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AMENDMENT 1
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Cardiovascular implants — Endovascular devices —

Part 1: Endovascular prostheses

AMENDMENT 1: Test methods

Implants cardiovasculaires — Dispositifs endovasculaires —

Partie 1: Prothèses endovasculaires

AMENDEMENT 1: Méthodes d'essai

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Contents

Page

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.

Amendment 1 to International Standard ISO 25539-1:2003 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This Amendment adds Annexes D and E to the document. These annexes are for information only.

Cardiovascular implants — Endovascular devices —

Part 1: Endovascular prostheses

AMENDMENT 1: Test methods

Page 42

Add the following annex before the Bibliography.

Annex D
(informative)

Test methods

D.1 General

The information included in this annex is intended to provide guidance for pre-clinical *in vitro* testing performed in order to verify the design of the endovascular system, and to provide guidance for reporting. It is recognized that testing intended to ensure that the device meets the specifications of this part of ISO 25539, during manufacture may not be conducted in accordance with the details outlined in this annex.

The intent of this annex is to identify the purpose of and important parameters for the testing described in this International Standard. To ensure consistency in the testing of devices, use of this annex is recommended in developing the methodology for the testing required by this International Standard. If the methods developed are not consistent with the guidance provided in this annex, the differences should be justified.

In some cases in this annex, one or more of the methods for the tests identified in the body of this International Standard have been combined into a single method. It was recognized during the drafting of these test methods that they should be combined to reflect the manner in which this testing is often conducted. It is also recognized that additional methods may be combined when testing is conducted for a specific device. For those tests performed simultaneously, the report should provide the individual test results for each of the tests listed in the body of this International Standard.

A test method for stent-free surface area has not been included in this annex. It was recognized during the drafting of the test methods that measurement of this parameter is generally not applicable for endovascular prostheses.

The methods included in this annex are grouped as follows:

— D.5.1 Endovascular system testing: dimensions (D.5.1.1 and D.5.1.2); simulated use (D.5.1.3 to D.5.1.5); strength (D.5.1.6);

— D.5.2 Delivery system testing: balloon inflation and deflation time; strength (D.5.2.2 to D.5.2.7);

— D.5.3 Implant (endovascular prosthesis): dimensions (D.5.3.1 to D.5.3.4); permeability (D.5.3.5 to D.5.3.7); strength (D.5.3.8 to D.5.3.17); stability (D.5.3.18 to D.5.3.20).

D.2 Sampling

A sampling plan should be utilized which will ensure that adequate representation of the data has been obtained for each parameter measured. The design characteristics of the graft material, stent/attachment system, endovascular prosthesis, delivery system and endovascular system must be verified to be representative of the devices to be released for distribution, including all sizes, configurations and components.

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

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

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

Additional recommendations regarding sampling are included with each test method as appropriate.

D.3 Conditioning of test samples

All samples should be subjected to sterilisation, 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, which may affect the test results. Conditioning may include loading the endovascular prosthesis on or inside the delivery catheter, preconditioning of the endovascular system as recommended in the instructions for use (IFU) and deployment of the prosthesis.

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

D.4 Reporting

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

The test report for the pre-clinical *in vitro* testing should 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 may be in tabular form. Consideration should 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 should 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 ISO 25539-1;

b) materials: list all materials (e.g. test articles, 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 should 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.

D.5 Test methods

NOTE 1 The tolerances and accuracy levels dictated throughout the following methods are stated as nominal acceptable levels. Depending upon design specification levels, equipment with tighter tolerances or higher levels of accuracy may be needed.

NOTE 2 As used within the context of this annex, “shall” indicates requirements strictly to be followed in order to conform to the recommended test method.

D.5.1 Endovascular system

D.5.1.1 Dimensional verification and component dimension compatibility

D.5.1.1.1 Purpose

The purpose of this test is to determine the endovascular system dimensions including, but not limited to, the outer diameter, guidewire lumen diameter and useable length, for verification to design specifications, and to evaluate the dimensional compatibility between the endovascular system and the recommended accessory devices listed in the product instructions for use (IFU). The relevant design evaluation sections of ISO 25539-1 include 7.2.1 Ability to access, 7.2.2 Ability to deploy and 7.2.3 Ability to withdraw.

D.5.1.1.2 Materials

D.5.1.1.2.1 Endovascular system

D.5.1.1.2.2 Accessory devices, necessary to accomplish deployment in accordance with the IFU.

D.5.1.1.2.3 Measuring equipment for diameters, (e.g. micrometer, optical profile projector, laser-micrometer) capable of measuring to an accuracy of ± 0,1 mm or appropriate profile hole gauges manufactured to a tolerance of ± 0,1 mm.

D.5.1.1.2.4 Measuring equipment for length, capable of measuring to an accuracy of ± 1 mm.

D.5.1.1.2.5 Wire mandrels/pin gauges, (for the delivery system inner lumen), manufactured to a tolerance of ± 0,03 mm.

D.5.1.1.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.1.1.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.1.5 Test method

Develop a test method based on the following:

a) Insert an appropriate guidewire or appropriately sized mandrel into the endovascular system lumen to verify the lumen dimension and guidewire compatibility;

b) measure the maximum outer diameter of the endovascular system using the appropriate measuring instrument or verify that the outer diameter fits through the appropriately sized profile hole gauge – it is only necessary to measure the region of the endovascular system intended to be passed through the specified introducer sheath;

c) measure the length of the endovascular system using an appropriate measuring instrument – it is only necessary to measure the region of the endovascular system intended to be passed through the introducer sheath;

d) measure all other appropriate dimensions;

e) verify compatibility with all types of recommended accessory components.

D.5.1.1.6 Expression of results

Length shall be expressed in centimetres (cm). Other dimensions shall be expressed in millimetres (mm). Results regarding the compatibility of the recommended accessory devices and the verification of the lumen and outer diameters, if applicable, shall be documented.

D.5.1.1.7 Test report

The test report shall be in accordance with Clause D.4. The test report shall include the maximum, minimum, mean and standard deviation of all measured dimensions, the results of any verified dimensions, and the results of the observations of the accessory compatibility.

NOTE Additional guidance may be found in ASTM F2081-01[28].

D.5.1.2 Profile/diameter test

D.5.1.2.1 Purpose

The purpose of this test is to determine the maximum diameter along sections of the endovascular system in order to evaluate the dimensional compatibility between the endovascular system and the vasculature, including the lesion to be treated. The relevant design evaluation section of ISO 25539-1 includes 7.2.1 Ability to access.

D.5.1.2.2 Materials

D.5.1.2.2.1 Endovascular system

D.5.1.2.2.2 Measuring equipment for diameters, (e.g. micrometer, optical profile projector, laser-micrometer), capable of measuring to an accuracy of ± 0,1 mm.

D.5.1.2.2.3 Recommended guidewire, or equivalent, as appropriate.

D.5.1.2.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.1.2.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.2.5 Test method

Develop a test method based on the following:

a) if applicable, insert an appropriate guidewire into the endovascular system such that it extends past the end of the endovascular system;

b) measure the maximum outer diameter of the endovascular system; consideration should be given to the potential for asymmetry, it is necessary to measure the region that is intended to pass through a vessel and/or vessel lesion, and the region that contains the implant.

D.5.1.2.6 Expression of results

Diameters measured shall be expressed in millimetres (mm).

D.5.1.2.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the maximum, minimum, mean and standard deviation of the measured outer diameter of the endovascular system and the diameter of the region containing the implant for each size tested.

NOTE Additional guidance may be found in ASTM F2081-01[28].

D.5.1.3 Assessment of haemostasis

D.5.1.3.1 Purpose

The purpose of this test is to evaluate the ability of any seal or valves in the system to maintain an adequate haemostatic seal. The relevant design evaluation section of ISO 25539-1 includes 7.2.5 Haemostasis.

D.5.1.3.2 Materials

D.5.1.3.2.1 Endovascular system

D.5.1.3.2.2 Accessory devices, necessary to accomplish deployment in accordance with the instructions for use (IFU).

D.5.1.3.2.3 Model (or fixture), representative of “worst-case” conditions for leakage (e.g. introduction, tortuosity, withdrawal). This may require the use of an appropriate anatomical model as described in D.5.1.4 Simulated use models.

D.5.1.3.2.4 Pressurized fluid fixture, capable of delivering water or appropriate fluid, at physiological temperature (37 ± 2) °C and appropriate pressure (e.g. 100 mm Hg).

D.5.1.3.2.5 A means for collecting and measuring the total fluid leakage from the endovascular system, to an accuracy of ± 5 % of the total leakage.

D.5.1.3.2.6 Timer, with an accuracy of ± 1 s.

D.5.1.3.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.1.3.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.3.5 Test method

Develop a test method based on the following:

a) connect the model to the fluid fixture;

b) place the reservoir(s) where it (they) collect(s) the fluid leakage;

c) insert the appropriate accessory devices (e.g. guidewire, introducer sheath) in the fixture and start timing;

d) using the IFU, follow the steps of deployment, including any modular components; insert, deliver and deploy the implant in the fixture or model;

e) the pressurized fluid exposure shall be representative of anticipated clinical conditions, simulating blood loss during introduction, deployment and withdrawal in the clinical setting;

f) withdraw the delivery system and stop timing;

g) measure and record the amount of fluid leakage and the elapsed time in which leakage occurred; leakage between the model and the introducer sheath need not be included.

D.5.1.3.6 Expression of results

Record all critical observations. The leakage rate shall be expressed in milliliters per minute (ml/min).

D.5.1.3.7 Test report

The test report shall be in accordance with Clause D.4 and include the maximum, minimum, mean and standard deviation of the leakage rate. The test fluid shall be identified, and should include the density and/or viscosity. Typical pressurized time in the clinical setting should be considered when interpreting results. Report any critical observations.

D.5.1.4 Simulated use models

D.5.1.4.1 Purpose

The purpose of this test is to evaluate the performance of the endovascular system using a model(s) that simulate(s) the intended use conditions. This test addresses the requirements for qualitative evaluation of simulated use, flex/kink, pushability, torquability and trackability of the endovascular system. Conformability of the deployed prosthesis to the vessel wall shall also be evaluated. The relevant design evaluation sections of ISO 25539-1 include 7.2.1 Ability to access, 7.2.2 Ability to deploy, 7.2.3 Ability to withdraw, 7.3.1 Ability to accurately deploy and 7.3.2 Fixation effectiveness.

D.5.1.4.2 Materials

D.5.1.4.2.1 Endovascular system

D.5.1.4.2.2 Accessory devices, necessary to accomplish deployment in accordance with the instructions for use (IFU).

D.5.1.4.2.3 Anatomical model, that includes a delivery pathway and a deployment location. The angulation and tortuosity of the intended implant location and delivery pathway should be considered in the design of the model.

D.5.1.4.2.4 Pressurized fluid fixture, capable of delivering water or appropriate fluid, at physiological temperature (37 ± 2) °C, pulsatile pressures, and antegrade or retrograde flow, as appropriate.

D.5.1.4.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.1.4.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.4.5 Test method

Develop a test method based on the following:

a) connect the anatomical model to the fluid fixture and allow the test system to stabilize at temperature and pressure;

b) insert the appropriate accessory devices (e.g. guidewire, introducer sheath) in the fixture;

c) using the IFU, follow the steps of deployment, including any modular components; insert, deliver and deploy the implant in the model and withdraw the delivery system;

d) evaluate the ease of advancing the delivery system into the model (pushability), the ability to transmit torque from the proximal end to the distal end of the catheter (torquability) and the ability of the delivery system to track over a guidewire during insertion around bends in the model (trackability);

e) note any anomalies, such as kinking or buckling of the system, the inability to fully and accurately deploy the implant, implant dislodgment while withdrawing the delivery system and any other appropriate observations;

f) visually inspect the deployed endovascular prosthesis in the anatomical model; note the conformance to the model vessel wall, the placement accuracy, kinks, bends, twisting, component separation, any damage and any other critical observations;

g) inspect the delivery system, note any damage and any other critical observations.

D.5.1.4.6 Expression of results

For each test, all critical observations and aspects of the ability to access, deploy, and withdraw the endovascular system should be documented.

D.5.1.4.7 Test report

The test report shall be in accordance with Clause D.4 and shall include all critical observations and aspects of the ability to access, deploy and withdraw the endovascular system. The test fluid shall be identified and

should include the density and/or viscosity. The results for flex/kink, pushability, torquability and trackability of the endovascular system should be individually documented as well as the conformity to the vessel wall of the implant. The report shall include a description of the anatomical model used, including the geometry and material of construction.

D.5.1.5 Visibility

D.5.1.5.1 Purpose

The purpose of this test is to evaluate the ability to visualize the endovascular system and/or endovascular prosthesis using the imaging techniques specified in the instructions for use (IFU). The relevant design evaluation sections of ISO 25539-1 include 7.2.1 Ability to access, 7.2.2 Ability to deploy, 7.2.3 Ability to withdraw and 7.3.1 Ability to accurately deploy.

D.5.1.5.2 Materials

D.5.1.5.2.1 Endovascular system

D.5.1.5.2.2 Radiological phantom tissue model, or equivalent, with appropriate accessories, such as radiopaque markers and a ruler.

D.5.1.5.2.3 X-ray/fluoroscopy machine, capable of operating at clinically relevant power levels.

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

D.5.1.5.2.4 Accessory devices, necessary to accomplish deployment in accordance with the IFU.

D.5.1.5.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.1.5.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.5.5 Test method

Develop a test method based on the following:

a) position the endovascular system and the phantom tissue model to simulate clinical conditions;

b) use the X-ray/fluoroscope to visualize the endovascular system and any radiopaque markers;

c) qualitatively examine the X-ray/fluoroscopic images for ease of visibility; e.g. the degree of visibility may be assessed by locating the exact ends, orientation of critical points and/or parts of the endovascular system, alternatively, the degree of visibility may be compared to a specified control device;

d) repeat a) to c) above for the prosthesis during deployment and after withdrawal of the delivery system.

D.5.1.5.6 Expression of results

This is a qualitative assessment. Record the degree of visibility for all applicable components at the various stages of testing and any comparison to a specified control.

D.5.1.5.7 Test report

The test report shall be in accordance with Clause D.4 and shall include the assessment of visibility and visual results (e.g. representative fluoroscopic images). The test report shall also include a model of the imaging equipment, the parameter settings and details of the phantom tissue model.

D.5.1.6 Force to deploy

D.5.1.6.1 Purpose

The purpose of this test is to determine the force to deploy the endovascular prostheses. All applicable steps of the deployment process are evaluated. The relevant design evaluation section of ISO 25539-1 includes 7.2.2 Ability to deploy.

D.5.1.6.2 Materials

D.5.1.6.2.1 Endovascular system

D.5.1.6.2.2 Accessory devices, necessary to accomplish deployment in accordance with the instructions for use (IFU).

D.5.1.6.2.3 Anatomical model, that includes a delivery pathway and a deployment location. The angulation and tortuosity of the intended implant location and delivery pathway should be considered in the design of the model.

D.5.1.6.2.4 Force measuring mechanism (e.g. force gauge, universal mechanical testing system), capable of measuring force to an accuracy of ± 5 % of the reported value.

D.5.1.6.2.5 Gripping fixture

D.5.1.6.2.6 Temperature controlled environment, (37 ± 2) °C.

D.5.1.6.3 Sampling

Sampling shall be in accordance with Clause D.2. Devices to be tested should represent worst-case deployment force conditions (e.g. greatest bulk within the sheath or cover, highest compression ratio). The effect of device diameter and length should be taken into consideration in the selection of devices for testing.

D.5.1.6.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.1.6.5 Test Method

Develop a test method based on the following:

a) prepare the endovascular system in accordance with the IFU;

b) insert the endovascular system into the anatomical model;

c) secure the endovascular system such that it remains stationary during testing;

d) attach the deployment mechanism to the load measuring equipment;

e) allow the device to stabilize at physiological temperatures;

f) initiate and complete the deployment in accordance with the IFU at a rate that simulates clinical use while measuring the force to deploy the implant;

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

D.5.1.6.6 Expression of results

The maximum force of each step required to deploy the implant is recorded in newtons (N). Also record any anomalous observations (e.g. buckling) for each test sample.

D.5.1.6.7 Test report

Test report shall be in accordance with Clause D.4 and shall include the maximum, minimum, mean and standard deviation of the deployment forces and any anomalous observations.

D.5.2 Delivery system

D.5.2.1 Balloon inflation and deflation time (balloon expandable or balloon assisted)

D.5.2.1.1 Purpose

The purpose of this test is to determine the time required to inflate the balloon to the maximum recommended inflation pressure, volume or diameter and to measure the time required to deflate the balloon. This test provides information that may be clinically useful for treatment planning (e.g. potential occlusion time). The relevant design evaluation section of ISO 25539-1 includes 7.2.2 Ability to deploy.

NOTE This test may also be of importance in evaluating the ability to withdraw.

D.5.2.1.2 Materials

D.5.2.1.2.1 Delivery system, or appropriate balloon sub-assembly.

D.5.2.1.2.2 Recommended guidewire, or equivalent.

D.5.2.1.2.3 Temperature controlled water bath, (37 ± 2) °C.

D.5.2.1.2.4 Contrast medium, in accordance with the instructions for use (IFU).

D.5.2.1.2.5 Inflation device, syringe or equivalent, fitted with a means of measuring pressure or volume to an accuracy of ± 5 % of the reported value, and of maintaining the inflation pressure or volume.

D.5.2.1.2.6 Rigid tube, of a diameter that represents the largest recommended prosthesis or vessel diameter for the compliant balloon under test. No tube is necessary for non-compliant balloon testing.

D.5.2.1.2.7 Timer, with an accuracy of ± 0,2 s.

D.5.2.1.3 Sampling

Sampling shall be in accordance with Clause D.2.

D.5.2.1.4 Conditioning

Conditioning shall be in accordance with Clause D.3.

D.5.2.1.5 Test method

Develop a test method based on the following:

a) insert the appropriate guidewire in the device;

b) submerge the device in the water bath and insert into the rigid tube, if appropriate;

c) allow it to reach the equilibrium test temperature;

d) inflate the balloon in accordance with the IFU, simulating clinical use;

e) time the balloon inflation period to the maximum inflation pressure, volume or diameter as indicated in the IFU;

f) deflate the balloon in accordance with the IFU and time the balloon deflation period.

D.5.2.1.6 Expression of results

The inflation and deflation times should be expressed in seconds.

D.5.2.1.7 Test report

The test report shall be in accordance with Clause D.4 and include the maximum, minimum, mean and standard deviation of the balloon inflation and deflation times. The definition of the inflation and deflation endpoints shall also be reported.

D.5.2.2 Balloon rated burst pressure (RBP) for non-compliant balloons (balloon expandable or balloon assisted)

D.5.2.2.1 Purpose

The purpose of this test is to determine the rated burst pressure (RBP) of the balloon. This is accomplished using burst pressures as measured by the test method and calculating an appropriate safety margin using the mean and standard deviation. The relevant design evaluation section of ISO 25539-1 includes 7.2.2 Ability to deploy.

NOTE This test may also be of importance in evaluating the ability to withdraw.

D.5.2.2.2 Materials

D.5.2.2.2.1 Delivery system, or appropriate balloon sub-assembly.

D.5.2.2.2.2 Temperature controlled water bath, (37 ± 2) °C.

D.5.2.2.2.3 Fluid for inflation, (e.g. room temperature water).

D.5.2.2.2.4 Leak detection mechanism, (e.g. dye in the test fluid, pressure drop monitor, flow rate monitor).

D.5.2.2.2.5 Inflation device, syringe or equivalent, fitted with a means of measuring pressure to an accuracy of ± 5 % of the reported value, and capable of maintaining the inflation pressure.

D.5.2.2.2.6 Timer, with an accuracy of ± 1 s.