leak or decrease in pressure.

e) Repeat steps c) and d) until a persistent leak or decrease in pressure is detected, whether due to failure of the balloon, shaft or proximal or distal seals.

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

g) Calculate the rated burst pressure. The rated burst pressure (RBP) 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 RBP can be calculated in the following manner.

Using a one-sided tolerance limit for a normal distribution:

$$RBP = X - K(SD) \quad (D.1)$$

where

X is the mean balloon burst pressure;

SD 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 0,999 (99,9 % reliability);

C 0,95 (95 % confidence);

N is the number of balloons tested.

D.5.1.1.1.6 Expression of results

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

D.5.1.1.1.7 Test report

The test report shall be in accordance with 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.5.1.1.2 Balloon deflation times

D.5.1.1.2.1 Purpose

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

D.5.1.1.2.2 Materials

The following materials apply:

— endovascular system for devices with balloons integral to the system or endovascular prosthesis and balloon catheter for balloons that are not integral to the system;

— recommended guide wire or equivalent;

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

— contrast medium or equivalent fluid, in accordance with the instructions for use (IFU);

— inflation device, syringe or equivalent, fitted with a means of measuring pressure or volume, and of maintaining the inflation pressure or volume;

— timer with an accuracy of ±1 s.

D.5.1.1.2.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.1.2.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.1.2.5 Test method

Develop a test method based on the following steps:

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

For self-expanding endovascular prostheses, submerge a deployed endovascular prosthesis in the water bath, insert the guide wire and advance the balloon over the guide wire into the endovascular prosthesis.

An endovascular system may be used to deploy the endovascular prosthesis in the water bath.

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.

D.5.1.1.2.6 Expression of results

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

D.5.1.1.2.7 Test report

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

D.5.1.1.3 Balloon rated fatigue

D.5.1.1.3.1 Purpose

The purpose of this test is to determine the ability of the balloon when inside of the endovascular prosthesis to withstand repeated inflation cycles to the maximum recommended pressure or volume, taking into consideration the number of inflation cycles expected clinically.

D.5.1.1.3.2 Materials

The following materials apply:

— endovascular system for devices with balloons integral to the system or endovascular prosthesis and balloon catheter for balloons that are not integral to the system;

— recommended guide wire 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 drop monitor, flow rate monitor);

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

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

— timer with an accuracy of ±1 s.

D.5.1.1.3.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.1.3.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.1.3.5 Test method

Develop a test method based on the following steps:

a) For balloon expandable endovascular prostheses, submerge the endovascular system in the water bath and deploy the endovascular prosthesis in the water bath or in the compliant tube, as appropriate, inflating the balloon using a clinically relevant rate, to the maximum pressure or volume as indicated in the instructions for use (IFU), for a minimum of 10 s or for the length of time stated in the IFU.

b) For self-expanding endovascular prostheses:

   1) submerge the deployed endovascular prosthesis in the water bath or in the compliant tube, as appropriate;

      An endovascular system may be used to deploy the endovascular prosthesis in the water bath.

   2) insert the guide wire and advance the balloon over the guide wire into the endovascular prosthesis;

3) inflate the balloon using clinically relevant rates to the maximum pressure or volume, as indicated in the instructions for use (IFU), for a minimum of 10 s or for the length of time stated in the IFU.

c) Deflate the balloon.

d) Repeat steps a) and b), with the balloon inside of the endovascular prosthesis, 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.

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

D.5.1.1.3.6 Expression of results

The maximum inflation diameter, pressure or volume used shall be expressed with diameter in millimetres (mm), pressure in atmospheres (atm) or volume in millilitres (ml).

D.5.1.1.3.7 Test report

The test report shall be in accordance with 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 diameter, pressure or volume. The selected tube diameter(s), if used for testing, shall be justified.

NOTE Additional information can be found in ISO 10555-4.

D.5.1.1.4 Balloon volume to burst for compliant balloons

D.5.1.1.4.1 Purpose

The purpose of this test is to determine the volume required to burst a compliant balloon when inside of an endovascular prosthesis.

D.5.1.1.4.2 Materials

The following materials apply:

— endovascular system for devices with balloons integral to the system or endovascular prosthesis and balloon catheter for balloons that are not integral to the system;

— recommended guide wire 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 drop monitor, flow rate monitor);

— inflation device, syringe or equivalent, fitted with a means of measuring volume and capable of maintaining the inflation volume;

— timer with an accuracy of ±1 s.

D.5.1.1.4.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.1.4.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.1.4.5 Test method

Develop a test method based on the following steps:

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

   For self-expanding endovascular prostheses, submerge a deployed endovascular prosthesis in the water bath, insert the guide wire and advance the balloon over the guide wire into the endovascular prosthesis.

   An endovascular system may be used to deploy the endovascular prosthesis in the water bath.

b) Using an inflation rate simulating clinical use, inflate the balloon to the diameter of the tube and hold the diameter for a minimum of 10 s. Record the volume (V_1).

c) Incrementally, increase the volume and hold the volume for a minimum of 10 s after each increment.

d) Monitor the system after each incremental increase for any persistent leak or decrease in volume.

e) Repeat steps c) and d) until a persistent leak or decrease of volume or pressure is detected, whether due to failure of the balloon, shaft or proximal or distal seals.

f) Record the volume at burst (V_2), describe the location of the failure and the failure mode [e.g. fragmentation, seal leaks, balloon rupture (including orientation of rupture)].

D.5.1.1.4.6 Expression of results

Volume shall be expressed in millilitres (ml).

D.5.1.1.4.7 Test report

The test report shall be in accordance with D.4 and shall include the maximum, minimum, mean and standard deviation of the volume at the specified diameter, the volume at failure and the observed failure location and failure mode(s).

D.5.1.2 Dimensional verification of the endovascular system

D.5.1.2.1 Purpose

The purpose of this test is to determine the endovascular system dimensions for verification to design specifications including the useable length, profile and all other appropriate dimensions.

NOTE Measure the delivery system with the endovascular prostheses loaded on the system. See D.5.2.7.1 for dimensional verification of the endovascular prosthesis.

D.5.1.2.2 Materials

The following materials apply:

— endovascular system;

— equipment for establishing the profile of the endovascular system:

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

  — appropriate profile hole gauges;

— measuring equipment for length.

D.5.1.2.3 Sampling

Sampling shall be in accordance with D.2. The sampling plan shall include each type of modular component unless justification is provided for exclusion of a component(s).

D.5.1.2.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.2.5 Test method

Develop a test method based on the following steps:

a) Establish the profile of the endovascular system using one of the following methods:

  1) measure the maximum outer diameter of the endovascular system using the appropriate measuring instrument, or

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

  It is only necessary to evaluate the region of the endovascular system intended to be passed through the specified introducer sheath. Consideration should be given to the potential for asymmetry.

b) Measure the length of the endovascular system using an appropriate measuring instrument. It is only necessary to measure the region of the endovascular system intended to be passed through the introducer sheath.

c) Measure all other appropriate dimensions.

D.5.1.2.6 Expression of results

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

D.5.1.2.7 Test report

The test report shall be in accordance with 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 guidance can be found in ASTM F2081.

D.5.1.3 Dislodgement force (pre-mounted, balloon expandable endovascular prostheses)

D.5.1.3.1 Purpose

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

D.5.1.3.2 Materials

The following materials apply:

— endovascular system;

— 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 endovascular prosthesis to be removed from the balloon, while minimizing interaction between the balloon and the fixture;

— recommended guide wire or equivalent;

— temperature controlled environment (37 ± 2) °C for endovascular systems with material properties that are sensitive to changes between ambient and physiological temperatures.

D.5.1.3.3 Sampling

Sampling shall be in accordance with D.2. The sampling plan shall include each type of modular component unless justification is provided for exclusion of a component(s).

D.5.1.3.4 Conditioning

Conditioning shall be in accordance with D.3 and shall include preconditioning and tracking through a tortuous anatomical model using appropriate accessory devices (e.g. introducer sheath).

D.5.1.3.5 Test method

Develop a test method based on the following steps:

a) insert the guide wire into the endovascular system;

b) secure the endovascular prosthesis in the gripping fixture;

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 endovascular prosthesis from the delivery system using a constant crosshead speed (e.g. 200 mm/min);

e) record the peak force needed to move the endovascular prosthesis beyond a pre-specified critical distance (e.g. the margin of the balloon);

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.5.1.3.6 Expression of results

Force shall be expressed in Newtons (N).

D.5.1.3.7 Test report

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

NOTE Additional guidance can be found in ASTM F2394.

D.5.1.4 Force to deploy for self-expanding endovascular prostheses

D.5.1.4.1 Purpose

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

D.5.1.4.2 Materials

The following materials apply:

— endovascular system;

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU);

— 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 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. The limits set in the IFU regarding anatomy are also important to consider when selecting the anatomical model (e.g. neck angulation and length). 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. guide wire, introducer sheath) and the endovascular system and the friction associated with the model material should also be considered in selecting the model material and any test fluid.

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

— gripping fixture;

— temperature controlled environment (37 ± 2) °C.

D.5.1.4.3 Sampling

Sampling shall be in accordance with D.2. Endovascular systems to be tested should be representative of the devices that have the potential for the highest deployment force (e.g. greatest bulk within the sheath or cover, highest compression ratio). The effect of diameters and lengths should be taken into consideration in the selection of devices for testing. The sampling plan shall include each type of modular component unless justification is provided for exclusion of a component(s).

D.5.1.4.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.4.5 Test method

Develop a test method based on the following steps:

a) Prepare the endovascular system per the IFU.

b) Insert the endovascular 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 prosthesis.

If multiple mechanisms are required for deploying a prosthesis (e.g. tether wire release, 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.5.1.4.6 Expression of results

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

D.5.1.4.7 Test report

Test report shall be in accordance with 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.5.1.5 Simulated use

D.5.1.5.1 Purpose

The purpose of this test is to evaluate the ability to access, deploy and withdraw the endovascular system, including pushability, flexibility, torquability, trackability and 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 endovascular system with accessory devices. Additionally, this test is intended to evaluate the conformability of the deployed endovascular prosthesis to the vessel wall, positioning (including orientation, if applicable) and absence of anomalies (e.g. kinks, twists, component separation, non-uniform expansion, prosthesis damage).

D.5.1.5.2 Materials

The following materials apply:

— endovascular system(s), including all components of the implant (e.g. main body, limbs, extenders);

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU) (e.g. guide wire, introducer sheath, balloons used to achieve adequate apposition of the prosthesis);

— 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 instructions for use regarding anatomy are also important to consider when selecting the anatomical model(s) (e.g. neck angulation and length). 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. guide wire, introducer sheath) and the endovascular system and the friction associated with the model material should also be considered in selecting the model material and test fluid.

— fixture capable of delivering water or appropriate fluid at physiological temperature (37 ± 2) °C and at other clinically relevant physiological conditions (e.g. pulsatile pressures, flow).

D.5.1.5.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.5.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.5.5 Test method

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 physiological conditions.

b) Following the IFU and using the appropriate accessory devices (e.g. guide wire, introducer sheath), insert, deliver and deploy the implant, including any modular components, while evaluating the following:

   1) evaluate the ability of the endovascular 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 endovascular system;

   2) for prostheses requiring rotational orientation for appropriate position, evaluate the ability of the endovascular system to provide sufficient rotation to the distal (leading) end in order to position the implant in the targeted deployment location of the anatomical model(s);

   3) evaluate the ease and ability to deploy the prosthesis;

   4) evaluate the accuracy of deployment;

   5) evaluate the ability to withdraw the delivery system and accessory devices from the anatomical model(s) and note any anomalies, such as prosthesis dislodgment or damage;

   6) evaluate the compatibility of the endovascular system with the accessory devices (e.g. guide wire, introducer sheath) and when appropriate, the compatibility of the accessory devices with the endovascular system (e.g. balloons used post-deployment).

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

d) Visually inspect the delivery system, and record the type and location of any damage or any other anomalies.

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

f) Visually inspect the test fluids for particulates that were generated during the test.

D.5.1.5.6 Expression of results

Results of the assessments shall be expressed descriptively.

D.5.1.5.7 Test report

The test report shall be in accordance with 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 viscosity and density and the model material of construction shall be reported and justified. The pressure and flow conditions shall be justified (i.e. whether or not these variables were included or controlled during the test). The results for pushability, flexibility, torquability, trackability, deployment accuracy, conformability of the deployed prosthesis to the vessel wall and compatibility between the accessory devices and the endovascular system should each be documented. The type and location of any prosthesis or delivery system damage and any clinically relevant accessory device damage shall be reported. If visible particle generation is observed during access, deployment and withdrawal of the endovascular system, this observation should be noted. The relevance of any observations should be explained in the context of the intended clinical use.

D.5.1.6 Tensile bond strength

D.5.1.6.1 Purpose

The purpose of this test is to determine the bond strength of the joints and/or fixed connections of the delivery system. 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.5.1.6.2 Materials

The following materials apply:

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

— recommended guide wire or equivalent, if appropriate;

— mechanical testing system with a constant rate of traverse, a suitable load cell and appropriate gripping fixtures;

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

D.5.1.6.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.6.4 Conditioning

Conditioning shall be in accordance with 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.5.1.5.2. Delivery systems from completed simulated use testing (see D.5.1.5) may be used for this test.

D.5.1.6.5 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 guide wire, 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.

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

D.5.1.6.6 Expression of results

Bond strength shall be expressed in Newtons (N).

D.5.1.6.7 Test report

The test report shall be in accordance with 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.5.1.7 Torsional bond strength

D.5.1.7.1 Purpose

The purpose of this test is to determine the torque required to cause failure of the joints and/or fixed connections in the appropriate segments of the delivery system (i.e. joints and/or fixed connections that are subjected to torsion during clinical use). 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 torsional bond strength determination.

D.5.1.7.2 Materials

The following materials apply:

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

— recommended guide wire or equivalent, if appropriate;

— torque testing system with a suitable torque gauge;

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

D.5.1.7.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.7.4 Conditioning

Conditioning shall be in accordance with 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.5.1.5.2. Delivery systems from completed simulated use testing (see D.5.1.5) may be used for this test.

D.5.1.7.5 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 guide wire, if appropriate.

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

c) Affix 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) Apply a torque at a rate characteristic of that used in typical clinical use to one end of the sample until the joint and/or delivery system breaks or loses functional integrity.

e) Record the torque at which failure occurs and the failure mode and location.

D.5.1.7.6 Expression of results

Torsional bond strength shall be expressed in Newton-meters (N·m).

D.5.1.7.7 Test report

The test report shall be in accordance with 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 necessary to access, deploy and withdraw the system.

D.5.1.8 Haemostasis

D.5.1.8.1 Purpose

The purpose of this test is to evaluate the ability of any haemostatic seal or valve in the delivery system to minimize leakage of blood.

D.5.1.8.2 Materials

The following materials apply:

— endovascular system;

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU);

— pressurized fluid fixture capable of delivering water or an appropriate fluid, at physiological temperature (37 ± 2) °C and appropriate pressure (e.g. 100 mmHg);

— reservoir for collecting and measuring the total fluid leakage from the endovascular system to a justified minimum accuracy (e.g. ±5 ml);

— timer with an accuracy of ±1 s.

D.5.1.8.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.8.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.8.5 Test method

Develop a test method based on the following steps:

a) Prepare the fixture for receipt of the endovascular system. For systems that do not have integral sheaths, place the appropriate accessory devices (e.g. guide wire, introducer sheath) in the fixture.

b) Prepare and insert the endovascular system into the fixture.

c) Place the reservoir(s) to collect the fluid leakage from any seal or valve in the delivery system and start timing.

   Leakage between the fixture and the introducer sheath should not be included. If appropriate, leakage between the introducer sheath and the endovascular system may be included.

d) Stop fluid collection and timer. The duration of test should be adequate to determine the leakage through the seal or valve.

e) Record the amount of fluid leakage and the elapsed time over which leakage occurred.

f) Repeat step c) through step e) for any devices intended to be inserted through the haemostatic valve of the endovascular system (e.g. additional delivery system, balloon, wire).

D.5.1.8.6 Expression of results

The leakage rate(s) shall be expressed in millilitres per minute (ml/min).

D.5.1.8.7 Test report

The test report shall be in accordance with D.4 and include the maximum, minimum, mean and standard deviation of each leakage rate. The test timing, pressure and fluid used shall be reported. If blood or simulated blood is used, the density, viscosity or treatments (e.g. anti-coagulants) shall be identified.

NOTE Guidance for introducer sheaths can be found in ISO 11070.

D.5.1.9 Visibility

D.5.1.9.1 Purpose

The purpose of this test is to evaluate the ability to visualize the endovascular system and endovascular prosthesis using the imaging techniques specified in the instructions for use (IFU).

D.5.1.9.2 Materials

The following materials apply:

— endovascular system;

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

— phantom tissue model, or equivalent (e.g. 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.5.1.9.3 Sampling

Sampling shall be in accordance with D.2.

D.5.1.9.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.1.9.5 Test method

Develop a test method based on the following steps:

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

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

c) Use the imaging machine to visualize the endovascular 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 endovascular system. Alternatively, the degree of visibility may be compared to a specified material or device with known visibility.

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

D.5.1.9.6 Expression of results

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

D.5.1.9.7 Test report

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

NOTE Additional information can be found in ASTM F640.

D.5.2 Implant (endovascular prosthesis)

D.5.2.1 Corrosion assessment

D.5.2.1.1 Purpose

The purpose of this assessment is to evaluate the susceptibility of the metallic materials of the endovascular prosthesis 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.5.2.1.2 Materials for corrosion testing

The following materials apply:

— endovascular prosthesis or appropriate test samples of the prosthesis (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.5.2.1.3 Sampling for corrosion testing

Sampling shall be in accordance with D.2.

D.5.2.1.4 Conditioning for corrosion testing

Conditioning shall be in accordance with D.3 and shall include actual or simulated loading and deployment.

D.5.2.1.5 Assessment

The susceptibility of the metallic materials of the prosthesis 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, text books, 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 F746, *Standard Test Method for Pitting or Crevice Corrosion of Metallic Surgical Implant Materials*

— 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.5.2.1.6 Expression of results for corrosion testing

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

D.5.2.1.7 Test report

The test report shall be in accordance with 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 metallic materials of the endovascular prosthesis. Applicable requirements indicated in the guidance documents used for testing should also be included.

D.5.2.2 Fatigue and durability — Computational analyses

D.5.2.2.1 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.

D.5.2.2.2 Model inputs and tools

The following model inputs and tools apply:

— structural design of the endovascular prosthesis 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 prosthesis 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, angulation, tortuosity);

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

D.5.2.2.3 Analysis

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

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 prosthesis 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 prostheses to be evaluated.

   2) Establish the prosthesis 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 prosthesis, 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 prosthesis to be modelled or when applying symmetry assumptions.

c) Establish the material properties.

Determine the properties of the materials of the finished prosthesis 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 prosthesis 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) prosthesis 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 prosthesis 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 prosthesis.

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.5.2.2.4 Expression of results

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

D.5.2.2.5 Report

NOTE The computational analysis report is intentionally different from the standard test reports described in 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 prostheses 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 prostheses selected for evaluation.

   4) If only a portion of the prosthesis 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 of 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 prosthesis 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, prosthesis 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 prosthesis is expected to experience *in vivo*.

3) Provide justification that the delivery system loading and prosthesis 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 prosthesis 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 prosthesis. 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 prosthesis.

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 prosthesis 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.

D.5.2.3 Fatigue and durability tests — *in vitro* testing

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.

D.5.2.3.1 General

The information included under this subclause are applicable to radial fatigue and durability, active fixation fatigue and durability, axial fatigue and durability, bending fatigue and durability and torsional 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 artery (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 endovascular prosthesis in response to a displacement(s) or an applied load(s).

NOTE Additional information can be found in ASTM F2477 and ASTM F2942.

D.5.2.3.1.1 Purpose

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

Appropriate test methods should be developed to simulate physiological deformations of the endovascular prosthesis. 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.

The long-term integrity of active fixation components (e.g. hooks, barbs, anchors) should also be evaluated. Information to aid in the development of an appropriate test method is presented below.

Potential failure modes that can be evaluated in these tests include: stent fracture, fracture of active fixation components, detachment of the stent from the graft material, tearing or other failure modes of the fabric or covering, and wear or abrasion between prosthesis components.

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

D.5.2.3.1.2 Materials

The following materials apply:

— endovascular system;

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

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU) (e.g. guide wire, introducer sheath, balloons used to achieve adequate apposition of the prosthesis);

— if applicable, a mock artery 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, high resolution X-ray, scanning electron microscopy (SEM)].

D.5.2.3.1.3 Sampling

Sampling shall be in accordance with D.2.

Sampling shall allow for the evaluation of the structural integrity of all relevant parts of the prosthesis and contact areas between components.

The endovascular prosthesis 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 prosthesis may be used as the test article if appropriately justified.

D.5.2.3.1.4 Conditioning

Conditioning shall be in accordance with D.3.

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

D.5.2.3.1.5 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 endovascular prosthesis 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 artery

There is no general guidance beyond those included in the general materials (see D.5.2.3.1.2). See a), 2) of 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 prosthesis and rate-dependent effects on material properties.

4) Displacement conditions/control

The gripping technique, slip between the mock artery (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) Setup

1) Either deploy the test article according to the IFU directly into the test fixture or deploy the endovascular prosthesis according to the IFU and secure the test article (i.e. either the complete prosthesis or a segment or portion of the prosthesis) to the test fixture. If appropriate, deploy additional overlapped components.

2) Inspect the test article(s) using appropriate visual aids and record the location and severity of any anomalies (e.g. in-folding of graft material, non-uniform prosthesis expansion).

3) Allow the test articles to reach the pre-defined test temperature before initiating the test.

c) Testing

1) 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 artery for the periodic inspection is not recommended. However, if removing the test article from a mock artery is necessary, care shall be taken to remove and re-deploy in a manner that minimizes the effect on the test article.

2) Termination

Terminate the test after the desired number of cycles has been achieved or a pre-specified endpoint has been observed.

3) Post-test inspection

Carefully remove the test articles from the test apparatus and mock artery, 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 endovascular prosthesis 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, high resolution X-ray) 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, fracture of active fixation components, detachment of the stent from the graft material, tearing or other failure modes of the fabric or covering (e.g. graft wear holes) and significant wear between prosthesis components;

— additional observations, such as perforation, suture breaks and suture hole elongation;

— failure modes that may be related to corrosion, wear between the prosthesis and the recipient vessel, or prosthesis 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).

D.5.2.3.1.6 Expression of results

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

D.5.2.3.1.7 Test report

The test report should be in accordance with 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 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 artery friction) and clinical relevance of the observations. Results should be considered and interpreted in relation to any applicable *in vivo* data.

D.5.2.3.2 Radial fatigue and durability

D.5.2.3.2.1 Purpose

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

D.5.2.3.2.2 Materials

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

D.5.2.3.2.3 Sampling

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

D.5.2.3.2.4 Conditioning

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

D.5.2.3.2.5 Test method

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

This test method describes a radial cyclic fatigue and durability test that subjects the test article to a specified amount of cyclic radial deformation. Testing is performed using a mock artery and fatigue tester that induces an expected physiologic radial deformation of the test article. Each test article is inspected periodically during the test for the occurrence of strut fracture, graft material holes 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 [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 prosthesis. 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. Dynamic radial compliance should be expressed as a percentage of the diameter change per 100 mmHg and defined per ISO 7198:2016, A.5.9.

$$\%\text{Compliance} = (D_{p2} - D_{p1}) \times 10^4/[D_{p1}(p_2 - p_1)] \quad \text{(D.2)}$$

where

D_{p1} is the inner diameter at the pressure of p_1;

D_{p2} 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 artery

Refer to the information regarding the mock artery in the general materials (see D.5.2.3.1.2) with the following.

The mock artery 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 artery 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 section [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 [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 artery as measured by a laser micrometer correlates with the intended deformation of the prosthesis (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 artery should be maintained.

b) Setup

Refer to the information in the general test method, set up [D.5.2.3.1.5, items b) 1) to 3)].

c) Testing

Refer to the information in the general test method, testing [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 artery 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 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 location and method for measuring diameter and deformation should be specified and justified.

d) Termination

Refer to the information in the general test method, termination [D.5.2.3.1.5, item d)].

e) Post-test inspection

Refer to the information in the general test method, post-test inspection [D.5.2.3.1.5, item e)].

D.5.2.3.2.6 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 $100(\Delta D/D_{diastolic})$ where D refers to the outer diameter of the test articles. The compliance is expressed as a percentage of the diameter change per 100 mmHg (%/100 mmHg).

D.5.2.3.2.7 Test report

Refer to the information in the general test method, test report (see D.5.2.3.1.7) with the following:

The intended and measured radial displacements of the test article shall be reported.

D.5.2.3.3 Active fixation fatigue and durability

D.5.2.3.3.1 Purpose

The purpose of this test is to evaluate the long-term structural integrity of the securement of the active fixation components (e.g. barbs, hooks, pins) to the attachment system (e.g. proximal stent) and the securement of the attachment system to the endovascular prosthesis body when subjected to cyclic loading conditions, appropriate for the device design and intended clinical use.

NOTE The evaluation of the securement of the active fixation components to the attachment system can be conducted separately from the evaluation of the securement of the attachment system to the endovascular prosthesis body.

D.5.2.3.3.2 Materials

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

D.5.2.3.3.3 Sampling

Refer to the information in the general sampling (see D.5.2.3.1.3) with the following:

The number of active fixation components and the total load on these components may vary with endovascular prosthesis size. The load on each active fixation component shall be considered when identifying the endovascular prosthesis size with the greatest potential for fatigue failure of the active fixation component. The endovascular prosthesis size selection can be justified using computational modelling (e.g. finite element analysis), engineering analysis and/or clinical data.

The number of connections between the attachment system and endovascular prosthesis body and the total load on these connections may vary with endovascular prosthesis size. The load on each connection shall be considered when identifying the endovascular prosthesis size with the greatest potential for fatigue failure of the connection between the attachment system and the endovascular prosthesis body. The endovascular prosthesis size selection can be justified using computational modelling (e.g. finite element analysis), engineering analysis and/or clinical data.

D.5.2.3.3.4 Conditioning

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

D.5.2.3.3.5 Test method

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

This test method describes a fatigue and durability test that subjects the active fixation components of the endovascular prosthesis and the connections between the attachment system to the endovascular prosthesis body to a specified number of cyclic loads. The direction of loading (e.g. axial) is selected and applied resulting in a minimum and a maximum load applied to the test article. Testing is performed with a fatigue tester that induces an expected physiologic loading to the test article and can be performed with or without a mock artery. Each test article is monitored during the test for the occurrence of component fracture, separation, strut fracture, graft tears, suture breaks and other aspects of structural integrity.

a) Define test conditions

   1) Establish loading condition

      Refer to the information in the general test method, establish loading conditions [D.5.2.3.1.5, item a) 1)] with the following:

      — the loading conditions of the test, that is, the intended displacement of or force applied to the test article are based on the expected clinical vascular pressures, diameter of the

vessel, the number of active fixation components and the number of connections between the attachment system to the endovascular prosthesis body. The load applied to each fixation component and/or the connections can also be affected by vessel angulation and the presence of calcification, resulting in non-uniform engagement of the active fixation components around the circumference of vessel. Force equilibrium models, finite element analysis or experimental evaluation can be used to establish the target minimum and maximum forces or displacements;

— determine the location(s) along the active fixation component (e.g. tip, distributed along the length) where the load will be applied. The location chosen for testing should be justified.

2) Mock artery (if applicable)

Refer to the information regarding the mock artery in the general materials (see D.5.2.3.1.2) with the following:

— the mock artery may or may not have a physiologically relevant compliance;

— the wall thickness of the mock artery should be appropriate to allow for engagement and loading of the active fixation component in order to obtain the desired deformation of the test article.

b) Test frequency

Refer to the information in the general test method, test frequency [D.5.2.3.1.5, item a) 3)].

c) Displacement conditions/control

Refer to the information in the general test method, displacement conditions/control [D.5.2.3.1.5, item a) 4)].

d) Setup

Refer to the information in the general test method, set up [D.5.2.3.1.5, items b) 1) to 3)] with the following.

Ensure that the locations of contact between the test fixture or mock artery and the fixation component match with the intended contact or loading location.

e) Testing

Refer to the information in the general test method, testing [D.5.2.3.1.5, item c)] with the following.

Set the frequency to the established rate and adjust the test system to achieve the intended minimum and maximum displacement of, or forces on, the test article. After the displacement or force targets are achieved, begin counting the cycles.

f) Termination

Refer to the information in the general test method, termination [D.5.2.3.1.5, item d)].

g) Post-test inspection

Refer to the information in the general test method, post-test inspection [D.5.2.3.1.5, item e)].

D.5.2.3.3.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). Diameters and displacements shall be expressed in millimetres (mm). Forces shall be express in Newtons (N).

D.5.2.3.3.7 Test report

Refer to the information in the general test method, test report (see D.5.2.3.1.7) with the following.

The intended and measured minimum and maximum test article displacement or forces shall be reported.

D.5.2.3.4 Axial fatigue and durability

D.5.2.3.4.1 Purpose

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

D.5.2.3.4.2 Materials

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

D.5.2.3.4.3 Sampling

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

D.5.2.3.4.4 Conditioning

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

D.5.2.3.4.5 Test method

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

This test method describes an axial cyclic 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 an expected physiologic axial deformation of the test article and can be performed with or without a mock artery. Each test article is inspected periodically during the test for the occurrence of strut fracture, graft material holes and other aspects of structural integrity.

The test article, with or without a mock artery, 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 artery and the load applied to the mock artery with appropriate justification.

a) Define test conditions

   1) Establish loading conditions

      Refer to the information in the general test method, establish loading conditions [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 artery (if applicable)

      Refer to the information regarding the mock artery in the general materials (see D.5.2.3.1.2) with the following.

      The mock artery may or may not have a physiologically relevant compliance.

3) Test frequency

Refer to the information in the general test method, test frequency section [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 [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 prosthesis, then this may be used to control the applied displacement during testing.

b) Setup

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

1) if a mock artery is used, and axial shortening of the test article is being evaluated, it may be appropriate to stretch the mock artery 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:

$$\%AS = \left[\frac{\left(L_{Free} - L_{Min}\right)}{L_{Free}}\right] \times 100 \quad \text{(D.3)}$$

where

%AS is the percent 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:

$$\%AL = \left[\frac{\left(L_{Max} - L_{Free}\right)}{L_{Free}}\right] \times 100 \quad \text{(D.4)}$$

where

%AL is the percent 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 [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 [D.5.2.3.1.5, item d)].

e) Post-test inspection

Refer to the information in the general test method, post-test inspection [D.5.2.3.1.5, item e)].

D.5.2.3.4.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). Diameters and displacements shall be expressed in millimetres (mm). Axial lengthening or shortening shall be expressed as a percentage (%).

D.5.2.3.4.7 Test report

Refer to the information in the general test method, test report (see D.5.2.3.1.7) with the following.

The intended and measured minimum and maximum test article displacement shall be reported.

D.5.2.3.5 Bending fatigue and durability

D.5.2.3.5.1 Purpose

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

D.5.2.3.5.2 Materials

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

D.5.2.3.5.3 Sampling

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

D.5.2.3.5.4 Conditioning

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

D.5.2.3.5.5 Test method

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

This test method describes bending fatigue and durability testing that subjects the test article to a specified amount of cyclic bending deformation. Bending deformation of the test article can be applied using several methods (e.g. column buckling, bend on a mandrel, bend in an arc without a mandrel). Testing is performed with a fatigue tester that induces an expected physiologic bending deformation of the test article and can be performed with or without a mock artery. Each test article is inspected periodically during the test for the occurrence of strut fracture, graft material holes and other aspects of structural integrity.

There is no standardized method for evaluating bending durability. An appropriate test method should be defined based upon prosthesis design and the intended clinical environment. The use of pressure within the mock artery and/or the test article might be helpful to aid in the reduction of the flattening of the mock artery and/or the test article lumen. Three potential methods for evaluating bending durability are provided in this document. An alternative method for evaluating bending fatigue and durability may be used.

The three methods are as follows.

a) Column buckling

If a mock artery is used, the test article is deployed into the mock artery and the mock artery is attached to a set of bending fixtures. If a mock artery is not used, the test article is directly attached to a set of bending fixtures. The bending fixtures are mounted on a machine capable of using rectilinear motion to impart consistent cyclic bending motion. A minimum and a maximum bending radius is selected and applied.

b) Bend on a mandrel

This test may be conducted with the test article directly attached to the apparatus or deployed in a mock artery which is attached to the apparatus. To create the bending action, the test article or the mock artery with the test article is deflected around a mandrel or deformed between two curved mating blocks, resulting in the target maximum and minimum radii of curvature.

c) Bend in an arc without a mandrel

To create the bending action, the end of the test article or the mock artery with the test article is moved in an arc or other defined path, resulting in the maximum and minimum radii of curvature.

a) Define test conditions

1) Loading conditions

Refer to the information in the general test method, establish loading conditions [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 bending conditions are based on the anticipated clinical bending deformation. Force equilibrium models, finite element analysis or experimental evaluation can be used to establish the target bending deformation.

2) Mock artery (if applicable)

Refer to the information regarding the mock artery in the general materials (see D.5.2.3.1.2) with the following.

The mock artery may or may not have a physiologically relevant compliance. The mock artery may be pressurized to aid in reduction of flattening of its lumen.

3) Test frequency.

Refer to the information in the general test method, test frequency [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 [D.5.2.3.1.5, item a) 4)].

b) Setup

Refer to the information in the general test method, set up [D.5.2.3.1.5, items b) 1) to 3)].

c) Testing

Refer to the information in the general test method, testing [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 bending conditions. For the selected test apparatus (column buckling, bend on a mandrel or bend in an arc without a mandrel), verify that the test article deformations are as intended. After the target bending conditions are achieved, begin counting the cycles;

2) verify the bending deformation at regular time intervals to ensure that the defined 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 [D.5.2.3.1.5, item d)].

e) Post-test inspection

Refer to the information in the general test method, post-test inspection [D.5.2.3.1.5, item e)].

D.5.2.3.5.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). Diameters shall be expressed in millimetres (mm). Bending radius of curvature or displacement of the test article shall be expressed in millimetres (mm).

D.5.2.3.5.7 Test report

Refer to the information in the general test method, test report (see D.5.2.3.1.7) with the following.

The test article intended and measured displacement or minimum and maximum radii of curvature shall be reported.

D.5.2.3.6 Torsional fatigue and durability

D.5.2.3.6.1 Purpose

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

D.5.2.3.6.2 Materials

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

D.5.2.3.6.3 Sampling

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

D.5.2.3.6.4 Conditioning

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

D.5.2.3.6.5 Test method

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

This test method describes a torsion durability test that subjects the test article to a specified amount of cyclic torsional deformation. A repeated torsional motion is applied to the test article (i.e. rotation with respect to the axis of the test article) or applied to a mock artery with the test article.

To induce cyclic torsion to the prosthesis, the ends of the mock artery in which the test article has been deployed are attached to an apparatus that cyclically rotates on one end of the mock artery while the opposite end of the mock artery remains fixed. It is also acceptable to apply cyclic torsion to the test article by securing both the test article and mock artery or the test article alone to the test apparatus. The testing apparatus should be adjusted so that the amount of rotation between the mock artery or test article attachment points is appropriate to induce the desired torsion in the test article. Each test article is monitored during the test for the occurrence of strut fracture, graft material holes and other aspects of structural integrity.

a) Define test conditions

1) Loading condition

Refer to the information in the general test method, establish loading conditions [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 torsional conditions are based on the anticipated clinical deformation. Force equilibrium models, finite element analysis or experimental evaluation can be used to establish the target deformation.

2) Mock artery

Refer to the information regarding the mock artery in the general materials (see D.5.2.3.1.2) with the following.

Localized instability during torsion testing may occur if the wall thickness of the mock artery is too thin. Thicker-walled tubes may be used in order to obtain the desired deformation of the endovascular prosthesis. The mock artery may or may not have a physiologically relevant compliance.

3) Test frequency

Refer to the information in the general test method, test frequency [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 [D.5.2.3.1.5, item a) 4)] with the following.

Establish the method to control torsional 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 torsional displacement of the test apparatus adequately correlates with the intended deformation of the test article, then this may be used to control the applied displacement during testing.

b) Setup

Refer to the information in the general test method, set up [D.5.2.3.1.5, items b) 1) to 3)] with the following.

Ensure that the prosthesis is not twisted during mounting.

Adjust the test apparatus to yield the desired torsional displacement (i.e. torsion per test article gage length).

c) Testing

Refer to the information in the general test method, testing [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 torsional displacement. Verify that the test article deformations are as intended. After the torsional displacement targets are achieved, begin counting the cycles;

2) verify minimum and maximum torsional displacement 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 [D.5.2.3.1.5, item d)].

e) Post-test inspection

Refer to the information in the general test method, post-test inspection [D.5.2.3.1.5, item e)].

D.5.2.3.6.6 Expression of results

The test frequency shall be expressed in cycles per second (Hz). Diameters shall be expressed in millimetres (mm). Torsional displacement shall be expressed in degrees per millimetre of length.

D.5.2.3.6.7 Test report

Refer to the information in the general test method, test report (see D.5.2.3.1.7) with the following.

The intended and measured minimum and maximum test article torsional displacement shall be reported.

D.5.2.4 Fixation and seal

D.5.2.4.1 Leakage at seal zone

D.5.2.4.1.1 Purpose

This test applies to a device design modification that may affect the seal zone(s).

Determine the leakage between the seal zone(s) of the endovascular prosthesis and a mock artery and compare the results to those for the unmodified device. This requirement can alternatively be met through evaluation of Type I endoleaks in a clinical study.

The evaluation of seal zone leakage is not necessary for endovascular prostheses intended for clinical uses for which seal zone leakage is unlikely to occur or would not likely be associated with adverse clinical sequelae (e.g. treatment of occlusive lesions).

D.5.2.4.1.2 Materials

The following materials apply:

— modified and unmodified endovascular prostheses;

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU);

— test fixture(s) incorporating a mock artery to simulate the proximal and distal landing zones

— pressurized fluid fixture capable of delivering water or appropriate fluid, at physiological temperature (37 ± 2) °C and appropriate pressure;

— a means of lowering the prosthesis graft material permeability to water or other test fluid so as to allow the necessary pressure differential across the graft material, if appropriate;

— a means for accurately measuring or determining the total leakage at the proximal and distal prosthesis seal zones;

— timer.

D.5.2.4.1.3 Sampling

Sampling shall be in accordance with D.2.

D.5.2.4.1.4 Conditioning

Conditioning shall be in accordance with D.3.

D.5.2.4.1.5 Test method

Develop a test method based on the following steps:

a) Insert the test article into the test fixture.

b) Connect the test fixture to the fluid system and allow the test system to stabilize at physiological temperature, flow and pressure.

c) Measure and record the amount of test fluid leaking between the mock artery and the test article (i.e. not through the test article wall) and the elapsed time over which leakage occurred.

D.5.2.4.1.6 Expression of results

The seal zone leakage shall be expressed in millilitres per minute (ml/min).

D.5.2.4.1.7 Test report

The test report shall be in accordance with D.4 and include the maximum, minimum, mean and standard deviation of the seal zone leakage rate and abnormal observations for the modified and unmodified devices. The test fluid viscosity and density, pressure and flow rate and the model material of construction shall be reported and justified.

D.5.2.4.2 Migration resistance

D.5.2.4.2.1 Purpose

The purpose of this test is to evaluate the ability of the endovascular prosthesis to resist migration when subjected to force or pressure.

D.5.2.4.2.2 Materials

The following materials apply:

— endovascular system;

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

— accessory devices necessary to accomplish deployment in accordance with the instructions for use (IFU);

— biological or synthetic mock artery with appropriate diameter, simulated seal zone length and mechanical properties for the endovascular prosthesis design (e.g. to accommodate hooks/barbs);

— test fixture capable of securely holding the mock artery and the endovascular prosthesis;