



BSI Standards Publication

Cardiovascular implants - Endovascular devices

Part 1: Endovascular prostheses

National foreword

This British Standard is the UK implementation of EN ISO 25539-1:2017. It supersedes BS EN ISO 25539-1:2009, which is withdrawn.

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

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

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Date	Text affected
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English Version

Cardiovascular implants - Endovascular devices - Part 1: Endovascular prostheses (ISO 25539-1:2017)

Implants cardiovasculaires - Dispositifs
endovasculaires - Partie 1: Prothèses endovasculaires
(ISO 25539-1:2017)

Kardiovaskuläre Implantate - Endovaskuläre
Implantate - Teil 1: Endovaskuläre Prothesen (ISO
25539-1:2017)

This European Standard was approved by CEN on 23 December 2016.

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EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Avenue Marnix 17, B-1000 Brussels

European foreword

This document (EN ISO 25539-1:2017) has been prepared by Technical Committee ISO/TC 150 “Implants for surgery” in collaboration with Technical Committee CEN/TC 285 “Non-active surgical implants” the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by September 2017 and conflicting national standards shall be withdrawn at the latest by March 2020.

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

This document supersedes EN ISO 25539-1:2009.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZA, which is an integral part of this document.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 25539-1:2017 has been approved by CEN as EN ISO 25539-1:2017 without any modification.

The following referenced documents are indispensable for the application of this document. For undated references, the latest edition of the referenced document (including any amendments) applies. For dated references, only the edition cited applies. However, for any use of this standard ‘within the meaning of Annex ZA’, the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this shall be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard, as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table — Correlations between undated normative references and dated EN and ISO standards

Normative references as listed in Clause 2	Equivalent dated standard	
	EN	ISO
ISO 10993 (all parts)	EN ISO 10993-1:2009 EN ISO 10993-2:2006 EN ISO 10993-3:2014 EN ISO 10993-4:2009 EN ISO 10993-5:2009 EN ISO 10993-6:2009 EN ISO 10993-7:2008 and EN ISO 10993-7:2008/AC:2009 EN ISO 10993-9:2009 EN ISO 10993-10:2013 EN ISO 10993-11:2009 EN ISO 10993-12:2012 EN ISO 10993-13:2010 EN ISO 10993-14:2009 EN ISO 10993-15:2009 EN ISO 10993-16:2010 EN ISO 10993-17:2009 EN ISO 10993-18:2009 - -	ISO 10993-1:2009 ISO 10993-2:2006 ISO 10993-3:2014 ISO 10993-4:2002 and Amd 1:2006 ISO 10993-5:2009 ISO 10993-6:2007 ISO 10993-7:2008 and ISO 10993-7:1/Cor 1:2009 ISO 10993-9:2009 ISO 10993-10:2010 ISO 10993-11:2006 ISO 10993-12:2012 ISO 10993-13:2010 ISO 10993-14:2001 ISO 10993-15:2000 ISO 10993-16:2010 ISO 10993-17:2002 ISO 10993-18:2005 ISO/TS 10993-19:2006 ISO/TS 10993-20:2006
ISO 11135	EN ISO 11135:2014	ISO 11135:2014
ISO 11137 (all parts)	EN ISO 11137-1:2015 EN ISO 11137-2:2015 EN ISO 11137-3:2006	ISO 11137-1:2006 and Amd 1:2013 ISO 11137-2:2013 ISO 11137-3:2006
ISO 11607-1	EN ISO 11607-1:2009 and EN ISO 11607-1:2009/A1:2014	ISO 11607-1:2006 and Amd 1:2014
ISO 14155	EN ISO 14155:2011	ISO 14155:2011 and Cor. 1:2011
ISO 14160	EN ISO 14160:2011	ISO 14160:2011
ISO 14630:2012	EN ISO 14630:2012	ISO 14630:2012
ISO 14937	EN ISO 14937:2009	ISO 14937:2009
ISO 14971	EN ISO 14971:2012	ISO 14971:2007
ISO 17665 (all parts)	EN ISO 17665-1:2006 CEN ISO/TS 17665-2:2009	ISO 17665-1:2006 ISO/TS 17665-2:2009

Annex ZA (informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC [OJ L 169] aimed to be covered

This European Standard has been prepared under a Commission's standardisation request M/023 concerning the development of European standards related to medical devices to provide a voluntary means of conforming to essential requirements of Council Directive 93/42/EEC of 14 June 1993 concerning medical devices [OJ L 169].

Once this standard is cited in the Official Journal of the European Union under that Directive, compliance with the clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Directive 93/42/EEC as amended by 2007/47/EC. This means that risks have to be reduced 'as far as possible', 'to a minimum', 'to the lowest possible level', 'minimized' or 'removed', according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with essential requirements 1, 2, 5, 6, 7, 8, 9, 11 and 12 of the Directive.

NOTE 3 This Annex ZA is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZA.1— Correspondence between this European Standard and Annex I of Directive 93/42/EEC [OJ L 169]

Essential Requirements of Directive 93/42/EEC	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
7.2	11.2	Partially covered by the sub-clause: There is a requirement for devices to be designed to protect patients from <i>sterilization</i> residuals when the device is used. Other contaminants and residues are not covered. Manufacturing and packing to minimize these risks are not covered.
8.1	11.1, 12.1.5	Partially covered by the sub-clauses: Requirements for ensuring sterility are included for devices that are supplied

		sterile (11.1) which would eliminate or reduce as far as possible the risk of infection to the patient. Maintenance of sterility in transit is covered in 12.1.5. Risk of infection to the user and third party are not covered. Minimizing contamination during use is not covered.
8.3	11.1, 12.1, 10 with 6.4(c)	Sterility assurance (11.1), manufacturing (10), packaging design and maintenance of sterility (12.1) are covered. 6.4(c) includes the requirement for the design attributes to take the need for sterility into account.
8.4	11.1, 10 with 6.4(c)	Manufacturing (10), sterilization validation and routine control (11.1) are covered, with the requirement for the design attributes to take the need for sterility into account (6.4(c)).
9.1	8.5.1.5, 12.3.2(i)	Endovascular systems may be designed to be used with accessory devices (e.g., guide wires, introducer sheaths). Accessory devices are evaluated for compatibility with the endovascular system in simulated use testing (8.5.1.5). Requirements regarding instructions for use include preparation and implantation techniques including the use of ancillary devices (12.3.2(i)).
9.2, first indent	4.3, 6.2, 6.3, 8.5.1.2, 8.5.2.7, 8.5.1.5	Partially covered by the sub-clauses: Device design is covered through the requirement to specify dimensions (4.3), design attribute requirements (6.2 and 6.3) and the requirements

		for dimensional verification (8.5.1.2, 8.5.2.7). The risk of injury to the patient is also covered through simulated use testing (8.5.1.5). Manufacturing to minimize risks associated with physical features is not covered.
9.2, second indent	6.3 (g), 8.5.2.9	Only risks associated with magnetic fields is covered through design attribute (6.3(g)) and MRI safety (8.5.2.9) requirements. The other environmental conditions are not applicable.
13.1	12.2, 12.3	The labelling (12.2) and instructions for use (12.3) sub-clauses cover this directive.
13.3(a)	12.2.1(a)	Partially covered by the sub-clause: This directive is covered with the exception of the requirement regarding the name and address of the authorised representative where the manufacturer does not have a registered place of business in the Community.
13.3(b)	12.2.1(b), (c), (d), (e), (f)	Identification of the device and the contents of the packaging is covered: 12.2.1 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);
13.3(c)	12.2.1(g)	The inclusion of the word 'STERILE' on the product label is covered by the requirement to include the words "STERILE—DO NOT RESTERILIZE—SINGLE USE

		ONLY”, or equivalent phrase or symbols, in prominent form per the sub-clause.
13.3(d)	12.2.1(k)	This directive is covered by the requirement to include the manufacturer’s batch or lot number per the sub-clause, but only if the batch code is preceded by the word ‘LOT.’
13.3(e)	12.2.1(j)	This directive is covered by the requirement to include the date of sterilization and/or expiration date per the sub-clause.
13.3(f)	12.2.1(g)	Partially covered by the sub-clause: This directive is covered by the requirement to include the words ‘SINGLE USE ONLY’ per the sub-clause. Consistency of marking across the community is not covered.
13.3(i)	12.2.1(m)	Partially covered by the sub-clause: This directive is covered by the requirement to include the manufacturers recommendations for storage (when applicable) per the sub-clause. Handling is not covered.
13.3(k)	12.2.1(l)	Partially covered by the sub-clause: The only warning that is included indicates not to use if the package is opened or damaged.
13.3(m)	12.2.1(h)	This directive is covered by the requirement to include the method of sterilization per the sub-clause.
13.4	12.3.2(d)	This directive is covered. The intended purpose is obvious, but the intended use is required to be specified in the instructions for use per the sub-clause.
13.6(a) [13.3(a),(b), (c), (f), (i), (j), (k)]	12.3.2(a), (b), (c), (i), (j), (l), (e)	Partially covered by the sub-clauses: This directive is covered as follows: • 13.3 (a) is covered by

		12.3.2 (a) with the exception of the name and address of the authorised representative where the manufacturer does not have a registered place of business in the Community, nor the method of sterilization. • 13.3(b) is covered by 12.3.2(b), (c) • 13.3(c) is covered by 12.3.2(j) • 13.3(f) is covered by 12.3.2(j) • 13.3(i) is covered by 12.3.2(l) with the exception of handling • 13.3(j) is covered by 12.3.2(i) • 13.3(k) is covered by 12.3.2(e)
13.6(b)	12.3.2(f), (g)	This directive is covered with respect to the inclusion of any undesirable side effects by the requirement to include the potential adverse events (12.3.2(f) and performance information by the requirement to include data from clinical studies (if applicable) (12.3.2(g)).
13.6(c)	12.3.2(i)	Use of endovascular systems involves the use of additional medical devices (e.g., syringes, wire guides). This directive is covered by the requirement to include recommended methods for the preparation of the endovascular system and implantation techniques per the sub-clause.
13.6(d)	12.3.2(i)	The requirement to include recommended methods for the preparation of the endovascular system and implantation techniques per the sub-clause covers the

		directive regarding proper installation and preparation for operation. The directive regarding maintenance and calibration is not applicable as endovascular prostheses do not require maintenance and calibration.
13.6(g)	12.2.1(l), 12.3.2(j)	Partially covered by the sub-clauses: This directive is covered under the labelling requirement regarding not to use the device if the package is opened or damaged (12.2.1(l)), but not under the instructions for use. The directive regarding resterilization is covered by the requirement to state not to resterilize in the instructions for use (12.3.2(j)).
13.6(i)	12.3.2(i)	The directive regarding details of further handling is covered by the requirement to include recommended methods for the preparation of the endovascular system and implantation techniques per the sub-clause.
13.6(l)	12.3.2(n)	Only precautions associated with magnetic fields are covered through the requirement to provide MRI safety information per the sub-clause. The other environmental conditions are not applicable.
13.6(q)	12.3.2 (o)	This directive is covered through the requirement to include the revision date for the instructions for use per the sub-clause.

WARNING 1: Presumption of conformity stays valid only as long as a reference to this European standard is maintained in the list published in the Official Journal of the European Union. Users of this standard should consult frequently the latest list published in the Official Journal of the European Union.

WARNING 2: Other Union legislation may be applicable to the product(s) falling within the scope of this standard.

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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 than 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;