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American National Standard

ANSI/AAMI/ISO 25539-1:2003

# Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses

AAMI Association for the Advancement of Medical Instrumentation

# The Objectives and Uses of AAMI Standards and Recommended Practices

It is most important that the objectives and potential uses of an AAMI product standard or recommended practice are clearly understood. The objectives of AAMI's technical development program derive from AAMI's overall mission: the advancement of medical instrumentation. Essential to such advancement are (1) a continued increase in the safe and effective application of current technologies to patient care, and (2) the encouragement of new technologies. It is AAMI's view that standards and recommended practices can contribute significantly to the advancement of medical instrumentation, provided that they are drafted with attention to these objectives and provided that arbitrary and restrictive uses are avoided.

A voluntary *standard* for a *medical device* recommends to the manufacturer the information that should be provided with or on the product, basic safety and performance criteria that should be considered in qualifying the device for clinical use, and the measurement techniques that can be used to determine whether the device conforms with the safety and performance criteria and/or to compare the performance characteristics of different products. Some standards emphasize the information that should be provided with the device, including performance characteristics, instructions for use, warnings and precautions, and other data considered important in ensuring the safe and effective use of the device in the clinical environment. Recommending the disclosure of performance characteristics often necessitates the development of specialized test methods to facilitate uniformity in reporting; reaching consensus on these tests can represent a considerable part of committee work. When a drafting committee determines that clinical concerns warrant the establishment of *minimum* safety and performance criteria, referee tests must be provided and the reasons for establishing the criteria must be documented in the rationale.

A *recommended practice* provides guidelines for the use, care, and/or processing of a medical device or system. A recommended practice does not address device performance *per se*, but rather procedures and practices that will help ensure that a device is used safely and effectively and that its performance will be maintained.

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a fume of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards health care professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decisionmaking.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

## INTERPRETATIONS OF AAMI STANDARDS AND RECOMMENDED PRACTICES

Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the Manager for Technical Development. An official interpretation must be approved by letter ballot of the originating committee and subsequently reviewed and approved by the AAMI Standards Board. The interpretation will become official and representation of the Association only upon exhaustion of any appeals and upon publication of notice of interpretation in the "Standards Monitor" section of the *AAMI News*. The Association for the Advancement of Medical Instrumentation disclaims responsibility for any characterization or explanation of a standard or recommended practice which has not been developed and communicated in accordance with this procedure and which is not published, by appropriate notice, as an *official interpretation* in the *AAMI News*.

American National Standard ANSI/AAMI/ISO 25539-1:2003

# Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses

Approved 27 January 2003 by
**Association for the Advancement of Medical Instrumentation**

Approved 21 February 2003 by
**American National Standards Institute, Inc.**

**Abstract:** Specifies requirements for endovascular prostheses, including requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization packaging, and information to be supplied by the manufacturer.

**Keywords:** attachment system, delivery system, design, performance

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## AAMI Standard

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## Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard.

NOTE—Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

| International designation | U.S. designation | Equivalency |
|---|---|---|
| IEC 60601-1-2:2001 | ANSI/AAMI/IEC 60601-1-2:2001 | Identical |
| IEC 60601-2-21:1994 and Amendment 1:1996 | ANSI/AAMI/IEC 60601-2-21 and Amendment 1:2000 (consolidated texts) | Identical |
| IEC 60601-2-24:1998 | ANSI/AAMI ID26:1998 | Major technical variations |
| ISO 5840:1996 | ANSI/AAMI/ISO 5840:1996 | Identical |
| ISO 7198:1998 | ANSI/AAMI/ISO 7198:1998/2001 | Identical |
| ISO 7199:1996 | ANSI/AAMI/ISO 7199:1996/(R)2002 | Identical |
| ISO 10993-1:1997 | ANSI/AAMI/ISO 10993-1:1997 | Identical |
| ISO 10993-2:1992 | ANSI/AAMI/ISO 10993-2:1993/(R)2001 | Identical |
| ISO 10993-3:1992 | ANSI/AAMI/ISO 10993-3:1993 | Identical |
| ISO 10993-4:2002 | ANSI/AAMI/ISO 10993-4:2002 | Identical |
| ISO 10993-5:1999 | ANSI/AAMI/ISO 10993-5:1999 | Identical |
| ISO 10993-6:1994 | ANSI/AAMI/ISO 10993-6:1995/(R)2001 | Identical |
| ISO 10993-7:1995 | ANSI/AAMI/ISO 10993-7:1995/(R)2001 | Identical |
| ISO 10993-8:2000 | ANSI/AAMI/ISO 10993-8:2000 | Identical |
| ISO 10993-9:1999 | ANSI/AAMI/ISO 10993-9:1999 | Identical |
| ISO 10993-10:2002 | ANSI/AAMI BE78:2002 | Minor technical variations |
| ISO 10993-11:1993 | ANSI/AAMI 10993-11:1993 | Minor technical variations |
| ISO 10993-12:2002 | ANSI/AAMI/ISO 10993-12:2002 | Identical |
| ISO 10993-13:1998 | ANSI/AAMI/ISO 10993-13:1999 | Identical |
| ISO 10993-14:2001 | ANSI/AAMI/ISO 10993-14:2001 | Identical |
| ISO 10993-15:2000 | ANSI/AAMI/ISO 10993-15:2000 | Identical |
| ISO 10993-16:1997 | ANSI/AAMI/ISO 10993-16:1997/(R)2003 | Identical |
| ISO 10993-17:2002 | ANSI/AAMI/ISO 10993-17:2002 | Identical |
| ISO 11134:1994 | ANSI/AAMI/ISO 11134:1993 | Identical |
| ISO 11135:1994 | ANSI/AAMI/ISO 11135:1994 | Identical |
| ISO 11137:1995 and Amendment 1:2001 | ANSI/AAMI/ISO 11137:1994 and A1:2002 | Identical |
| ISO 11138-1:1994 | ANSI/AAMI ST59:1999 | Major technical variations |
| ISO 11138-2:1994 | ANSI/AAMI ST21:1999 | Major technical variations |
| ISO 11138-3:1995 | ANSI/AAMI ST19:1999 | Major technical variations |

| International designation | U.S. designation | Equivalency |
|---|---|---|
| ISO TS 11139:2001 | ANSI/AAMI/ISO 11139:2002 | Identical |
| ISO 11140-1:1995 and Technical Corrigendum 1:1998 | ANSI/AAMI ST60:1996 | Major technical variations |
| ISO 11607:2003 | ANSI/AAMI/ISO 11607:2000 | Identical |
| ISO 11737-1:1995 | ANSI/AAMI/ISO 11737-1:1995 | Identical |
| ISO 11737-2:1998 | ANSI/AAMI/ISO 11737-2:1998 | Identical |
| ISO TR 13409:1996 | AAMI/ISO TIR 13409:1996 | Identical |
| ISO 13485:1996 | ANSI/AAMI/ISO 13485:1996 | Identical |
| ISO 13488:1996 | ANSI/AAMI/ISO 13488:1996 | Identical |
| ISO 14155-1:2003 | ANSI/AAMI/ISO 14155-1:2003 | Identical |
| ISO 14155-2:2003 | ANSI/AAMI/ISO 14155-2:2003 | Identical |
| ISO 14160:1998 | ANSI/AAMI/ISO 14160:1998 | Identical |
| ISO 14161:2000 | ANSI/AAMI/ISO 14161:2000 | Identical |
| ISO 14937:2000 | ANSI/AAMI/ISO 14937:2000 | Identical |
| ISO 14969:1999 | ANSI/AAMI/ISO 14969:1999 | Identical |
| ISO 14971:2000 | ANSI/AAMI/ISO 14971:2000 | Identical |
| ISO 15223:2000 | ANSI/AAMI/ISO 15223:2000 | Identical |
| ISO 15223/A1:2002 | ANSI/AAMI/ISO 15223:2000/A1:2001 | Identical |
| ISO 15225:2000 | ANSI/AAMI/ISO 15225:2000 | Identical |
| ISO 15674:2001 | ANSI/AAMI/ISO 15674:2001 | Identical |
| ISO 15675:2001 | ANSI/AAMI/ISO 15675:2001 | Identical |
| ISO 25539-1:2003 | ANSI/AAMI/ISO 25539-1:2003 | Identical |
| ISO TS 15843:2000 | ANSI/AAMI/ISO TIR15843:2000 | Identical |
| ISO TR 15844:1998 | AAMI/ISO TIR15844:1998 | Identical |
| ISO TR 16142:1999 | ANSI/AAMI/ISO TIR16142:2000 | Identical |

 

## Committee representation

**Association for the Advancement of Medical Instrumentation**

**Vascular Prostheses Committee**

The adoption of ISO 25539-1:2003 as an American National Standard was initiated by the AAMI Vascular Prostheses Committee, which also functions as the U.S. Technical Advisory Group to the relevant work in the International Organization for Sterilization (ISO). The AAMI Vascular Prostheses Committee functions under the auspices of the U.S. Technical Advisory Group (TAG) for ISO/TC 150/SC 2, Cardiovascular implants. U.S. representatives from the AAMI Vascular Prostheses Committee (U.S. Sub-TAG for ISO/TC 150/SC 2/WG 3) played an active part in developing the ISO standard.

At the time this document was published, the **AAMI Vascular Prostheses Committee Committee (U.S. Sub-TAG for ISO/TC 150/SC 2/WG 3)** had the following members:

| | |
|---|---|
| *Cochairs:* | Dorothy Abel |
| | Louis J. Smith |
| *Members:* | Dorothy Abel, U.S. Food and Drug Administration/Center for Devices and Radiological Health |
| | Scott E. Anderson, PE, EnduraTEC Systems Corporation |
| | Richard W. Bianco, University of Minnesota |
| | James C. Conti, PhD, Dynatek Dalta Scientific Instruments |
| | Frank J. Criado, MD, Union Memorial/Center for Vascular Intervention |
| | Mark Dehdashtian, Edwards LifeSciences |
| | Kristen Honl, Guidant Corporation |
| | Martin W. King, PhD, Hospital Saint Francoise D'Assise/Quebec Biomaterials Institute |
| | James Machek, Medtronic Inc. |
| | Scott Rush, Johnson & Johnson |
| | Louis J. Smith, WL Gore & Associates Inc. |
| | Ann C. Tunstall, PhD, Salamandra LLC |
| | Frank J. Veith, MD, Montefiore Medical Center |
| | Cynthia A. Walcott, RN, CR Bard |
| | Matthew S. Waninger, PhD, Med Institute Inc. |
| | Steven L. Weinberg, PhD, Biomedical Consultants & Labs |
| | Robert G. Whirley, TriVascular Inc. |
| | Rodney A. White, MD, Harbor–UCLA Medical Center |
| | Christopher K. Zarins, MD, Stanford University Hospital |
| *Alternates:* | Heather Bartholf, Johnson & Johnson |
| | Brian Hudson, CR Bard |
| | Michael F. Wolf, Medtronic Inc. |

NOTE—Participation by federal agency representatives in the development of this standard does not constitute endorsement by the federal government or any of its agencies.

## Background of ANSI/AAMI adoption of ISO 25539-1:2003

As indicated in the foreword to the main body of this document (page ix), the International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard.

International Standard ISO 25539-1 was developed by Working Group (WG) 3, *Vascular prostheses* of ISO Technical Committee (TC) 150, Subcommittee (SC) 2, Cardiovascular implants, to fill a need for basic requirements for endovascular prostheses and the methods of test which will enable evaluation of these devices to the standard.

U.S. participation in this ISO SC is organized through the U.S. Technical Advisory Group (TAG) for ISO/TC 150/SC 2, administered by the Association for the Advancement of Medical Instrumentation (AAMI) on behalf of the American National Standards Institute. The U.S. made a considerable contribution to this International Standard.

Upon review of ISO 25539-1, the AAMI Vascular Prostheses Committee decided to adopt ISO 25539-1 verbatim.

AAMI serves as the Secretariat for ISO/TC 150/SC 2 and the AAMI Vascular Prostheses Committee serves as the U.S. Sub-TAG for ISO/TC 150/SC 2/WG 3. Members of the U.S. Sub-TAG participated in the development of this International Standard. The goal of the U.S. adoption of this International Standard was to harmonize U.S. requirements with International ones where possible.

AAMI and ANSI procedures require that standards be reviewed and, if necessary, revised every five years to reflect technological advances that may have occurred since publication.

AAMI (and ANSI) have adopted other ISO standards. See the Glossary of Equivalent Standards for a list of ISO standards adopted by AAMI which gives the corresponding U.S. designation and the level of equivalency with the ISO standard.

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data come to light.

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

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NOTE—Beginning with the ISO foreword on page ix, this American National Standard is identical to ISO 25539-1, *Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses*.

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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 25539-1 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants*.

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

— *Part 1: Endovascular prostheses*

— *Part 2: Vascular stents*

— *Part 3: Vena cava filters*

## Introduction

This part of ISO 25539 has been prepared in order to provide minimum requirements for endovascular prostheses and the methods of test that will enable their evaluation. It is the first part of a proposed three-part International Standard. ISO/TS 15539, from which this part of ISO 25539 is derived, serves as a rationale for the requirements. The technical specification was developed by first identifying the design requirements for endovascular implants and listing the potential implant 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.

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, acceptable standardized *in vitro* tests and clinical results are not always available. As further scientific and clinical data becomes available, appropriate revision of this part of ISO 25539 will be undertaken.

 

**American National Standard** **ANSI/AAMI/ISO 25539-1:2003**

# Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses

## 1 Scope

**1.1** This part of ISO 25539 specifies requirements for endovascular prostheses, 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.

**1.2** This part of ISO 25539 is applicable to endovascular prostheses used to treat arterial aneurysms, arterial stenoses, or other appropriate vascular abnormalities.

**1.3** This part of ISO 25539 is applicable to delivery systems if they comprise an integral component of the deployment of the endovascular prostheses.

**1.4** This part of ISO 25539 is not applicable to vascular occluders, with the exception of contra-lateral iliac occluders when used as an integral part of an aorto-uni-iliac device. See ISO 14630 for excluded products.

**1.5** This part of ISO 25539 is not applicable to procedures and devices used prior to the introduction of the endovascular system (defined in 3.6), such as balloon angioplasty devices.

## 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 7198:1998, *Cardiovascular implants—Tubular vascular prostheses*.

ISO 11134:1994, *Sterilization of health care products—Requirements for validation and routine control—Industrial moist heat sterilization*.

ISO 11135:1994, *Medical devices—Validation and routine control of ethylene oxide sterilization*.

ISO 11137:1995, *Sterilization of health care products—Requirements for validation and routine control—Radiation sterilization*.

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

ISO 11607:1997, *Packaging for terminally sterilized medical devices*.

ISO 13485, *Medical devices—Quality management systems—Requirements for regulatory purposes*.

ISO 13488:1996, *Quality systems—Medical devices—Particular requirements for the application of ISO 9002*.

ISO 14155 (all 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 14630:1997, *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 14971:2000, *Medical devices—Application of risk management to medical devices*.

 

## 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.

**3.1 attachment system:** System integral to the endovascular prosthesis that is designed to interface directly with vessel wall in order to prevent migration.

NOTE—The system may also prevent blood flow on the outside of the prostheses at the attachment sites.

**3.2 delivery system:** System or mechanism used to deliver the endovascular prosthesis to the targeted position.

NOTE—The delivery system is removed after implant placement.

**3.3 determine:** Quantitatively appraise or analyze.

**3.4 endoleak:** Persistence of blood flow outside the lumen of an endovascular prosthesis but within an aneurysm sac or adjacent vascular segment being treated by the graft.

NOTE—Endoleaks are catagorized as follows:

— a Type I endoleak is periprosthetic and occurs at the proximal or distal attachment zone;

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

— a Type III endoleak arises from a defect in the graft material or from an inadequate seal between modular graft components;

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

**3.5 endovascular prosthesis, endovascular graft, endovascular implant:** Transluminally placed vascular prosthesis, residing partially or completely within a vascular conduit to form an internal bypass or shunt between sections of the vascular system.

**3.6 endovascular system**: System used to treat a vascular lesion from within the vessel, typically comprised of an endovascular prosthesis and its delivery system.

NOTE 1—An abdominal aortic aneurysm is an example of a vascular lesion which can be treated with an endovascular system.

NOTE 2—For the purposes of this part of ISO 25539, the delivery system as well as the implant are included within this definition.

**3.7 evaluate:** Qualitatively appraise or analyze.

**3.8 graft material:** Non-metallic component of the endovascular prosthesis.

**3.9 reportable clinical events:** Complications or failures that may be observed with clinical use of the endovascular system.

## 4 Intended performance

The requirements of Clause 4 of ISO 14630:1997 shall apply.

## 5 Design attributes

### 5.1 General

The requirements of Clause 5 of ISO 14630:1997 shall apply. In addition, the following shall be taken into account:

a) with regard to oxidation potential: the possibility of crevice corrosion passivation level over the relevant parts;

b) with regard to wear: fretting corrosion;

c) with regard to interface between implant and body:

   1) fixation hooks if present;

   2) relative movement between implant and tissue;

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

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

 

d) expected ingrowth, penetration, perforation, tilting, and migration;

e) introduction and delivery systems.

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

### 5.2 Delivery 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 implant;

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;

e) the ability of the system to minimize blood loss (hemostasis);

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

### 5.3 Implant

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

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

b) the ability of the implant to ensure effective fixation within the vasculature;

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

d) the ability of the implant to prevent blood from flowing through the implant wall as appropriate to its intended use;

Changes in wall permeability after implantation shall be taken into account.

e) the appropriate interaction between and among the modules of endovascular systems designed with modular components (modularity);

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

g) the ability of the implant to maintain adequate blood flow through the lumen (patency);

h) the compatibility of the implant with exposure to magnetic resonance imaging (MRI) fields;

i) the compliance of the implant with the requirements of ISO 10993-1 and appropriate other parts of the ISO 10993 series;

j) the visibility of the implant under fluoroscopy or other technologies.

## 6 Materials

The requirements of Clause 6 of ISO 14630:1997 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.

## 7 Design evaluation

### 7.1 General

The requirements of Clause 7 of ISO 14630:1997 shall apply. A risk analysis shall be carried out in accordance with the requirements of ISO 14971.

NOTE—All testing may not be appropriate for all prosthesis designs.

Justification shall be provided for the properties not measured for characterization.

It is impossible to take into consideration all future and emerging technologies. These emerging-technology prostheses will need to follow the basic test protocols of this part of ISO 25539 to characterize the endovascular system. Testing beyond the scope of this part of ISO 25539 may also be necessary to characterize new emerging-technology prostheses. Consideration shall be given to the failure modes of the prostheses and their effects on the performance of the implant in identifying the appropriate testing. For compound prostheses, as defined in ISO 7198:1998, 3.9, although it may be appropriate to conduct some of the testing described in this part of ISO 25539 on components of the prosthesis, testing of the endovascular system as a whole is also required. In addition, if the compound prosthesis is partially constructed of a resorbable component, the non-resorbable portion of the implant shall be characterized as well as the implant as a whole.

Each segment of a composite prosthesis, as defined in ISO 7198:1998, 3.8, shall be tested. In addition, any manufactured anastomosis shall satisfy the requirements of this part of ISO 25539 relating to leakage and factory anastomotic strength.

Retesting shall be performed whenever significant changes are made in materials, construction, configuration, application, or processing methods.

A complete description of the validated test methods and sample preparation procedures used to address the requirements of this part of ISO 25539 shall be documented by the manufacturer. The method and sample size chosen shall be justified. Where acceptance criteria are not specified, the manufacturer shall evaluate the acceptability of the results against predetermined criteria.

For certain design attributes, the use of a reference device should be considered.

If it can be justified that sterilization has no effect on the characteristics of the devices that are under evaluation, the required tests may be carried out on non-sterilized devices.

### 7.2 Delivery (and/or endovascular) system

#### 7.2.1 Ability to access

##### 7.2.1.1 General

The ability of the system to permit safe, consistent, and accurate access to the intended location shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) guidewire not crossing the lesion;

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

c) delivery system not advancing to target site;

d) emboli generation;

e) implant dislodgement.

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

— access failure;

— vascular trauma;

— neurological deficit;

— ischemia;

— spinal neurological deficit;

— embolization.

Testing shall include the following items listed in 7.2.1.2 through 7.2.1.12, as appropriate to the design of the endovascular system.

##### 7.2.1.2 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, deploy, and withdraw the system.

 

#### 7.2.1.3 Component dimension compatibility

Determine the dimensions of the endovascular system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible.

#### 7.2.1.4 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.2.1.5 Flex/kink

Evaluate the ability of the endovascular system to bend in order to accommodate the minimum radius or angle to be negotiated during access and delivery.

#### 7.2.1.6 Profile

Determine the maximum diameter along defined sections of the endovascular system.

#### 7.2.1.7 Pushability

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

#### 7.2.1.8 Visibility

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

#### 7.2.1.9 Simulated use

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

#### 7.2.1.10 Torquability

Evaluate the ability of the endovascular system to provide sufficient rotation to the distal (leading) end to deliver the implant within the anatomy in accordance with the design constraints of the system.

#### 7.2.1.11 Torsional bond strength

Determine the torque required to break joints and/or materials in the appropriate delivery system components. The results shall be evaluated in relation to the force(s) necessary to access, deploy, and withdraw the system.

#### 7.2.1.12 Trackability

Evaluate the ability of the endovascular system to advance over the recommended guidewire and to follow the guidewire tip along the path of the vessel, including in narrow, tortuous vessels.

### 7.2.2 Ability to deploy

#### 7.2.2.1 General

The ability of the system to permit safe, consistent, and accurate deployment of the implant shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) inability to fully and properly deploy the prosthesis;

b) disproportionate dimensions and properties, such as balloon compliance and burst pressure, of balloon relative to endovascular system and vessel (if applicable);

c) implant dislodgement;

d) balloon failure (if applicable);

e) damage of implant components by other components;

f) inadequate visualization;

g) emboli generation.

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

— delivery system failure;

— spinal neurological deficit;

— neurological deficit;

— vascular trauma;

— ischemia;

— embolization;

— damage to implant.

Testing shall include the following items listed in 7.2.2.2 through 7.2.2.14, as appropriate to the design of the endovascular system.

#### 7.2.2.2 Bond strength

Determine the longitudinal bond strength between parts of the delivery system. All bonds shall remain intact under recommended conditions of use.

#### 7.2.2.3 Balloon inflation time

Determine the time required to expand the balloon to the maximum recommended inflation pressure.

#### 7.2.2.4 Balloon deflation time

Determine the time required to deflate the balloon and characterize the ability to remove the deflated balloon.

#### 7.2.2.5 Balloon mean burst pressure

Determine the mean burst pressure.

#### 7.2.2.6 Balloon rated burst pressure

Determine the burst pressure with an appropriate safety margin including reliability parameters.

Designate the maximum recommended inflation pressure and operating pressure(s).

#### 7.2.2.7 Balloon rated fatigue

Determine the maximum number of recommended inflation cycles to the recommended inflation pressure including reliability parameters.

Designate the maximum recommended number of inflation cycles.

#### 7.2.2.8 Component dimension compatibility

Determine the dimensions of the endovascular system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible.

#### 7.2.2.9 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.2.2.10 Force to deploy

Determine the force to deploy the implant.

#### 7.2.2.11 Visibility

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

#### 7.2.2.12 Simulated use

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

 

#### 7.2.2.13 Torsional bond strength

Determine the torque required to break joints and/or materials in the appropriate delivery system components.

#### 7.2.2.14 Tubing tensile strength

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

### 7.2.3 Ability to withdraw

#### 7.2.3.1 General

The ability of the system to permit safe and consistent withdrawal of the delivery system shall be evaluated.

Hazards to be evaluated 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) emboli generation;

e) diameter mismatch;

f) implant dislodgement;

g) damage of endovascular system components by other components;

h) delivery system snags on the implant;

i) inadequate visualization.

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

— delivery system failure;

— neurological deficit;

— vascular trauma;

— ischemia;

— spinal neurological deficit;

— embolization;

— damage to implant.

Testing shall include the following items in 7.2.3.2 through 7.2.3.9, as appropriate to the design of the endovascular system.

#### 7.2.3.2 Bond strength

Determine the longitudinal bond strength between parts of the delivery system. All bonds shall remain intact under recommended conditions of use.

#### 7.2.3.3 Component dimension compatibility

Determine the dimensions of the endovascular system for compatibility with the dimensions of recommended accessories. All components shall be dimensionally compatible.

#### 7.2.3.4 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.2.3.5 Flex/kink

Evaluate the ability of the delivery system to bend in order to accommodate the minimum radius or angle to be negotiated during withdrawal.

#### 7.2.3.6 Visibility

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

#### 7.2.3.7 Simulated use

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

#### 7.2.3.8 Torsional bond strength

Determine the torque required to break joints and/or materials in the appropriate delivery system components.

#### 7.2.3.9 Tubing tensile strength

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

### 7.2.4 Biocompatibility

Biocompatibility should be tested in accordance with ISO 10993-1 and appropriate other parts of the ISO 10993 series.

### 7.2.5 Hemostasis

#### 7.2.5.1 General

The ability of the system to minimize blood loss shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) size mismatch;

b) seal incompetence;

c) other leakage.

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

— procedural bleeding;

— hematoma.

Testing shall include the following items listed in 7.2.5.2 and 7.2.5.3, as appropriate to the design of the endovascular system.

#### 7.2.5.2 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.2.5.3 Assessment of hemostasis

Evaluate the ability of any seal or valve in the delivery system to maintain an adequate hemostatic seal.

## 7.3 Implant

### 7.3.1 Ability to accurately deploy

#### 7.3.1.1 General

The ability of the system to permit safe, consistent, and accurate deployment of the implant at the intended lesion location shall be evaluated.

Hazards to be evaluated 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 can result in reportable clinical events, including but not limited to the following:

— branch vessel occlusion;

— delivery system failure;

— attachment site leak;

— prosthesis migration;

— lumen obstruction;

— ischemia;

— aneurysm enlargement;

— aneurysm rupture;

— vascular trauma.

Testing shall include the following items listed in 7.3.1.2 through 7.3.1.4, as appropriate to the design of the endovascular system.

#### 7.3.1.2 Implant length to diameter relationship

Determine the relationship between implant length and expanded implant diameter.

#### 7.3.1.3 Visibility

Evaluate the ability to visualize the implant during deployment and after withdrawal using fluoroscopy. The use of other technologies shall be justified.

#### 7.3.1.4 Simulated use

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

### 7.3.2 Fixation effectiveness

#### 7.3.2.1 General

The ability of the system to permit effective fixation of the implant within the vasculature shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) incomplete apposition to vessel wall;

b) excessive or inadequate radial outward force.

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

— attachment site leak;

— prosthesis migration;

— lumen obstruction;

— vascular trauma;

— trauma to adjacent structures;

— branch vessel occlusion;

— aneurysm enlargement;

— aneurysm rupture.

Testing shall include the following items in 7.3.2.2 through 7.3.2.8, as appropriate to the design of the endovascular system.

#### 7.3.2.2 Conformability to vessel wall

Evaluate the ability of the implant to maintain adequate contact with the vessel wall.

#### 7.3.2.3 Crush resistance

Determine the minimum force at which permanent deformation or full collapse occurs.

#### 7.3.2.4 Local compression

Determine the elastic deformation of the implant in response to localized compressive force.

#### 7.3.2.5 Migration resistance

Determine the ability of the implant to remain stationary under simulated use.

#### 7.3.2.6 Radial outward force

The force exerted by a self-expanding implant shall be measured as a function of the implant diameter.

#### 7.3.2.7 Recoil

Determine the amount of device diameter elastic recoil (percent of device diameter reduction) after the deployment of the implant. Correlate this recoil to recommended sizing.

#### 7.3.2.8 Simulated use

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

### 7.3.3 Implant integrity

#### 7.3.3.1 General

The ability of the implant to maintain integrity shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) structural failure of implant;

b) loss of complete apposition to vessel wall;

c) leaking.

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

— stent/attachment system fracture;

— graft dilatation/rupture;

— implant thrombosis;

— prosthesis migration;

— attachment site leak;

— aneurysm enlargement;

— aneurysm rupture;

— transgraft leak;

— vascular trauma;

— lumen obstruction/stenosis;

— ischemia;

— trauma to adjacent structures.

Testing shall include the following items listed in 7.3.3.2 through 7.3.3.9, as appropriate to the design of the endovascular system.

 

#### 7.3.3.2 Burst/circumferential strength

Determine the burst strength and/or the circumferential strength of the appropriate components of the implant and of the finished product in accordance with ISO 7198:1998, 8.3.3 or 8.3.1, respectively.

#### 7.3.3.3 Corrosion

Evaluate the susceptibility of the material(s) to corrosion in an actual or simulated environment.

#### 7.3.3.4 Factory anastomotic strength

Determine the tensile strength of any manufactured anastomosis in accordance with ISO 7198:1998, 8.3.2.4.

#### 7.3.3.5 Durability

##### 7.3.3.5.1 General

The following items shall be considered in evaluating durability:

— potential failure modes, such as wear, strut fracture, weave separation, delamination, and suture breaks;

— radial and axial loads, and other *in vivo* loads.

These items shall be considered in the context of anatomic variability and morphologic changes.

##### 7.3.3.5.2 Stress/strain analysis

Evaluate the stress/strain characteristics of the implant when subjected to a worst-case physiological load using appropriate tools, such as Finite Element Analysis (FEA).

##### 7.3.3.5.3 Fatigue

Evaluate the long-term dimensional and structural integrity of the implant. This includes the integrity of all parts of the implant and their connections and contact areas among each other.

Fatigue testing of the implant shall include *in vitro* testing until 10 years equivalent cycles (at least 380 million) have been applied to each device under test. If the intended implant life is less than 10 years, shorter duration fatigue testing may be appropriate and shall be justified.

The test conditions shall be justified, and include but are not limited to the number of samples, implant sizes tested, and the frequency used in the testing.

The frequency of the test shall be set such that the deformation of the implant under test is no less than the deformation of the implant at physiologic heart rates. Fatigue testing shall be conducted using physiologic temperatures, not less than 37 °C.

#### 7.3.3.6 Longitudinal tensile strength

Determine the longitudinal tensile strength of the implant.

#### 7.3.3.7 Strength after repeated puncture (for arterial-venous shunt for vascular access)

Assess the ability of the implant to withstand repeated punctures.

#### 7.3.3.8 Strength of stent/attachment system to graft bond (e.g., adhesive, sutures)

Evaluate the strength of the connection of the graft to the stent/attachment system.

#### 7.3.3.9 Visual inspection

The prosthesis shall show no discontinuities in construction, and shall show no dirt, soiled areas, spots, stains, loose particles, or other defects that would render the prosthesis unsuitable for its intended use.

### 7.3.4 Permeability

#### 7.3.4.1 General

The ability of the implant to be impermeable to blood flow through the implant wall shall be evaluated.

Changes in permeability after implantation shall be taken into consideration.

Hazards to be evaluated include, but are not limited to, the following:

a) leaking.

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

— transgraft leak;

— aneurysm enlargement;

— aneurysm rupture.

Testing shall include the following items listed in 7.3.4.2 and 7.3.4.3, as appropriate to the design of the endovascular system.

#### 7.3.4.2 Porosity, water permeability, and water entry pressure

Evaluate the porosity, water permeability, and water entry pressure as appropriate to the implant in accordance with ISO 7198:1998, 8.2.1, 8.2.2, 8.2.4. Justification shall be provided for the property (or properties) selected to be measured.

#### 7.3.4.3 Integral water permeability/leakage

Determine the integral water permeability/leakage of the finished implant in accordance with ISO 7198:1998, 8.2.3.

### 7.3.5 Modularity

#### 7.3.5.1 General

The ability of the system to permit appropriate interaction between and among the modules as appropriate shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) dimensional mismatch;

b) inaccurate positioning or orientation;

c) separation between modules;

d) damage to or obstruction of modules by other modules;

e) angulation or kink between modules.

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

— prosthesis migration;

— attachment site leak/intracomponent leak;

— vascular trauma;

— branch vessel occlusion;

— aneurysm enlargement;

— aneurysm rupture;

— lumen obstruction;

— ischemia.

Testing shall include the following items listed in 7.3.5.2 through 7.3.5.5, as appropriate to the design of the endovascular system.

#### 7.3.5.2 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.3.5.3 Flex/kink

Determine the minimum radius of curvature that the implant can accommodate without kinking.

#### 7.3.5.4 Migration resistance

Determine ability of the implant to remain stationary under simulated use.

#### 7.3.5.5 Pull test for modular components

Determine the force required to disengage modular components under simulated use conditions.

### 7.3.6 Sizing

#### 7.3.6.1 General

The ability of the system to permit adequate fixation of the implant within the vasculature by appropriate sizing through consistent dimensions shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) inappropriate sizing.

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

— stent/attachment system failure;

— prosthesis migration;

— implant thrombosis;

— attachment site leak;

— aneurysm enlargement;

— aneurysm rupture;

— branch vessel occlusion;

— vessel trauma;

— trauma to adjacent structures;

— lumen obstruction;

— ischemia.

Testing shall include the following items listed in 7.3.6.2 through 7.3.6.6, as appropriate to the design of the endovascular system.

#### 7.3.6.2 Implant length to diameter relationship

Determine the relationship between implant length and expanded implant diameter.

#### 7.3.6.3 Dimensional verification

Determine the appropriate dimensions for conformance with design specifications.

#### 7.3.6.4 Recoil

Determine the amount of elastic recoil after deployment of the implant. Correlate this recoil to recommended sizing.

#### 7.3.6.5 Simulated use

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

#### 7.3.6.6 Implant diameter to balloon inflation pressure

For balloon expandable implants, determine the relationship between the implant diameter and the balloon inflation pressure.

### 7.3.7 Patency

#### 7.3.7.1 General

The ability of the implant to maintain an open lumen shall be evaluated.

Hazards to be evaluated include, but are not limited to, the following:

a) kinking;

b) twisting;

c) inaccurate deployment;

d) deformation;

e) thrombus generation.

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

— implant thrombosis;

— lumen obstruction;

— restenosis;

— abrupt reclosure;

— angina;

— recurrence of portal hypertension;

— myocardial infarction;

— ischemia;

— pulmonary embolism.

Testing shall include the following items listed in 7.3.7.2 through 7.3.7.7, as appropriate to the design of the endovascular system.

#### 7.3.7.2 Radial outward force

The force exerted by a self-expanding implant shall be measured as a function of the implant diameter.

#### 7.3.7.3 Crush resistance

Determine the minimum force at which permanent deformation or full collapse occurs.

#### 7.3.7.4 Simulated use

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

#### 7.3.7.5 Stent free surface area

Determine the percentage change in free or open area as a function of stent diameter.

#### 7.3.7.6 Local compression

Determine the elastic deformation of the implant in response to localized compressive force.

#### 7.3.7.7 Flex/link

Determine the minimum radius of curvature that the implant can accommodate without kinking.

### 7.3.8 Magnetic resonance imaging (MRI) compatibility

Evaluate the safety and compatibility of the implant with the use of MRI.

 

Hazards to be evaluated include, but are not limited to, the following:

a) lack of quality imaging (artifact);

b) movement or heating of the implant.

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

— vascular trauma;

— implant migration.

NOTE—The MRI artifact generated caused by some implants can compromise the effectiveness and limit the use of MRI in patients with these implants.

### 7.4 Preclinical *in vivo* evaluation

#### 7.4.1 Purpose

The purpose of preclinical *in vivo* testing is to evaluate the deployment of the endovascular graft and the capacity of the prosthesis to maintain physiological function, and to determine the response of both the host and the prosthesis. The study(s) shall evaluate the suitability of the endovascular system for its intended use in clinical investigation.

#### 7.4.2 Specific aims

Specific aims of the study shall be stated and may include the following, as appropriate.

a) Evaluate the ability to access the target location with the delivery system.

b) Evaluate the handling and visualization of the delivery system and visualization of the implant.

c) Verify the accuracy and efficacy of deployment.

d) Characterize the ability to withdraw the delivery system.

e) Evaluate the appropriateness of implant sizing.

f) Evaluate the functional hemostasis of the delivery system and sheath introducer.

g) Evaluate the position, structural and material integrity, and functionality of the implant acutely and over time and at explantation.

h) Evaluate histology and pathology of explants and pertinent tissues/organs.

i) Record adverse events.

#### 7.4.3 Protocol

Each type of prosthesis shall be tested by implantation at the intended, or an analogous, vascular site in at least six animals for at least 26 weeks in each animal, unless a justification for a shorter study is provided. The type and intervals of interim assessments shall be specified and justified. For novel technologies, interim sacrifices and longer implant durations may be indicated. As far as permitted by the limitations of the animal model, all devices used shall be of clinical quality and size, and of the design intended for clinical use.

All animals in the study shall be regularly examined, and ailing animals 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. Histological and pathological assessment of explants and appropriate tissues/organs shall be provided. A control may be appropriate for comparison purposes.

The design of the preclinical *in vivo* testing, including the experimental protocol, measurement methods, and data analysis, shall be justified. 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 instructions for clinical use as far as permitted by the limitations of the animal model.

NOTE—See ISO/IEC 17025 for guidance on appropriate laboratory practices.

#### 7.4.4 Data acquisition

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

a) identification data:
   1) source of animals;
   2) animal identification;
   3) gender;
   4) date of birth;
   5) mass;

b) pre-operative data:
   1) verification of health status, including appropriate blood testing;
   2) medication (e.g., prophylactic antibiotics);

c) operative data:
   1) date of procedure;
   2) name of person performing procedure;
   3) description of the implant procedure including:
      i) prosthesis identification number;
      ii) *in situ* length and diameter of prosthesis;
      iii) amount of oversizing;
      iv) use of systemic antiplatelet/anticoagulant therapy;
   4) assessment of accuracy and efficacy of insertion of delivery system and deployment of the endovascular implant;
   5) assessment of handling and visualization of the delivery system and visualization of the implant;
   6) assessment of efficacy of withdrawal of delivery system;
   7) assessment of appropriateness of sizing and sizing scheme;
   8) amount and location of blood loss;
   9) assessment of position, structural and material integrity, and functionality of the implant;
   10) adverse perioperative events;

d) post-operative and follow-up data:
   1) medications, including those that affect coagulation;
   2) observation of endoleaks, structural integrity, functionality and position of implant, method of visualization, and date;
   3) adverse events, date of occurrence, therapy, and outcome;
   4) any major deviation from protocol;

e) termination data:
   1) observation of endoleaks, structural integrity, functionality, patency and position of implant, method of visualization, and date of sacrifice;
   2) gross alteration in the dimensional, chemical, and physical properties of the implant and components;
   3) histological and pathological assessment of explants and appropriate tissues/organs.

 

#### 7.4.5 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 species;

   2) implantation site;

   3) implantation periods;

   4) methods of assessment;

   5) intervals of observation;

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

c) summary of results:

   1) animal accountability, including rationale for exclusion of data;

   2) success rates per objectives;

   3) summary of adverse events;

   4) summary of early deaths or sacrifices for cause;

   5) operator opinion of ease of deployment, visualization, and handling;

   6) significant and/or relevant deviations from protocol;

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

   8) summary of any changes in position, structural and material integrity, and functionality of the implant;

   9) conclusions from study;

   10) summary of quality assurance and data auditing procedures.

### 7.5 Clinical evaluation

#### 7.5.1 Purpose

The purpose of clinical evaluation is to evaluate the performance of the delivery system and assess the safety and efficacy of an endovascular prosthesis. This evaluation is not intended to demonstrate the long-term performance of the prosthesis. An investigation shall be carried out for each new prosthesis or new clinical application of a prosthesis prior to market approval, using the principles given in ISO 14155 or an equivalent publication. Significant design changes that can impact safety and performance shall require clinical evaluation. Additional prosthesis sizes outside the previously evaluated range may require clinical evaluation. The prosthesis shall have satisfied all appropriate preclinical testing requirements of this part of ISO 25539 before the clinical investigation is begun.

#### 7.5.2 Specific aims

Specific aims of the study shall be stated and may include the following, as appropriate.

a) Evaluate the ability to access the target location with the delivery system.

b) Evaluate the handling and visualization of the delivery system and visualization of the implant.

c) Verify the accuracy and efficacy of deployment.

d) Characterize the ability to withdraw the delivery system.

e) Evaluate the appropriateness of implant sizing.

f) Evaluate the functional hemostasis of the delivery system and sheath introducer.

g) Evaluate the position, structural and material integrity, and functionality of the implant acutely and over time.

h) Monitor lesion characteristics and implant positioning (over time).

i) Report the early and late conversions and the cause.

j) Evaluate histology and pathology of any explants and pertinent tissues/organs.

k) Record reportable clinical events.

### 7.5.3 Protocol

A multicenter study (at a minimum of three investigational sites) shall be performed. A justification for the number of investigational sites shall be provided. A statistical justification for the number of patients studied shall also be provided based upon the clinical hypotheses.

The clinical investigation shall be continued for a minimum of 12 months for each patient unless a justification for a different duration of follow-up is provided. Duration of follow-up should be related to the standard of care for the intended clinical application. All patients implanted with either test or control prostheses, including those excluded from the final analysis, shall be recorded and reported. The final report shall include current follow-up data on all patients, with a minimum of 12 months follow-up data on the last patient enrolled. Patient follow-up intervals shall include a minimum of a baseline assessment at discharge and at 12 months after surgery. A justification will be required for follow-up intervals. Patient follow-up is advised for a minimum of 5 years after the last prosthesis has been implanted.

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. The control should be appropriate to the questions being addressed in the study.

A specific question or set of questions shall be defined prospectively. These questions shall delineate the appropriate endpoints to be measured and include definitions of success and failure for each endpoint.

Patient selection and exclusion criteria shall be clearly established. 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 to participate fully in the study). An appropriate epidemiological approach shall be utilized for recruiting subjects to minimize bias.

### 7.5.4 Data acquisition

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

NOTE—Exceptions for the control population are noted below.

a) identification data:

   1) patient identification;

   2) sex;

   3) date of birth;

   4) name of investigator;

   5) name of institution;

b) pre-operative data:

   1) risk factors, such as hypertension, diabetes, hyperlipidemia, tobacco use, obesity, anesthesia risk, and any other cardiovascular risk factors, with some measure of severity and current treatment;

   2) summary of previous vascular interventions, including non-surgical interventions, and vascular prostheses implanted;

   3) urgency of intervention (i.e., emergency or elective);

   4) diagnostic criteria:

      i) clinical assessment;

 

ii) objective assessment of lesion and access vessel characteristics and other relevant factors (such as sizes, degree of calcification, tortuosity, and angle of attachment sites);

c) operative data:

1) name of implanting physician;

2) date of procedure;

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

4) details of procedure, including any adjunctive vascular procedures performed;

5) relevant medications;

6) assessment of handling, visualization, deployment, and withdrawal;

7) assessment of endoleaks;

8) assessment of patency, positioning, and integrity of the prosthesis;

9) reportable clinical events (see annex C);

10) date of hospital discharge;

11) comparison of intended and actual implant location;

12) for exclusion of aneurysm, length of implant in contact with non-aneurysmal tissue;

13) luminal diameter of implant;

14) confirmation of implant placement and conformity to vessel;

d) post-operative data:

1) date of each follow-up visit;

2) summary of vascular interventions since last follow-up;

3) clinical evaluation (assessment protocol may differ between the control group and the treatment group);

i) clinical assessment;

ii) objective assessment of prosthesis function (endoleak, migration, patency, percentage of diameter stenosis, component integrity);

iii) objective assessment of targeted lesion characteristics and implant positioning;

4) implant relevant medications, such as anticoagulants or antibiotics;

5) reportable clinical events;

i) event, date of occurrence, severity, management, outcome;

ii) documentation of prosthesis involvement (i.e., does the complication involve the prosthesis?);

iii) documentation of probable causative factors (i.e., is the complication caused by prosthesis, patient factors, technical factors, or other?);

e) patient withdrawal:

1) date;

2) months of study completed;

3) reason for withdrawal (lost to follow-up, death).

#### 7.5.5 Final report

The clinical report shall include the following:

a) study protocol;

b) definitions of reportable clinical events;

c) rationale for selection of the following:

1) study size;

2) choice of control;

3) measurement methods;

4) statistical analyses employed;

5) patient follow-up intervals;

d) post-operative and follow-up data:

1) patient accountability, including rationale for exclusion of data;

2) significant and/or relevant deviations from protocol;

3) summary of patients not completing study (e.g., lost to follow-up or death);

4) summary of periprocedural (less than or equal to 30 days, or prior to discharge if longer than 30 days) and late reportable clinical events;

i) by type of event;

ii) detail of any events associated with other events in individual patients;

5) summary of delivery system performance;

6) summary of prosthesis performance over time (e.g., endoleak, migration, patency, component integrity, change in shape);

7) summary of lesion characteristics over time (e.g., aneurysm size changes);

8) summary of lesion characteristics related to implant performance over time (e.g., aneurysm size changes related to endoleaks);

9) summary of vascular interventions;

10) summary of peri-procedural and late conversions to open surgery;

11) summary of periprocedural and late deaths;

12) summary of pathology, if appropriate, including representative gross photographs and micrographs;

13) comparison of results for test and control groups;

14) conclusions from study.

## 8 Manufacturing

The requirements of ISO 13485 and ISO 13488 or Clause 8 of ISO 14630:1997 shall apply.

## 9 Sterilization

### 9.1 Products supplied sterile

**9.1.1** Implants that are labeled “Sterile” shall comply with national or regional standards. Implants which are labeled “Sterile” shall have a sterility assurance level (SAL) of $10^{-6}$.

NOTE—For example, see EN 556 [17] and ANSI/AMI ST67 [20].

 

**9.1.2** Sterilization processes shall be validated and routinely controlled as follows:

a) If endovascular systems are to be sterilized by ethylene oxide, ISO 11135 shall apply.

b) If endovascular systems are to be sterilized by moist heat, ISO 11134 shall apply.

c) If endovascular systems are to be sterilized by radiation, ISO 11137 shall apply.

d) If single-use endovascular systems incorporating animal tissue are to be sterilized using liquid chemical sterilants, ISO 14160 shall apply.

e) If endovascular systems are to be sterilized by other sterilization processes, ISO 14937 shall apply.

NOTE—Separate International and European Standards have been developed that address validation and routine control of some sterilization processes. For European purposes, EN 550 applies for ethylene oxide sterilization, EN 554 applies for moist heat sterilization, and EN 552 applies for radiation sterilization. At the time of the publication of this part of ISO 25539, efforts were underway to harmonize the separate International and European Standards for validation and routine control of sterilization processes.

### 9.2 Products supplied non-sterile

The requirements of 9.2 of ISO 14630:1997 shall apply.

### 9.3 Sterilization residuals

The requirements of 9.3 of ISO 14630:1997 shall apply.

## 10 Packaging

### 10.1 Protection from damage in storage and transport

#### 10.1.1 General

The requirements of 10.1 of ISO 14630:1997 shall apply.

#### 10.1.2 Unit container

Each prosthesis shall be packaged in a unit container. It shall be readily apparent if the unit container has been opened.

#### 10.1.3 Outer container

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

#### 10.1.4 Shipping container

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

#### 10.1.5 Maintenance of sterility in transit

For prostheses supplied sterile, the unit container shall be designed to maintain the sterility of the prosthesis under nominal conditions of handling, transit, and storage, and to permit the contents to be presented for use in an aseptic manner.

The packaging shall conform to ISO 11607.

NOTE—Separate International and European Standards have been developed that address packaging for sterilized medical devices. For European purposes, EN 868-1 applies for sterilization packaging for medical devices.

### 10.2 Marking

#### 10.2.1 Container label

Each endovascular system shall be accompanied by a label(s) on an appropriate container(s). At least the following information shall be provided on the label(s):

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

b) the material of construction and type of construction;

c) the configuration. A symbol may be substituted for a written description of the prosthesis;

d) the nominal length(s);

e) the nominal diameter(s);

f) if appropriate, porosity, mean water permeability, integral water permeability/leakage, and/or water entry pressure;

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

h) manufacturer's batch or lot number;

i) sterile lot number;

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

k) for prostheses supplied sterile, a warning against the use of the prosthesis if the package is open or damaged;

l) manufacturer's recommendations for storage, when applicable;

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

NOTE—If the manufacturer's batch or lot number (h) and the sterile lot number (i) can be traced to the same information, only one number need be given.

#### 10.2.2 Record label

Each prosthesis shall be supplied with at least three adhesive record labels suitable for attachment to the records of the patient receiving the implant. The record label shall include the following information:

a) manufacturer's identification;

b) product name;

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

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

### 10.3 Information supplied by the manufacturer

#### 10.3.1 General

The requirements of Clause 11 of ISO 14630:1997 shall apply. Further information is contained in Table A.2 in annex A.

#### 10.3.2 Information and instructions for use

Each unit container or outer container of which the contents are identical shall be supplied with instructions for the use of the prosthesis. The instructions shall include the following:

a) indications for use;

b) contraindications, cautions, and warnings that are applicable;

c) recommended methods for the aseptic presentation and the preparation of the prosthesis, including any pre-treatment and implantation techniques;

d) the statement STERILE—DO NOT RESTERILIZE—SINGLE USE ONLY in prominent form, if applicable;

e) resterilization information, if applicable;

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

g) recommendations for storage, if applicable;

h) date of or reference relating to the publication of the text, indicating if the text has been revised;

i) recommendations for visualization;

j) MRI compatibility information.

 

# Annex A
(informative)

## Attributes of endovascular devices—Technical and clinical considerations

Tables A.1 through A.3 provide a logical method for identifying a set of biocompatibility, bench, animal, and clinical tests to assess device performance. Annex B includes a list of the bench tests identified in the table, with a description of the purpose of each test, and annex C includes definitions for the reportable clinical events listed in the table.

The table headings and explanations are listed in Table A.1 below. In addition, a form is given to help provide the proper context for the information contained within the matrix.

**Table A.1—Table headings and explanations**

| Column number | Title | Explanation | Context |
|---|---|---|---|
| *1* | Implant/procedure related attributes | Individual design goals | The implant should have an adequate _____ (column *1*). |
| *2* | Problem(s) | Difficulties that may be encountered that could result in not meeting the individual design goal | If the implant does not have an adequate _____ (column *1*), there could be a problem with _____ (column *2*). |
| *3* | Reportable clinical events | Complications or failures that may be observed with clinical use if the problems occur | If there is a problem with _____ (column *2*), _____ (column *3*) could occur and should be documented. |
| *4* | Bench and analytical tests | A list of tests, exclusive of animal and clinical studies, that may be conducted to validate the individual design goal | The following tests may be conducted to evaluate the adequacy of the _____ (column *1*):<br>_____ (column *4*). |
| *5* | Animal studies | Specific aims of animal studies to validate and verify the individual design goal | In order to evaluate the adequacy of the _____ (column *1*) in an *in vivo* environment, the animal study should _____ (column *5*). |
| *6* | Clinical studies | Specific aims of clinical studies to verify the individual design goal | In order to evaluate the adequacy of the _____ (column *1*) in a clinical environment, the clinical study should _____ (column *6*). |
| *7* | Information supplied by the manufacturer | Information to be supplied by the manufacturer to minimize the potential for failures to occur | To minimize the risk of _____ (column *2*) or _____ (column *3*), _____ (column *7*) should be provided by the manufacturer. |

**Table A.2—Attributes of endovascular devices—Technical and clinical considerations for delivery systems**

| Delivery system | | | | | | |
|---|---|---|---|---|---|---|
| **Device/ procedure-related attributes** | **Problem(s)** | **Reportable clinical events** | **Bench and analytical tests** | **Preclinical *in vivo* studies** | **Clinical studies** | **Information supplied by the manufacturer** |
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Ability to access | – Wire not crossing the lesion<br>– Introducer and delivery system not matching the access site (i.e., size mismatch)<br>– Delivery system not advancing to target site<br>– Emboli generation<br>– Implant (e.g., stent) dislodgement | – Access failure<br>– Vascular trauma<br>– Neurological deficit<br>– Ischemia<br>– Spinal neurological deficit<br>– Embolization | – Component dimension compatibility<br>– Flex/kink<br>– Torsional bond strength<br>– Bond strength<br>– Torquability<br>– Pushability<br>– Trackability<br>– Simulated use<br>– Dimensional verification<br>– Profile<br>– Visibility | – Evaluate ability to access<br>– Assess handling and visualization<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Evaluate ability to access<br>– Assess handling and visualization<br>– Evaluate reportable clinical events | – Implant profile, wire dimensions compatible with delivery system<br>– Sizing recommendations<br>– For user-mounted implants, manufacturer-supplied information should include recommendations or specifications for delivery components<br>– Information should include recommendations or specifications for accessory devices |

 

**Table A.2** *(continued)*

| Delivery system | | | | | | |
|---|---|---|---|---|---|---|
| **Device/ procedure-related attributes** | **Problem(s)** | **Reportable clinical events** | **Bench and analytical tests** | **Preclinical *in vivo* studies** | **Clinical studies** | **Information supplied by the manufacturer** |
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Ability to deploy:<br>Balloon-expandable | – Inability to activate deployment mechanism<br>– Disproportionate dimensions and properties, such as balloon compliance and burst pressure, of balloon relative to vessel<br>– Implant (e.g., stent) dislodgment<br>– Balloon failure<br>– Damage of implant components by other components<br>– Inadequate visualization<br>– Emboli generation | – Deployment system failure<br>– Spinal neurological deficit<br>– Neurological deficit<br>– Vascular trauma<br>– Embolization<br>– Damage to implant | – Component dimension compatibility<br>– Torsional bond strength<br>– Bond strength<br>– Simulated use<br>– Dimensional verification<br>– Balloon deflation<br>– Balloon mean burst<br>– Balloon rated burst<br>– Balloon rated fatigue<br>– Balloon inflation time<br>– Visibility | – Verify efficacy of deployment<br>– Assess handling and visualization<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Verify efficacy of deployment<br>– Assess handling and visualization<br>– Evaluate reportable clinical events | – For user-mounted implants, manufacturer-supplied information should include recommendations or specifications for delivery components<br>– Information should include recommendations or specifications for accessory devices |

**Table A.2** *(continued)*

| Delivery system | | | | | | |
|---|---|---|---|---|---|---|
| **Device/ procedure-related attributes** | **Problem(s)** | **Reportable clinical events** | **Bench and analytical tests** | **Preclinical *in vivo* studies** | **Clinical studies** | **Information supplied by the manufacturer** |
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Ability to deploy:<br>Self-expanding | – Inability to activate deployment mechanism<br>– Disproportionate dimensions of "modeling" balloon relative to implant/ vessel<br>– Balloon failure<br>– Damage of implant components by other components<br>– Inadequate visualization<br>– Emboli generation<br>– Implant (e.g., stent) dislodgment | – Deployment system failure<br>– Neurological deficit<br>– Vascular trauma<br>– Spinal neurological deficit<br>– Remobilization<br>– Damage to implant | – Component dimension compatibility<br>– Torsional bond strength<br>– Bond strength<br>– Simulated use<br>– Dimensional verification<br>– Visibility<br>– Deployment force | – Verify efficacy of deployment<br>– Assess handling and visualization<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Verify efficacy of deployment<br>– Assess handling and visualization<br>– Evaluate reportable clinical events | – For user-mounted implants, manufacturer-supplied information should include recommendations or specifications for delivery components<br>– Information should include recommendations or specifications for accessory devices |

 

**Table A.2** *(continued)*

| Delivery system | | | | | | |
|---|---|---|---|---|---|---|
| **Device/ procedure-related attributes** | **Problem(s)** | **Reportable clinical events** | **Bench and analytical tests** | **Preclinical *in vivo* studies** | **Clinical studies** | **Information supplied by the manufacturer** |
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Ability to withdraw:<br>Balloon-expandable | – Improper balloon deflation<br>– Balloon winging<br>– Lack of structural integrity<br>– Emboli generation<br>– Diameter mismatch<br>– Implant dislodgment<br>– Damage of implant components by other components<br>– Delivery system snagging on the implant<br>– Inadequate visualization | – Deployment system failure<br>– Neurological deficit<br>– Vascular trauma<br>– Ischemia<br>– Spinal neurological deficit<br>– Embolization<br>– Damage to implant | – Tubing tensile strength<br>– Component dimension compatibility<br>– Torsional bond strength<br>– Bond strength<br>– Simulated use<br>– Dimensional verification<br>– Flex/kink<br>– Visibility | – Verify efficacy of withdrawal<br>– Assess handling and visualization<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Verify efficacy of withdrawal<br>– Assess handling and visualization<br>– Evaluate reportable clinical events | – Information should include recommen-dations or specifications for accessory devices |
| Ability to withdraw:<br>Self-expanding | – Diameter mismatch<br>– Lack of structural integrity<br>– Emboli generation<br>– Implant dislodgment<br>– Damage of implant components by other components<br>– Delivery system snagging on the implant<br>– Inadequate visualization | – Deployment system failure<br>– Neurological deficit<br>– Vascular trauma<br>– Ischemia<br>– Spinal neurological deficit<br>– Embolization<br>– Damage to implant | – Tubing tensile strength<br>– Component dimension compatibility<br>– Torsional bond strength<br>– Bond strength<br>– Simulated use<br>– Dimensional verification<br>– Flex/kink<br>– Visibility | – Verify efficacy of withdrawal<br>– Assess handling and visualization<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Verify efficacy of withdrawal<br>– Assess handling and visualization<br>– Evaluate reportable clinical events | – Information should include recommen-dations or specifications for accessory devices |

**Table A.2** *(continued)*

| Delivery system | | | | | | |
|---|---|---|---|---|---|---|
| **Device/ procedure-related attributes** | **Problem(s)** | **Reportable clinical events** | **Bench and analytical tests** | **Preclinical *in vivo* studies** | **Clinical studies** | **Information supplied by the manufacturer** |
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Biocompat-ibility | – Lack of appropriate biocompati-bility | – Complica-tions attributable to a lack of appropriate biocompat-ibility | – ISO 10993 | – ISO 10993<br>– Appropriate histological and pathological investiga-tions of explants<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Evaluate reportable clinical events | N/A |
| Sterility | – Non-sterile product | – Infection | – Sterilization assurance | N/A | – Evaluate reportable clinical events | – Appropriate handling instructions<br>– Whether single or multiple use |
| Hemostasis | – Size mismatch<br>– Hemostasis valve incompe-tency<br>– Leaking | – Procedural bleeding<br>– Hematoma | – Assessment of hemostasis<br>– Dimensional verification | – Evaluate appropriate-ness of sizing<br>– Assess blood loss<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Evaluate appropriate-ness of sizing<br>– Assess blood loss<br>– Evaluate reportable clinical events | – Sizing recommen-dations<br>– Specifications for accessory devices |

 

**Table A.3—Attributes of endovascular devices—Technical and clinical considerations for implants**

| Device/ procedure-related attributes | Problem(s) | Reportable clinical events | Bench tests | Animal studies | Clinical studies | Information supplied by the manufacturer |
|---|---|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Ability to accurately deploy | – Inaccurate positioning or orienta-tion<br>– Improper deployment configuration<br>– Incomplete deployment<br>– Inadequate visualization | – Branch vessel occlusion<br>– Deployment system failure<br>– Attachment site leak<br>– Prosthesis migration<br>– Lumen obstruction<br>– Aneurysm enlargement<br>– Aneurysm rupture<br>– Ischemia | – Simulated use<br>– Implant length to diameter relationship<br>– Visibility | – Assess visualization<br>– Verify accuracy and efficacy of deployment<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Assess visualization<br>– Verify accuracy and efficacy of deployment<br>– Evaluate reportable clinical events | – Location and description of radio-opaque landmarks whenever present |
| Fixation effective-ness | – Incomplete apposition to vessel wall<br>– Excessive or inadequate radial force | – Attachment site leak<br>– Prosthesis migration<br>– Lumen obstruction<br>– Vascular trauma<br>– Trauma to adjacent structures<br>– Branch vessel occlusion<br>– Aneurysm enlargement<br>– Aneurysm rupture | – Radial force<br>– Crush resistance<br>– Recoil<br>– Local compression<br>– Conform-ability to vessel wall<br>– Migration resistance<br>– Simulated use | – Assess position, integrity, and functionality<br>– Appropriate histological and pathological investigation of explants<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Assess position, integrity, and functionality<br>– Monitor lesion morphology<br>– Appropriate histological and pathological investigation of explants if occurring<br>– Evaluate reportable clinical events | – Directions regarding restrictions and requirements to assure proper fixation |

**Table A.3** *(continued)*

| Device/ procedure-related attributes | Problem(s) | Reportable clinical events | Bench tests | Animal studies | Clinical studies | Information supplied by the manufacturer |
|---|---|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Implant integrity | – Structural failure of implant<br>– Loss of complete apposition to vessel wall<br>– Leaking | – Stent/ attachment system fracture<br>– Graft dilata-tion/rupture<br>– Implant thrombosis<br>– Prosthesis migration<br>– Attachment site leak<br>– Aneurysm enlargement<br>– Aneurysm rupture<br>– Transgraft leak<br>– Vascular trauma<br>– Lumen obstruction<br>– Venous thrombosis<br>– Trauma to adjacent structures<br>– Ischemia | – Fatigue and durability<br>– Stress/strain analysis<br>– Corrosion<br>– Longitudinal tensile strength<br>– Burst/ circumferen-tial strength<br>– Factory anastomotic strength<br>– Strength of stent/attachme nt system to graft bond (e.g., adhesive, sutures)<br>– Strength after repeated puncture for vascular access<br>– Visual inspection | – Assess position, integrity, and functionality<br>– Appropriate histological and pathological investigation of explants<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Assess position, integrity, and functionality<br>– Appropriate histological and pathological investigation of explants if occurring<br>– Evaluate reportable clinical events | N/A |
| Permeability | – Inadequate healing<br>– Leaking | – Transgraft leak<br>– Aneurysm enlargement<br>– Aneurysm rupture | – Porosity, water permeability, integral water permeability/le akage and water entry pressure | – Evaluate adverse events with particular attention to events listed in column *3* | – Monitor lesion morphology<br>– Evaluate reportable clinical events | N/A |

 

**Table A.3** *(continued)*

| Device/ procedure-related attributes | Problem(s) | Reportable clinical events | Bench tests | Animal studies | Clinical studies | Information supplied by the manufacturer |
|---|---|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Modularity | – Dimension-al mismatch<br>– Inaccurate positioning or orientation<br>– Separation between modules<br>– Damage to or obstruction of modules by other modules<br>– Angulation or kink between modules | – Prosthesis migration<br>– Attachment site leak<br>– Vascular trauma<br>– Branch vessel occlusion<br>– Aneurysm enlargement<br>– Aneurysm rupture<br>– Lumen obstruction<br>– Ischemia | – Pull test for modular components<br>– Dimensional verification<br>– Migration resistance<br>– Flex/kink | – Assess position, integrity, and functionality<br>– Appropriate histological and pathological investigation of explants<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Assess position, integrity, and functionality<br>– Monitor lesion morphology<br>– Appropriate histological and pathological investigation of explants if occurring<br>– Evaluate reportable clinical events | – Location and description of radio-opaque landmarks whenever present<br>– Directions regarding restrictions and requirements to assure proper fixation |
| Appropriate sizing | – Inappropriate sizing | – Stent/ attachment system failure<br>– Prosthesis migration<br>– Implant thrombosis<br>– Attachment site leak<br>– Aneurysm enlargement<br>– Aneurysm rupture<br>– Branch vessel occlusion<br>– Vessel trauma<br>– Trauma to adjacent structures<br>– Lumen obstruction<br>– Ischemia | – Simulated use<br>– Implant length to diameter relationship<br>– Recoil<br>– Dimensional verification<br>– Implant diameter to balloon inflation pressure | – Verify sizing scheme<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Evaluate reportable clinical events | – Sizing recommen-dations |

**Table A.3** *(continued)*

| Device/ procedure-related attributes | Problem(s) | Reportable clinical events | Bench tests | Animal studies | Clinical studies | Information supplied by the manufacturer |
|---|---|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| Patency | – Kinking<br>– Twisting<br>– Inaccurate deployment<br>– Deformation<br>– Thrombus generation | – Implant thrombosis<br>– Lumen obstruction<br>– Restenosis<br>– Abrupt reclosure<br>– Angina<br>– Recurrence of portal hypertension<br>– Myocardial infarction<br>– Ischemia<br>– Pulmonary embolism | – Radial force<br>– Crush resistance<br>– Simulated use<br>– Stent free surface area<br>– Local compression<br>– Flex/kink | – Assess position, integrity, and functionality<br>– Appropriate histological and pathological investigation of explants<br>– Evaluate adverse events with particular attention to events listed in column *3* | – Assess position, integrity, and functionality<br>– Monitor lesion morphology<br>– Appropriate histological and pathological investigation of explants if occurring<br>– Evaluate reportable clinical events | N/A |
| Magnetic resonance imaging (MRI) compatibility | – Lack of quality imaging<br>– Movement of implant or heating of wire | – Vascular trauma<br>– Implant migration | – MRI compatibility | N/A | – Evaluate reportable clinical events | – Describe MRI safety and compatibility of the device |
| Biocompat-ibility | – Lack of appropriate biocompat-ibility | – Complica-tions attributable to a lack of appropriate biocompat-ibility | – ISO 10993 | – ISO 10993<br>– Appropriate histological and pathological investiga-tions of explants | – Evaluate reportable clinical events | – List of materials utilized |
| Sterility | – Non-sterile product | – Infection | – Sterilization assurance | N/A | – Evaluate reportable clinical events | – Appropriate handling instructions<br>– Whether single or multiple use |

 

## Annex B
(informative)

## Bench and analytical tests

**Table B.1—Bench and analytical tests**

| Tests | Description of test and requirements | Relevant design evaluation section(s) |
|---|---|---|
| Assessment of hemostasis | Evaluate ability of system to maintain adequate hemostatic seal. | 7.2.5 Hemostasis |
| Balloon deflation | Determine time required to deflate balloon and evaluate ability to remove deflated balloon. | 7.2.2 Ability to deploy |
| Balloon inflation time | Determine time required to expand balloon to maximum recommended inflation pressure. | 7.2.2 Ability to deploy |
| Balloon mean burst | Determine mean burst pressure. | 7.2.2 Ability to deploy |
| Balloon rated burst | Determine burst pressure with appropriate safety margin including reliability parameters. | 7.2.2 Ability to deploy |
| Balloon rated fatigue | Determine maximum number of recommended inflation cycles to recommended inflation pressure including reliability parameters. | 7.2.2 Ability to deploy |
| Bond strength | Determine longitudinal bond strength between parts of delivery system. All bonds shall remain intact under recommended conditions of use. | 7.2.3 Ability to withdraw |
| Burst/circumferential strength | Determine burst strength and/or circumferential strength of appropriate components of implant. (ISO 7198:1998, 8.3.3) | 7.3.3 Implant integrity |
| Component dimension compatibility | Evaluate dimensions of implant for compatibility with dimensions of recommended accessories. All components shall be dimensionally compatible. | 7.2.1 Ability to access<br>7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw |
| Conformability to vessel wall | Evaluate ability of implant to maintain adequate contact with vessel wall. | 7.3.2 Fixation effectiveness |
| Corrosion | Evaluate susceptibility of material(s) to corrosion in an actual or simulated environment. | 7.3.3 Implant integrity |
| Crush resistance | Determine minimum force at which permanent deformation or full collapse occurs. | 7.3.7 Patency |
| Implant diameter to balloon inflation pressure | For balloon-expandable implants, determine relationship between implant diameter and balloon inflation pressure. | 7.3.6 Sizing |
| Implant length to diameter relationship | For balloon-expandable and self-expanding implants, determine relationship between implant length and expanded implant diameter. | 7.3.1 Ability to accurately deploy |
| Dimensional verification | Determine appropriate dimensions for conformance with design specifications. | 7.2.1 Ability to access<br>7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw<br>7.3.5 Modularity |
| Factory anastomotic strength | Determine tensile strength of any factory anastomosis. (ISO 7198:1998, 8.3.2.4) | 7.3.3 Implant integrity |

**Table B.1** *(continued)*

| Tests | Description of test and requirements | Relevant design evaluation section(s) |
|---|---|---|
| Fatigue and durability | Evaluate long-term dimensional and structural integrity of implant. | 7.3.3 Implant integrity |
| Flex/kink | Evaluate ability of implant and endovascular system to bend in order to accommodate the minimum radius or angle to be negotiated during access and delivery.<br>Also, determine minimum radius of curvature that implant can accommodate without kinking. (ISO 7198:1998, 8.9) | 7.2.1 Ability to access<br>7.2.3 Ability to withdraw<br>7.3.5 Modularity<br>7.3.7 Patency |
| Force to deploy | Determine force to deploy implant from delivery system. | 7.2.2 Ability to deploy |
| Integral water permeability | Determine the volume of clean, filtered liquid (with a viscosity approximating that of water) which passed through wall of a prosthesis in a specified time under a specific pressure, in accordance with ISO 7198:1998, 8.2.3. | 7.3.4 Permeability |
| Local compression | Determine elastic deformation of implant in response to localized compressive force. | 7.3.2 Fixation effectiveness |
| Longitudinal tensile strength | Determine longitudinal tensile strength of prosthesis. (ISO 7198:1998, 8.3.2) | ISO 7198:1998, 8.3.2 |
| Migration resistance | Evaluate ability of implant to remain stationary under simulated use. | 7.3.2 Fixation effectiveness<br>7.3.5 Modularity |
| MRI compatibility | Evaluate MRI safety and compatibility. | 7.3.8 MRI compatibility |
| Porosity | Determine porosity of implant material by estimating ratio of the void within a material to the total volume occupied by the material including the voids. (ISO 7198:1998, 8.2.1) | 7.3.4 Permeability |
| Profile | Determine maximum diameter along defined sections of the endovascular system. | 7.2.1 Ability to access |
| Pull test for modular components | Determine force required to disengage modular components under simulated use conditions. | 7.3.5 Modularity |
| Pushability | Evaluate ability of endovascular system to be pushed or positioned by an operator without bending or buckling. | 7.2.1 Ability to access |
| Radial outward force (hoop strength) | Determine force exerted by a self-expanding implant as a function of implant diameter. | 7.3.2 Fixation effectiveness<br>7.3.7 Patency |
| Recoil | Determine amount of elastic recoil after the deployment of implant. Correlate this recoil to recommended sizing. | 7.3.6 Sizing |
| Simulated use | Evaluate performance of implant using a model that simulates intended use conditions. | 7.2.1 Ability to access<br>7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw<br>7.3.1 Ability to accurately deploy<br>7.3.2 Fixation effectiveness |
| Stent free surface area | Determine percentage change in free or open area as a function of stent diameter. | 7.3.7 Patency |

 

**Table B.1** *(continued)*

| Tests | Description of test and requirements | Relevant design evaluation section(s) |
|---|---|---|
| Strength after repeated puncture | Assess structural integrity after repeated puncture. | 7.3.3 Implant integrity |
| Strength of stent/ attachment system to graft bond | Determine strength of connection between the graft and stent. | 7.3.3 Implant integrity |
| Stress/strain analysis | Determine stress/strain characteristics of implant when subjected to a worst-case physiological load using appropriate tools such as Finite Element Analysis (FEA). | 7.3.3 Implant integrity |
| Torquability | Evaluate ability of endovascular system to provide sufficient rotational rigidity to distal end of implant. | 7.2.1 Ability to access |
| Torsional bond strength | Determine torque required to break joints and/or materials in appropriate delivery system components. | 7.2.1 Ability to access<br>7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw |
| Trackability | Evaluate ability of endovascular system to advance over a guidewire, following the guidewire tip, along path of the vessel, including narrow, tortuous vessels. | 7.2.1 Ability to access |
| Tubing tensile strength | Determine strength of tubing used in delivery system as appropriate to material. | 7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw |
| Visibility | Evaluate ability to visualize implant under simulated use. | 7.2.1 Ability to access<br>7.2.2 Ability to deploy<br>7.2.3 Ability to withdraw<br>7.3.1 Ability to accurately deploy |
| Visual inspection | Verify that prosthesis shows no defects that would render the prosthesis unsuitable for its intended use. (ISO 7198:1998, 8.1) | 7.3.3 Implant integrity |
| Water entry pressure | Determine pressure at which water passes from inner wall to outer wall of a vascular prosthesis, in accordance with ISO 7198:1998, 8.2.4. | 7.3.4 Permeability |
| Water permeability | Determine amount of fluid flow through material of appropriate components of implant. (ISO 7198:1998, 8.2.2) | 7.3.4 Permeability |

## Annex C
(informative)

## Definitions of reportable clinical events

**Table C.1—Definitions of reportable clinical events**

| Event | Definition |
|---|---|
| Abrupt reclosure | Obstructed flow in a dilated lesion which was previously documented to be patent with antegrade flow. |
| Access failure | Failure to reach the intended site with the implant due to mechanical failure or patient anatomy. Whether or not successful implant deployment was achieved should be documented. |
| Accessory device failure | Inability to use the accessory device as intended due to mechanical failure or patient anatomy. Whether or not the failure contributed to an unsuccessful implant deployment should be documented. |
| Adynamic ileus | Inability to tolerate oral intake without supplemental IV therapy developing more than 48 h after, but within 30 days, of the procedure. The duration of the event should also be reported. |
| Aneurysm enlargement | Any enlargement of the diameter or volume of the aneurysm sac greater than documented measurement error, as determined by contrast-enhanced CT or other appropriate modality. |
| Aneurysm rupture | Rupture of the native aneurysm sac. |
| Angina | Chest, neck, arm, or other pain related to decreased coronary blood flow. |
| Arrythmia | Development of a new atrial or ventricular arrythmia or exacerbation of a prior arrythmia requiring treatment (i.e., medical therapy, cardioversion, pacemaker) within 30 days of the procedure. |
| Atelectasis/ pneumonia | Atelectasis or pneumonia documented by chest X-ray within 30 days of the procedure and requiring treatment with antibiotics, inhalation therapy, intubation, or suctioning. The type of treatment required should be reported. |
| Attachment site leak (Type I endoleak) | Blood flow into the aneurysm sac arising at or from the attachment site occurring at any time after endovascular repair as determined by contrast CT scan, ultrasound, angiography, or direct observation at surgery or autopsy. |
| Branch flow (Type II endoleak) | Retrograde flow from patent branch arteries, for example, lumbar and intercostal, occurring at any time after endovascular repair as determined by contrast CT scan, ultrasound, angiography, or direct observation at surgery or autopsy. |
| Branch vessel occlusion | Clinically significant, unplanned exclusion of a major branch vessel. |
| Coagulopathy | Development of a bleeding disorder documented by appropriate laboratory studies within 30 days of the procedure. The specific syndrome should also be noted. |
| Congestive heart failure | Development of an acute episode or exacerbation of existing low cardiac output accompanied by distal and/or pulmonary edema. The need for treatment and the type of treatment administered, as well as the duration of the episode, should be reported. |
| Damage to implant | Damage to the implant caused by an accessory device or the delivery system. |
| Deployment system failure | Inability to deploy the implant at the intended site due to mechanical failure or patient anatomy. Whether or not successful implant deployment was achieved should be documented. |

 

**Table C.1** *(continued)*

| Event | Definition |
|---|---|
| Implant infection | Development of a confirmed implant infection. The etiology (i.e., device sterility, endocarditis, etc.) should be reported if known. |
| Implant thrombosis | Hemodynamically significant thrombus formation within the lumen of the endovascular implant. The degree of narrowing should be specified. |
| Embolization | Migration of intraluminal debris in the presence of clinical sequelae. This is a reportable category that may encompass events reported under other categories. |
| Endoleak | Persistence of blood flow outside the lumen of an endovascular prosthesis but within an aneurysm sac or adjacent vascular segment being treated by the graft. Endoleaks are categorized as follows:<br>— Type I endoleak is periprosthetic and occurs at the proximal or the distal attachment zones.<br>— Type II endoleak is caused by retrograde flow from patent branch arteries, for example, lumbar and intercostal.<br>— Type III endoleak arises from a defect in the graft material or from an inadequate seal between modular graft components.<br>— Type IV endoleak is due to graft permeability. |
| Graft dilatation/rupture | Graft dilatation to more than 50 % of the manufacturer's labeled diameter or any graft rupture. |
| Hematoma | Development of a hematoma related to the endovascular procedure requiring surgical intervention, evacuation, and/or transfusion. If the patient requires transfusion, the volume of replaced blood should be reported. If surgical intervention is required, this should also be reported. |
| Hepatic encephalopathy | Neurological dysfunction due to inadequate metabolism by the liver. |
| Hypotension | Low blood pressure. |
| Impotence | Subjective report of failure to resume the degree of sexual function registered preoperatively within 6 months of the procedure. |
| Ischemia | Development of the clinical picture of acute or chronic ischemia within 30 days of the procedure. The cause of the ischemia should be diagnosed and reported (i.e., embolism, thrombosis, or dissection). Define severity and location. |
| Lumen obstruction | Unintentional obstruction of flow through the vascular lumen due to twisting or kinking of the prosthesis, oversizing, failure of the implant to fully open, or any other cause. |
| Lymphocele/lymph fistula | Cystic accumulation of lymph or groin wound drainage occurring at the incision site. Any intervention required to resolve the event should also be reported. |
| Myocardial infarction | Myocardial infarction documented by the presence of raised cardiac enzymes within 30 days of the procedure. Clinical symptoms, EKG changes, and/or hemodynamic instability associated with the event should also be reported. |
| Neurological deficit | Development of a new transient or permanent neurological deficit or exacerbation of a prior deficit as determined by CT/MRI scan and/or clinical exam that occurs within 30 days of the procedure. Whether the deficit was permanent or transient should also be reported. |
| Post-procedure bleeding | Procedure-related bleeding which occurs after the patient leaves the OR resulting in the need for transfusion. The volume of replaced blood, the source of the bleeding, and whether or not surgical intervention was required to stop the bleeding should also be reported. |

**Table C.1** *(continued)*

| Event | Definition |
|---|---|
| Procedural bleeding | Any blood loss requiring intervention (i.e., transfusion, medical therapy). The volume of blood lost during the procedure should be determined from the operative report. The need for transfusion and the volume and source (banked, autologous, autotransfused) of transfused blood should also be reported. |
| Prosthesis migration | Longitudinal movement of all or part of a stent or attachment system for a distance of greater than 1 cm relative to anatomical landmarks that were determined prior to discharge. |
| Prosthesis realignment | Clinical symptoms associated with movement of the aorta relative to the implant as a result of post-implantation morphological changes. The clinical symptoms should be specified. |
| Pulmonary embolism | Clinical evidence of pulmonary embolism confirmed by high probability VQ scan or pulmonary angiography occurring within 30 days after the procedure. |
| Recurrence of portal hypertension | Recurrent high blood pressure in the portal venous system. |
| Renal failure | Rise in creatine greater than 50 % above the pre-procedure level resulting in a creatine level above high normal that does not spontaneously resolve. The need for and the duration of dialysis treatment should also be reported. |
| Respiratory failure | Need for mechanical ventilation beyond the first 24 h after the procedure or the need for reintubation or ventilator support any time between 24 h and 30 days post-operative (unless the patient was ventilator dependent when he/she entered the study). The duration of ventilator support should be reported. |
| Restenosis | Reduction in diameter when compared to the reference diameter. |
| Spinal neurological deficit | Neurological deficit related to spinal cord ischemia developing within 30 days of the procedure. |
| Stent/attachment system fracture | Fracture or breakage of any portion of the stent or attachment system including metallic fracture or breakage of any of the suture material used to construct the stent or secure the stent or attachment system to the graft material. |
| Transgraft leak (Type IV endoleak) | The documented leakage of blood through the graft wall. |
| Trauma to adjacent structures | Injury to adjacent structures associated with vascular trauma (see definition below). |
| Vascular trauma | Injuries to vessels as a result of an endovascular procedure, including dissections or perforations, false or true aneurysms. The specific site and source of the injury as well as the clinical sequelae should be reported. All required surgical or interventional procedures required to repair the injury should also be reported. |

 

## Annex D

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