BRITISH STANDARD

BS EN ISO 25539-2:2009

Incorporating corrigenda February 2011 and March 2012

Cardiovascular implants — Endovascular devices

Part 2: Vascular stents (ISO 25539-2:2008)

ICS 11.040.40

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British Standards

Full document details: BS EN ISO 25539-2:2009

National foreword

This British Standard is the UK implementation of EN ISO 25539-2:2009, incorporating corrigendum February 2011. It is identical to ISO 25539-2:2008. It supersedes BS EN ISO 25539-2:2008, which is withdrawn. Together with BS EN ISO 25539-1:2009, it supersedes BS EN 14299:2004, which is withdrawn. Together with BS EN ISO 25539-1:2009 and BS EN ISO 25539-3:2011, it supersedes BS EN 12006-3:1998+A1:2009, which is withdrawn.

The UK participation in its preparation was entrusted by Technical Committee CH/150, Implants for surgery, to Subcommittee CH/150/2, Cardiovascular implants.

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

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

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EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 25539-2

May 2009

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Supersedes EN ISO 25539-2:2008
Incorporating corrigendum February 2011

English Version

Cardiovascular implants - Endovascular devices - Part 2: Vascular stents (ISO 25539-2:2008)

Implants cardiovasculaires - Dispositifs endovasculaires - Partie 2: Stents vasculaires (ISO 25539-2:2008)

Kardiovaskuläre Implantate - Endovaskuläre Implantate - Teil 2: Gefäßstents (ISO 25539-2:2008)

This European Standard was approved by CEN on 20 April 2009.

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This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN Management Centre has the same status as the official versions.

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Foreword

The text of ISO 25539-2:2008 has been prepared by Technical Committee ISO/TC 150 “Implants for surgery” of the International Organization for Standardization (ISO) and has been taken over as EN ISO 25539-2:2009 by 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 November 2009, and conflicting national standards shall be withdrawn at the latest by March 2010.

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 25539-2:2008 and EN 12006-3:1998+A1:2009.

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.

For relationship with EU Directive, 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, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 25539-2:2008 has been approved by CEN as a EN ISO 25539-2:2009 without any modification.

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Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Communities under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in table ZA 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.

Table ZA — Correspondence between this European Standard and Directive 93/42/EEC

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4	1, 2, 4, 7.1	
5	1, 2, 3, 4, 5, 7.1, 7.2, 7.3, 7.5, 8, 9.2	
6	1, 2, 7.1, 7.2, 7.3, 7.5, 8.2, 9.2	
7	1, 2, 3, 4, 6, 6a., 7.1, 7.2, 8, 9.2,	
8	1, 2, 3, 5, 7.1, 7.2	
9	1, 2, 3, 7.2, 8.1, 8.3, 8.4	
10	1, 2, 3, 5, 7.2, 8.3, 8.4	
11	1, 2, 8.7, 13.1, 13.3, 13.4, 13.6	Part of 13.3 a relating to the authorised representative is not covered. Part of ER 13.3 f concerning single use is not addressed in this European Standard. 13.6 h) concerning single use is not addressed in this European Standard.

WARNING — Other requirements and other EU Directives 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.

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

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

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

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

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

— *Part 1: Endovascular prostheses*

— *Part 2: Vascular stents*

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Introduction

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

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INTERNATIONAL STANDARD

Cardiovascular implants — Endovascular devices —

Part 2:
Vascular stents

1 Scope

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

NOTE Due to the variations in the design of implants covered by this part of ISO 25539 and in some cases due to the relatively recent development of some of these implants (e.g. bioabsorbable stents, polymeric stents), acceptable standardized *in vitro* tests and clinical results are not always available. As further scientific and clinical data become available, appropriate revision of this document will be necessary.

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

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

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

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

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

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

2 Normative references

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

ISO 10993 (all parts), *Biological evaluation of medical devices*

ISO 11135-1, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

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

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

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

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

ISO 14630, *Non-active surgical implants — General requirements*

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

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

ISO 17665-1, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

3 Terms and definitions

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

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

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

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

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

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

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

3.4
determine
to quantitatively appraise or analyse

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

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

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

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

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

3.8
evaluate
to qualitatively appraise or analyse

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

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

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

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

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

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

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

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

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

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

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

3.15.1
articulated stent
stent constructed of segments with distinct connections

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3.15.2
bare stent
stent without a coating or covering

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

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

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

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

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

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

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

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

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

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

4 General requirements

4.1 Classification

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

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4.2 Size

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

a) external diameter;

   1) self-expanding:

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

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

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

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

4.3 Intended clinical use designation

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

a) abdominal aorta;

b) arterio-venous shunt for vascular access;

c) carotid;

d) coronary;

e) femoral;

f) iliac;

g) popliteal;

h) renal;

i) thoracic aorta;

j) thoraco-abdominal aorta;

k) tibial;

l) other arterial vessels to be specified;

m) other venous vessels to be specified.

5 Intended performance

The requirements for intended performance of ISO 14630 shall apply.

6 Design attributes

6.1 General

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

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

b) fretting, galvanic and pitting corrosion;

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c) interface between implant and body:

1) fixation hooks if present;

2) relative movement between stent and tissue;

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

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

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

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

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

6.2 Delivery system and stent system

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

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

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

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

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

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

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

6.3 Implant

6.3.1 Stent

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

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

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

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

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

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

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

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

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

6.3.2 Coating

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

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

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

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

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

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

6.3.3 Drug

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

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

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

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

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

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

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

7 Materials

The requirements for materials of ISO 14630 apply. Additional testing specific to certain materials (e.g. metals, polymers, drugs) shall be performed to determine the appropriateness of the material for use in the design. For example, Nitinol materials dependent on shape memory properties shall be subjected to testing in order to assess transformation properties. In addition, for drug-eluting stents drug identity testing shall be performed, including the identification of impurities and degradants. Electro-chemical potentials of differing metals (stents, guidewires, other accessory devices) might require additional types of testing.

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8 Design evaluation

8.1 General

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

Justification shall be provided for the properties not measured.

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

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

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

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

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

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

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

8.2 Sampling

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

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

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

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

1) International Conference on Harmonisation guidelines.

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8.3 Conditioning of test samples

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

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

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

8.4 Reporting

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

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

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

Individual test reports should include the following information:

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

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

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

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

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

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

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

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

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8.5 Delivery system and stent system

8.5.1 Ability to access

8.5.1.1 General

This covers the ability of the system to permit safe, consistent and accurate access to the intended location.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) guidewire not crossing the lesion;

b) introducer and delivery system not matching the access site (i.e., size mismatch);

c) delivery system not advancing to target site;

d) embolism and air embolization;

e) stent dislodgement.

These hazards might result in reportable clinical events, including but not limited to the following:

— access failure;

— vascular trauma;

— neurological deficit;

— ischemia;

— spinal neurological deficit;

— embolization;

— procedural bleeding.

Testing shall include the following items listed in 8.5.1.2 to 8.5.1.13, as appropriate to the design of the stent system.

8.5.1.2 Bond strength

Determine the longitudinal bond strength between parts of the delivery system. All bonds shall remain intact under recommended conditions of use. The results shall be evaluated in relation to the force(s) necessary to access the intended location.

8.5.1.3 Component dimension compatibility

Evaluate the dimensions of the stent system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible. The need for contrast to be able to pass through the lumen of the guide catheter or introducer with the stent system in place should be considered.

8.5.1.4 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

8.5.1.5 Dislodgement force (pre-mounted balloon expandable stents)

Determine the force required to dislodge the premounted stent from the crimped position on the non-expanded balloon and to completely separate the stent from the non-expanded balloon during clinical use.

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8.5.1.6 Flex/kink

Evaluate the ability of the stent system to bend in order to accommodate the predetermined clinically relevant radius or angle it will be required to negotiate during access and delivery.

8.5.1.7 Profile/diameter test

Determine the maximum diameter along sections of the stent system.

8.5.1.8 Pushability

Evaluate the ability of the stent system to be pushed or positioned by an operator without undesirable bending or buckling.

8.5.1.9 Simulated use

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

8.5.1.10 Torquability

Evaluate the ability of the stent system to provide sufficient rotation to the distal (leading) end to deliver the stent within the anatomy, if appropriate for the intended clinical use.

8.5.1.11 Torsional bond strength

Determine the torque/rotation required to break joints and/or materials in the appropriate delivery system components, if appropriate for the intended clinical use. The results shall be evaluated in relation to the torque necessary to access the system.

8.5.1.12 Trackability

Evaluate the ability of the stent system to advance through the vessel to the target site using the recommended accessories. Evaluate the potential for displacement of the guidewire from its intended position during the advancement of the stent system, as appropriate for the intended use of the stent (e.g. loss of side-branch access during stenting).

8.5.1.13 Visibility

Evaluate the ability to visualize the delivery system and/ or stent system during access using fluoroscopy. The use of other technologies for visualization shall be justified.

8.5.2 Ability to deploy

8.5.2.1 General

This covers the ability of the system to permit safe, consistent and accurate deployment of the stent.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) inability to fully and properly deploy the stent;

b) stent dislodgement;

c) balloon failure (if applicable);

d) stent or delivery system damage;

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e) inadequate visualization;

f) embolism and air embolization.

These hazards might result in reportable clinical events, including, but not limited to, the following:

— delivery system failure;

— deployment failure;

— spinal neurological deficit;

— neurological deficit;

— vascular trauma;

— ischemia;

— embolization;

— damage to stent;

— procedural bleeding.

Testing shall include the following items listed in 8.5.2.2 to 8.5.2.13, as appropriate to the design of the stent system.

8.5.2.2 Bond strength

Determine the longitudinal bond strength between parts of the delivery system. All bonds shall remain intact under recommended conditions of use. The results shall be evaluated in relation to the force(s) necessary to deploy the stent.

8.5.2.3 Balloon inflation time (balloon expandable or balloon assisted stents)

Determine the time required to expand the balloon to the maximum recommended inflation pressure, volume or diameter. The stent system should be used for this test if the stent is intended to be mounted on the balloon during inflation.

8.5.2.4 Balloon deflation time (balloon expandable or balloon assisted stents)

Determine the time required to deflate the balloon and evaluate the ability to remove the deflated balloon from within the stent.

8.5.2.5 Balloon rated burst pressure (RBP) (balloon expandable or balloon assisted stents)

Determine the burst pressure with an appropriate safety margin. The stent system should be used for this test if the stent is intended to be mounted on the balloon during inflation.

Designate the maximum recommended inflation pressure. This pressure should not exceed the RBP.

8.5.2.6 Balloon rated fatigue (balloon expandable stents)

Evaluate the ability of the balloon to withstand a clinically justified number of repeated inflation cycles to the rated burst pressure. The stent system should be used for this test if the stent is intended to be mounted on the balloon during inflation.

Designate the maximum recommended number of inflation cycles.

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8.5.2.7 Component dimension compatibility

Evaluate the dimensions of the stent delivery system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible. The need for contrast to be able to pass through the lumen of the guide catheter with the stent system in place should be considered.

8.5.2.8 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

8.5.2.9 Dislodgement force (pre-mounted balloon expandable stents)

Determine the force required to dislodge the premounted stent from the crimped position on the non-expanded balloon and to completely separate the stent from the non-expanded balloon during clinical use.

8.5.2.10 Dogboning (balloon expandable stents)

Determine the diameter(s) of the balloon extending beyond the ends of the stent that are greater than the stent outer diameter(s) at the maximum recommended inflation pressure.

8.5.2.11 Force to deploy (self-expanding stents)

Determine the force to deploy the stent from the delivery system.

8.5.2.12 Simulated use

Evaluate the performance of the stent-system using a model that simulates the intended use conditions.

8.5.2.13 Visibility

Evaluate the ability to visualize the stent and delivery system during placement and deployment using fluoroscopy. The use of other technologies for visualization shall be justified.

8.5.3 Ability to withdraw

8.5.3.1 General

This covers the ability of the system to permit safe and consistent withdrawal of the delivery system.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) improper balloon deflation (balloon expandable);

b) balloon winging (balloon expandable);

c) lack of structural integrity;

d) embolism;

e) diameter mismatch;

f) stent dislodgement;

g) stent or delivery system damage;

h) delivery system snags on, or adheres to the stent;

i) inadequate visualization.

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These hazards might result in reportable clinical events, including, but not limited to, the following:

— delivery system failure;

— deployment failure

— neurological deficit;

— vascular trauma;

— ischemia;

— spinal neurological deficit;

— embolization;

— damage to stent;

— procedural bleeding.

Testing shall include the following items in 8.5.3.2 to 8.5.3.9, as appropriate to the design of the stent system.

8.5.3.2 Bond strength

Determine the longitudinal bond strength between parts of the delivery system. All bonds shall remain intact under recommended conditions of use. The results shall be evaluated in relation to the force(s) necessary to withdraw the system.

8.5.3.3 Component dimension compatibility

Evaluate the dimensions of the stent delivery system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible. The need for contrast to be able to pass through the lumen of the guide catheter with the stent system in place should be considered.

8.5.3.4 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

8.5.3.5 Flex/kink

Evaluate the ability of the stent system to bend in order to accommodate the predetermined clinically relevant radius or angle it will be required to negotiate during access and delivery.

8.5.3.6 Simulated use

Evaluate the performance of the delivery system using a model that simulates the intended use conditions.

8.5.3.7 Torsional bond strength

Determine the torque/rotation required to break joints and/or materials in the appropriate delivery system components, if appropriate for the intended clinical use. The results shall be evaluated in relation to the torque necessary to withdraw the system.

8.5.3.8 Tubing tensile strength

Determine the strength of the tubing used in the delivery system as appropriate to the material.

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8.5.3.9 Visibility

Evaluate the ability to visualize the delivery system during withdrawal using fluoroscopy. The use of other technologies for visualization shall be justified.

8.5.4 Biocompatibility

Biocompatibility shall be tested in accordance with ISO 10993-1 and appropriate other parts of the ISO 10993 series of International Standards. For extraction tests, the stent should be tested separately from the delivery system.

8.5.5 Haemostasis

8.5.5.1 General

This covers the ability of the system to minimise blood loss.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) component dimensional incompatibility (size mismatch);

b) seal incompetence;

c) other leakage.

These hazards might result in reportable clinical events, including, but not limited to, the following:

— procedural bleeding;

— haematoma.

Testing shall include the following items listed in 8.5.5.2 to 8.5.5.4, as appropriate to the design of the stent system.

8.5.5.2 Component dimension compatibility

Evaluate the dimensions of the stent delivery system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible.

8.5.5.3 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

8.5.5.4 Assessment of haemostasis

Evaluate the ability of any seal or valves in the delivery system to maintain an adequate haemostatic seal when used with appropriate accessory devices.

8.6 Stent

8.6.1 Ability to accurately deploy

8.6.1.1 General

This covers the ability to permit safe, consistent and accurate deployment of the stent at the intended lesion location.

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For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) inaccurate positioning or orientation;

b) improper deployment configuration;

c) incomplete deployment;

d) inadequate visualization.

These hazards might result in reportable clinical events, including, but not limited to, the following:

— branch vessel occlusion;

— delivery system failure;

— deployment failure;

— stent migration;

— intraprocedural vessel occlusion;

— ischemia;

— vascular trauma.

Testing shall include the following items listed in 8.6.1.2 to 8.6.1.5, as appropriate to the design of the stent.

8.6.1.2 Stent length-to-diameter relationship

Determine the relationship between stent length and expanded stent diameter.

8.6.1.3 Profile effect/flaring (balloon expandable stents)

Determine the change in distance between the external diameter of the stent and the external diameter of the balloon after tracking through a tortuous path.

8.6.1.4 Simulated use

Evaluate the performance of the stent using a model that simulates the intended use conditions.

8.6.1.5 Visibility

Evaluate the ability to visualize the stent during deployment and after withdrawal of the delivery system using fluoroscopy. The use of other technologies for visualization shall be justified.

8.6.2 Fixation effectiveness

8.6.2.1 General

This covers the ability of the stent to remain in its deployed position.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) incomplete apposition to vessel wall;

b) excessive or inadequate radial outward force.

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These hazards might result in reportable clinical events, including, but not limited to, the following:

— stent migration;

— intraprocedural vessel occlusion;

— vascular trauma;

— trauma to adjacent structures;

— branch vessel occlusion.

Testing shall include the following items in 8.6.2.2 to 8.6.2.8, as appropriate to the design of the stent.

NOTE Four tests are listed below, which determine forces related to the deformation of the stent. Although similar, crush resistance with a radially applied load, crush resistance using parallel plates, local compression and radial force tests measure different attributes of the stent, as follows:

— the crush resistance test with a radially applied load measures the ability of a balloon-expandable stent to resist permanent deformation when subjected to a circumferentially uniform radial load;

— the crush resistance test using parallel plates measures the ability of a stent to resist permanent deformation along the entire length of the device when subjected to a load uniformly applied over the length of the device;

— the local compression test measures the ability of a stent to resist permanent deformation under a localized (e.g. point) load;

— the radial force test measures the force exerted by a self-expanding stent on the vessel in the deployed state during expansion and compression.

8.6.2.2 Conformability to vessel wall

Evaluate the ability of the stent to adequately contact the vessel wall upon deployment.

8.6.2.3 Crush resistance with a radially applied load (balloon expandable stents)

Determine the load/deformation characteristics of the stent while a circumferentially uniform radial load is applied.

8.6.2.4 Crush resistance with parallel plates

Determine the load required to cause clinically relevant buckling or a deflection reduction of at least 50 % of the original distance between the plates and the load required to permanently deform or fully collapse the stent. This test is required for stents that can experience direct compression in a clinical setting.

8.6.2.5 Local compression

Determine the load/deformation characteristics of the stent in response to a localized compressive force, perpendicularly applied to the longitudinal axis of the device, and its ability to recover to its original geometry. The plate deflection should be reduced by at least 50 % at the point of contact. This test is required for stents of a design with the potential for a different response to local compression as compared to a radial or flat plate compressive force and for which this test is clinically relevant.

8.6.2.6 Radial force

Determine the force (expansion and compression) exerted by a self-expanding stent as a function of the stent outer diameter.

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8.6.2.7 Recoil (balloon expandable stents)

Determine the percent change of the stent outer diameter from the maximum outer diameter obtained with balloon inflation, to the final outer diameter after balloon removal. The sizing scheme recommended for the stent in the IFU should take into consideration this recoil.

8.6.2.8 Simulated use

Evaluate the performance of the stent using a model that simulates the intended use conditions.

8.6.3 Stent integrity

8.6.3.1 General

This covers the ability of the stent to resist structural failure.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) structural failure of the stent, including the coating, if applicable;

b) loss of complete apposition to vessel wall;

c) excessive, unintended stent expansion non-uniformity.

These hazards might result in reportable clinical events, including, but not limited to, the following:

— stent fracture;

— residual stenosis;

— in-segment restenosis;

— in-stent restenosis;

— restenosis;

— vessel occlusion, intraprocedural;

— vessel occlusion, periprocedural;

— vessel occlusion, late;

— stent migration;

— vascular trauma;

— ischemia due to emboli or in-stent thrombosis;

— trauma to adjacent structures.

Testing shall include the following items listed in 8.6.3.2 to 8.6.3.6, as appropriate to the design of the stent.

8.6.3.2 Acute coating integrity

Evaluate any damage to the coating due to loading, tracking, deployment and delivery system withdrawal.

8.6.3.3 Coating dimensions and other coating parameters (e.g. porosity, density distribution)

Determine the appropriate dimensions of the stent coating for conformance with design specifications.

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8.6.3.4 Corrosion

Evaluate the susceptibility of the stent to corrosion in an actual or simulated environment. These corrosion mechanisms can include pitting, fretting, crevice and galvanic corrosion.

Coating artefacts and coating manufacturing processes might affect corrosion potential of final product and should be considered.

8.6.3.5 Durability

8.6.3.5.1 General

The evaluation of long-term durability under anticipated physiological conditions shall be performed. If not all stent sizes and configurations are evaluated, the size(s) and configurations to be evaluated shall be selected to represent the greatest potential for fatigue failure, so that conclusions regarding the acceptable durability can be reasonably applied to other sizes and configurations not tested. Results from the testing and the analyses to evaluate the durability of the stent are complementary and should be interpreted both independently and in combination.

The following items shall be considered in evaluating stent durability:

— overlapping stents, as appropriate;

— potential failure modes, such as, strut or bridge fracture, wear, permanent deformation, loss of coating integrity (e.g. delamination, particle shedding or dehiscence);

— *in vivo* loads, as appropriate to the specific intended site of implantation (e.g. bending, radial, axial, torsion, crush);

— limitations of the test and associated potential artefacts.

Testing has not yet been standardized for the evaluation of the effects of physiological loads beyond radial loading. Testing and/or analyses in addition to those listed below might be necessary to fully evaluate all physiologic loading and potential failure modes. Anatomic variability and post-implant morphologic changes should be considered in establishing appropriate boundary conditions for test and/or analysis.

8.6.3.5.2 Stress/strain analyses

Determine the critical stresses and/or strains in the stent due to manufacturing, catheter loading, delivery, deployment and *in vivo* loading, using appropriate tools such as finite element analysis (FEA). The material properties shall be selected as those appropriate to the specific stage of manufacturing and deployment being analysed. The results of this stress/strain analysis can be used to determine appropriate design safety margins and can be used to establish the appropriate test conditions and to select the appropriate test articles (e.g. stent sizes) for durability testing.

8.6.3.5.3 Fatigue safety factor determination

Conduct an appropriate fatigue analysis. Evaluation of the stent fatigue safety factor requires an engineering approach such as stress-life, and/or strain-life. In general, all sizes and configurations shall be analysed, unless it can be reasonably demonstrated that a worst-case exists. Stress-life or strain-life fatigue safety analysis requires that the mean and cyclic stresses or strains be determined by stress/strain analysis, and compared to the appropriate material properties (e.g. ultimate and endurance strength or strain). Safety factor can be expressed based on stress, strain or fatigue life.

8.6.3.5.4 Fatigue durability testing

Evaluate the long-term structural integrity of the stent when subjected to simulated worst-case physiologic loads. Durability shall be evaluated for all relevant fatigue loading modes, which shall be justified based on the intended clinical use (implant location) and conditions (e.g. oversizing, overlap). Fatigue testing of the stent

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shall include *in vitro* testing until ten-year equivalent cycles have been applied to each stent under test. If the intended stent life is less than ten years, shorter duration fatigue testing might be appropriate and shall be justified. The frequency of the test shall be such that the deformation of the stent under test is no less than the deformation of the stent under the determined physiological conditions. The testing shall be conducted in an appropriate test solution, such as phosphate buffered saline, unless testing in a different environment, such as distilled water, can be justified. The testing shall be conducted at physiological temperature, unless otherwise justified.

Test conditions shall be documented and justified, and shall include the number of samples, stent sizes tested, test frequency, and other parameters used in simulating the physiological conditions. Loading/deformation modes and magnitudes and the requisite number of test cycles shall be justified by appropriate physiological models and analyses. The stent size(s) and configurations to be tested shall be selected to represent the greatest potential for fatigue failure, so that conclusions regarding the acceptable durability can be reasonably applied to other sizes and configurations not tested.

Testing to fracture shall be considered, but is not a requirement. While test methods have not yet been standardized, durability testing to fracture has several potential advantages; including identification of failure modes, verification of device fatigue analysis and appropriateness of factor of safety.

8.6.3.5.5 Coating durability

Evaluate the ability of the coating to resist delamination (e.g. flaps, bare spots) when subjected to simulated worst-case physiologic loads in a manner consistent with 8.6.3.5.4.

Examination of the coating under appropriate magnification shall be conducted. Inspection results shall be compared to baseline characteristics to determine the effective life of the coating. Results shall be analysed with respect to available preclinical *in vivo* and clinical performance.

Examinations at pre-specified intervals should be considered.

8.6.3.5.6 Coating particulate generation

Determine the size and amount of particles generated from the coating when subjected to simulated *in vivo* conditions.

8.6.3.6 Visual inspection

The stent shall conform to the manufacturer's specifications with respect to surface defects and contamination. The stent shall be free of defects that would render the stent unsuitable for its intended use.

8.6.4 Sizing

8.6.4.1 General

This covers the ability of the stent to remain in its placed position within the vasculature, by appropriate sizing.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) inappropriate sizing.

These hazards might result in reportable clinical events, including, but not limited to, the following:

— stent migration;

— stent thrombosis;

— branch vessel occlusion;

— vascular trauma;

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— trauma to adjacent structures;

— residual stenosis;

— in-segment restenosis;

— in-stent restenosis;

— restenosis;

— vessel occlusion, intraprocedural;

— vessel occlusion, periprocedural;

— vessel occlusion, late;

— ischemia.

Testing shall include the following items listed in 8.6.4.2 to 8.6.4.6, as appropriate to the design of the stent.

8.6.4.2 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

8.6.4.3 Stent diameter to balloon inflation pressure (balloon expandable stents)

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

8.6.4.4 Recoil (balloon expandable stents)

Determine the percent change of the stent outer diameter from the maximum outer diameter obtained with balloon inflation to the final outer diameter after balloon removal. The sizing scheme recommended for the stent in the IFU should take into consideration this recoil.

8.6.4.5 Simulated use

Evaluate the performance of the stent using a model that simulates the intended use conditions.

8.6.4.6 Stent length to diameter relationship

Determine the relationship between stent length and its expanded diameter.

8.6.5 Patency

8.6.5.1 General

This covers the ability of the stent to maintain an open lumen.

For estimating risks, the hazards to be considered include, but are not limited to, the following:

a) kinking;

b) twisting;

c) inaccurate deployment;

d) deformation, including stent closure;

e) thrombogenicity.

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These hazards might result in reportable clinical events, including, but not limited to, the following:

— stent thrombosis;

— residual stenosis;

— in-segment restenosis;

— in-stent restenosis;

— restenosis;

— vessel occlusion, intraprocedural;

— vessel occlusion, periprocedural;

— vessel occlusion, late;

— angina;

— recurrence of portal hypertension (for TIPS);

— myocardial infarction;

— ischemia;

— embolism;

— neurological deficit.

Testing shall include the following items listed in 8.6.5.2 to 8.6.5.8, as appropriate to the design of the stent.

NOTE There are four tests listed below that determine forces related to the deformation of the stent. Although similar, crush resistance with a radially applied load, crush resistance using parallel plates, local compression and radial force tests measure different attributes of the stent, as follows:

— the crush resistance test with a radially applied load measures the ability of the stent to resist permanent deformation along the entire length of the device when subjected to a radially applied load;

— the crush resistance test using parallel plates measures the ability of the stent to resist permanent deformation along the entire length of the device when subjected to a load uniformly applied over the length of the device;

— the local compression test measures the ability of the stent to resist permanent deformation under a localized (e.g. point) load;

— the radial force test measures the force exerted by the stent on the vessel in the deployed state.

8.6.5.2 Crush resistance test with a radially applied load (balloon expandable stents)

Determine the load required to cause clinically relevant buckling or a diameter reduction of at least 50 %.

8.6.5.3 Crush resistance with parallel plates

Determine the load required to cause clinically relevant buckling or a deflection equivalent to a diameter reduction (lumen reduction) of at least 50 % and the load required to permanently deform or fully collapse the stent. This test is required for stents that can experience direct compression in a clinical setting.

8.6.5.4 Flex/Kink

Determine the minimum radius of curvature that the stent can accommodate without kinking or exhibiting a diameter reduction (lumen reduction) of greater than 50 % and if the stent recovers its original geometry after testing.

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