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Standard**

ISO 25539-3

**Cardiovascular implants —
Endovascular devices —**

**Part 3:
Vena cava filters**

*Implants cardiovasculaires — Dispositifs endovasculaires —
Partie 3: Filtres de veine cave*

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights.

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC2, *Cardiovascular implants and extracorporeal systems*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 285, *Non-active surgical implants*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

The second edition cancels and replaces the first edition (ISO 25539-3:2011), which has been technically revised.

The main changes are as follows:

- the testing and clinical use related to vena cava filters has been updated;
- the consistency in nomenclature and reporting requirements has been improved.

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

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

This document was prepared to provide guidance on the minimum requirements for vena cava filter systems. The rationale for the requirements for bench tests and analyses to assess device performance and safety, guidance on the identification of appropriate testing to evaluate a specific device design, and guidance for developing test methods are provided in informative annexes. Further clarification of terminology is provided in [Annexes B, C and E](#).

This document has been updated to reflect current knowledge regarding the testing and clinical use related to vena cava filters, reflected in modifications to the requirements in the main body and in the guidance for developing test methods in [Annex D](#). In addition, revisions have been made to improve consistency in nomenclature and reporting and to enhance the utility of this document.

This revised document introduces methodology to identify appropriate testing and analyses applicable to intended clinical use, design and potential failure modes for a specific vena cava filter system, designated as the device evaluation strategy. The requirement regarding the device evaluation strategy is in the main body. [Annex A](#) provides guidance for developing a focused device evaluation strategy table that is specific to the unique characteristics of a device, device design modifications or changes in intended use. [Annex A](#) also provides guidance for the development of a comprehensive device evaluation strategy table that may be used when it is not sufficient to focus only on the unique characteristics or changes.

The guidance on the development of methods to address the requirement for evaluating fatigue and durability through computational analyses has been modified to include recommendations regarding verification of the solution and validation of the computational model, as well as reporting. The guidance on the model development for simulated use has also been significantly revised to improve the clinical relevance of this testing.

In addition to modifications to specific design evaluation requirements, guidance has been provided regarding the assessment of the acceptability of test results. When the requirement is to quantitatively appraise or analyse a parameter, test results generally may be compared to a quantitative value (i.e. acceptance criteria). For characterization tests, it is appropriate to provide an explanation of the relevance of the results. Additionally, some testing can include a comparison to test data or existing data from a previously evaluated device.

For design evaluation, requirements regarding sampling, conditioning of test samples and reporting have been incorporated in the main body. Guidance on these elements of testing and documentation were previously only included in [Annex D](#).

The revisions to the annexes to this document are given in [Table 1](#).

Table 1 — Revisions to the annexes in this document

Annex of ISO 25539-3:2011	Changes in ISO 25539-3:2024
Annex A – Attributes of endovascular devices – Vena cava filters – Technical and clinical considerations	Annex A now includes the relationship between testing requirements, device attributes, and potential failure modes and guidance for the creation of a device evaluation strategy.
Annex B – Descriptions of potential device effects of failure and failure modes and descriptions of detrimental clinical effects	Annex B now includes a description of potential clinical effects of failure.
Annex C – Bench and analytical tests	The list of tests is included in Table D.1 . Annex C now includes a description of potential device effects of failure.
Annex D – Test methods	Annex D – Test methods

Many filter systems have been shown to be safe and effective in clinical use – this update is not intended to require additional evaluations of these devices to remain in compliance with this document as the testing would not provide useful information regarding the expected clinical performance of the device. Manufacturers may rely on historical data gathered under the guidance of the previous edition of this document (i.e. ISO 25539-3:2011). Similarly, for device modifications or changes in intended clinical use, this

edition of this document is not intended to require additional evaluation of aspects of the device that are not expected to change clinical performance.

NOTE The relationship between testing requirements, device attributes and potential failure modes is provided in [Clause A.1](#). [Clause A.1](#) also provides general information regarding device evaluation strategies. [Tables A.3](#) to [A.9](#) provide the rationale for the requirements specified in this document for bench tests and analyses to assess device performance and safety. An explanation of the table headings for [Tables A.3](#) to [A.9](#) is given in [Table A.1](#).

Guidance for the creation of a device-specific evaluation strategy is provided in [Clause A.2](#). Two approaches to create a device-specific evaluation strategy are provided:

- a) focused device evaluation strategy in [A.2.1](#);
- b) comprehensive device evaluation strategy in [A.2.2](#).

[Annex B](#) provides a description of the potential clinical effects of failure identified in [Annex A](#).

[Annex C](#) provides a description of the potential device effects of failure identified in [Annex A](#).

Additional descriptions of clinical and device effects of failure are included in [Annexes B](#) and [C](#), respectively.

[Annex D](#) provides information to consider in developing appropriate bench test and analytical methods.

[Annex E](#) provides examples of terms for clinical use related to vena cava filters.

Cardiovascular implants — Endovascular devices —

Part 3: Vena cava filters

1 Scope

This document specifies the requirements for the evaluation of vena cava filter systems (filters and delivery systems) and the requirements with respect to nomenclature, design attributes and information supplied by the manufacturer. Guidance for the development of in vitro test methods is included in [Annex D](#). This document is intended to be used in conjunction with ISO 14630, which specifies general requirements for the performance of non-active surgical implants.

NOTE 1 Due to the variations in the design of implants covered by this document, and in some cases due to the emergence of novel types of such implants, acceptable standardized in vitro tests and clinical results are not always available. As further scientific and clinical data become available, a revision of this document will be necessary.

This document is applicable to vena cava filters intended to prevent symptomatic pulmonary embolism by capturing blood clots in the inferior vena cava (IVC). While this document can be useful with respect to filters implanted in other venous locations (e.g. superior vena cava, iliac veins), it does not specifically address the use of filters in other implantation sites.

This document is also applicable to permanent filters together with their associated delivery systems, optional filters that can be retrieved and their associated retrieval systems, and convertible filters and their associated conversion systems. While this document can be useful with respect to the evaluation of repositioning filters after chronic implantation, it does not specifically address filter repositioning.

This document is not applicable to

- temporary filters (e.g. tethered) that need to be removed after a defined period of time,
- issues associated with viable tissues and non-viable biological materials, and
- procedures and devices (e.g. venous entry needle) used prior to the vena cava filter procedure.

Although absorbable filters and filters with absorbable coatings are within the scope of this document, this document is not comprehensive with respect to the absorbable properties of these devices.

NOTE 2 Absorbable implants are covered in ISO/TS 17137.

Although coated filters and coated filter systems are within the scope of this document, this document is not comprehensive with respect to coatings.

NOTE 3 Vascular device-drug combination products are covered in ISO 12417-1 and some coating properties are covered in ISO 25539-4.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

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

ISO 11137 (all parts), *Sterilization of health care products — Radiation*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

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

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

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

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

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

ASTM F2503, *Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment*

3 Terms and definitions

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

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

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <https://www.electropedia.org/>

3.1

absorption

<biomaterial> action of a non-endogenous (foreign) material or substance or its degradation products passing through or being assimilated by cells and/or tissue over time

3.2

absorbable coating

implant coating (3.20) that is intended to be absorbed

Note 1 to entry: Drugs are excluded from this definition of absorbable coatings.

3.3

access site

vein that is used for accessing the vena cava

EXAMPLE Jugular vein, femoral vein, subclavian vein, antecubital vein.

3.4

adverse event

unfavourable change in health that occurs in a subject who participates in a study while receiving the treatment or within a specified time after receiving treatment

Note 1 to entry: For the purpose of this document, clinical effects of failure are a subset of adverse events and are described separately.

Note 2 to entry: Adverse events are categorized by the system affected (e.g. cardiac, vascular, respiratory, neurological, renal, gastro-intestinal) and the severity of the event.

3.5**caval perforation/penetration**

imaging [e.g. venography, computed tomography (CT)] showing filter components (e.g. struts, anchors) extending more than 5 mm outside the wall of the vena cava

3.6**clinical effect of failure**

specific detrimental clinical observations potentially associated with device failures

Note 1 to entry: The clinical effects of failure are described in [Annex B](#).

3.7**clinical perforation/penetration**

protrusion of filter components (e.g. struts, anchors) through the vena cava wall causing haemorrhage or hematoma, or interacting with another organ (e.g. liver, bowel, aorta, psoas muscle, vertebral body, lymph nodes), and resulting in adverse clinical symptoms (e.g. abdominal or back pain) or autopsy findings

3.8**conversion system**

components that are intended to structurally alter a *convertible filter* ([3.23.2](#)) after implantation so that it no longer functions as a filter

Note 1 to entry: A conversion system may also be used to inject contrast media (e.g. to obtain a cavagram) if indicated in the instructions for use (IFU).

3.9**delivery system**

components of the *filter system* ([3.18](#)) used to deliver the filter to the target position and to deploy the filter

Note 1 to entry: The delivery system may also be used to inject contrast media (e.g. to obtain a cavagram) if indicated in the instructions for use (IFU).

3.10**determine**

appraise or analyse quantitatively

Note 1 to entry: Also see *evaluate* ([3.15](#)).

3.11**device effect of failure**

consequence to the device potentially associated with device failure

Note 1 to entry: The device effects of failure are described in [Annex C](#).

3.12**device evaluation strategy**

rationale for testing selected for a specific vena cava *filter system* ([3.18](#)), based on requirements of the device design and potential *failure modes* ([3.16](#))

3.13**comprehensive device evaluation strategy table**

optional communication tool to present the *device evaluation strategy* ([3.12](#)) for a specific vena cava *filter system* ([3.18](#)) that addresses attributes of *failure modes* ([3.16](#))

3.14**focused device evaluation strategy table**

optional communication tool to present the *device evaluation strategy* ([3.12](#)) for a specific vena cava *filter system* ([3.18](#)) that focuses on the unique characteristics of the device design or procedure and unique aspects of the intended use

3.15

evaluate

qualitatively appraise or analyse

Note 1 to entry: Also see *determine* ([3.10](#)).

3.16

failure mode

type of difficulty or failure of the *filter system* ([3.18](#)) that can be encountered (hazards) in preclinical in vivo or clinical use and can result in consequences (harm) to the subject

3.17

filter formation

manufacturer's specified final expanded geometric configuration of the filter in the vena cava

3.18

filter system

component consisting of the *vena cava filter* ([3.23](#)) and the *delivery system* ([3.9](#))

3.19

filter system orientation

orientation (e.g. jugular, femoral) of the loaded filter within the *delivery system* ([3.9](#)), based on the designated *access site* ([3.3](#)) (e.g. jugular, femoral, subclavian, antecubital)

3.20

implant coating

surface coating ([3.24](#)) or *surface modification* ([3.25](#))

Note 1 to entry: Implant coating is considered a constituent of an implant.

Note 2 to entry: A laminate, i.e. a composite material made of multiple layers of the same or different materials with the same or different internal structures assembled sandwich-like and bonded by heat, pressure, welding, soldering or adhesives, is not in itself considered an implant coating but the exposed surface of the laminate can be an implant coating.

Note 3 to entry: A covering, for example additional material (e.g. a graft) added to a structure (e.g. a stent) specifically to bridge elements of the structure for the sole purpose of reducing the permeability of the structure, is not considered an implant coating.

[SOURCE: ISO 17327-1:2018, 3.1]

3.21

implantation site

location of *vena cava filter* ([3.23](#)) placement within the body

3.22

retrieval system

components that are intended to remove a specific filter

Note 1 to entry: A retrieval system may also be used to inject contrast media (e.g. to obtain a cavagram) if indicated in the instructions for use (IFU).

3.23

vena cava filter

filter implant

transluminally placed implant, which is used to prevent pulmonary embolism by capturing blood clots traveling in the inferior vena cava (IVC)

3.23.1

absorbable filter

filter, or filter with a component, that is designed to be *absorbed* ([3.1](#))

Note 1 to entry: A filter with a component designed to be absorbed can function as a *convertible filter* ([3.23.2](#)) without intervention.

3.23.2

convertible filter

filter that can be altered structurally after implantation such that some permanent implant remains that no longer functions as a filter (e.g. functions as a stent)

3.23.3

optional filter

filter that can be removed (retrievable filter) or can be left as an implant that permanently functions as a filter

3.23.4

permanent filter

filter that is designed as an implant which permanently functions as a filter

Note 1 to entry: All *optional filters* ([3.23.3](#)) are also permanent filters. Permanent filters can incorporate design characteristics that allow for retrieval or conversion and can be labelled for use of these optional features, if applicable.

3.24

surface coating

layer of material with any different property than the natural surface of the substrate that is intentionally added to the substrate

Note 1 to entry: The coating can partially or fully cover the substrate surface.

Note 2 to entry: The term includes surface coatings created as a result of additive manufacturing.

[SOURCE: ISO 17327-1:2018, 3.2]

3.25

surface modification

intentional conversion or reconstruction of the surface of the original substrate to form a new surface material consisting of components of the substrate's own material and possibly foreign material and forming a surface layer with different properties

[SOURCE: ISO 17327-1:2018, 3.3]

3.26

unacceptable filter tilting

clinically significant rotation of the filter relative to the longitudinal axis of the vena cava and resulting in performance failure (e.g. inadequate filtration, excessive filtration, filter migration, filter embolization, *caval perforation/penetration* ([3.5](#)), *clinical perforation/penetration* ([3.7](#)), inability to retrieve the filter as applicable, inability to convert the filter as applicable)

4 General requirements

4.1 Classification

A filter system shall be designated by its access site (see [3.3](#)), orientation (see [3.17](#)), implantation site (see [3.19](#)), type (see [3.22](#)), materials of construction, as well as surface modifications, coatings and/or drugs.

4.2 Materials of construction for filter system

Materials of the filter system (e.g. wire, imaging markers, coatings) shall be described by their generic or chemical names.

4.3 Configuration and size designation for filters

The configuration of a filter shall be designated by its geometry (e.g. conical) and whether it is permanent, optional or convertible. The size of a filter shall be designated by the minimum and maximum intended caval lumen diameters.

4.4 Intended clinical use designation

Vena cava filters are intended to prevent symptomatic pulmonary embolism by capturing blood clots in the IVC.

5 Intended performance

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

6 Design attributes

6.1 General

The requirements for design attributes in [6.2](#) to [6.10](#) and of ISO 14630:2012, Clause 5 apply. General design attributes for the filter system, the filter, the filter retrieval system and the filter conversion system are listed in [Tables A.3](#) and [A.9](#) with reference to the nonclinical testing necessary for the evaluation of the design. It is recognized that not all tests identified in a category are necessary or practical for any given filter and/or system. The tests considered and the rationale for selection and/or waiving of tests shall be documented.

6.2 Filter system

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

- a) the ability to permit safe and consistent deliverability of the filter to the intended deployment location;
- b) the ability to permit accurate and safe deployment of the filter;
- c) the ability to inject contrast via the delivery system if indicated in the IFU;
- d) the ability to permit safe withdrawal of the delivery system following deployment;
- e) the ability to maintain adequate structural integrity.

6.3 Vena cava filter

The design attributes of the vena cava filter shall at least take into account the following:

- a) the ability to ensure effective fixation in the intended location within the inferior vena cava;
- b) the ability to maintain adequate integrity;
- c) the ability to capture clots in the blood, while allowing acceptable blood flow;
- d) the ability to prevent clinical perforation/penetration;
- e) the compatibility of the filter dimensions for use with the specified caval diameters;
- f) the compatibility with exposure to magnetic resonance imaging (MRI) fields.

6.4 Optional filter

In addition to the attributes listed in [6.3](#), the design attributes of the optional filter shall at least take into account the following:

- a) the ability to be engaged;
- b) the ability to be retrieved;
- c) the ability to maintain adequate structural integrity through retrieval.

6.5 Convertible filter

In addition to the attributes listed in [6.3](#), the design attributes of the convertible filter shall at least take into account the following:

- a) the ability to be engaged;
- b) the ability to be converted (e.g. into a stent);
- c) the ability to maintain adequate structural integrity through and after conversion.

6.6 Retrieval system

The design attributes of the retrieval system shall at least take into account the following:

- a) the ability to safely reach the filter location;
- b) the ability to safely engage the filter;
- c) the ability to safely retrieve the filter;
- d) the ability to inject contrast via the retrieval system if indicated in the IFU;
- e) the ability to be safely withdrawn.

6.7 Conversion system

The design attributes of the conversion system shall at least take into account the following:

- a) the ability to safely reach the filter location;
- b) the ability to safely engage the conversion component of the filter;
- c) the ability to safely convert the filter;
- d) the ability to inject contrast via the conversion system if indicated in the IFU;
- e) the ability to be safely withdrawn.

6.8 Filter system, retrieval system and conversion system

In addition to the general requirements, the design attributes of the filter system, the retrieval system and the conversion system, as applicable, shall at least take into account the following:

- a) visibility under fluoroscopy or other applicable imaging modalities;
- b) compliance with the requirements of ISO 10993-1 and other appropriate parts of the ISO 10993 series;
- c) the sterility of the systems;
- d) the ability to minimize blood loss (haemostasis);

- e) the ability to maintain adequate resistance to unintended particulate generation;
- f) the ability to meet specifications under conditions of transit and storage.

6.9 Coating on delivery system or filter

The design attributes of a coating on a delivery system or filter shall at least take into account the following:

- a) the ability of the coating to maintain adequate integrity in accordance with design specifications (e.g. freedom from significant delamination, flaps and bare spots);
- b) the ability of the coating to maintain adequate resistance to unintended particulate generation;
- c) conformance of the coating dimensions, functional requirements (e.g. lubricity) and other coating parameters (e.g. porosity, density, distribution) to the design requirements.

6.10 Absorbable filter or coating

The design attributes of an absorbable filter, and a filter containing an absorbable component or an absorbable coating, shall at least take into account the following:

- a) the ability to degrade or absorb as designed over time;
- b) appropriate mechanical properties over time;
- c) the ability of the absorbable filter, absorbable component or absorbable coating to maintain adequate resistance to unintended particulate generation over time;
- d) the potential biological effects of degradants;
- e) the ability to safely use MRI on a patient with an absorbable filter or filter with absorbable coating without negatively affecting the absorbable properties (e.g. due to heating).

7 Materials

The requirements for materials of ISO 14630:2012, Clause 6 apply. Additional testing specific to certain materials should be performed to determine the appropriateness of the materials 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.

NOTE Additional information regarding nitinol materials can be found in ASTM F2063 and ASTM F2082.

8 Design evaluation

8.1 General

The requirements of ISO 14630:2012, Clause 7, apply. A risk analysis shall be carried out in accordance with the requirements of ISO 14971.

Because optional filters can be used as permanent filters, testing appropriate for a permanent filter shall be conducted for optional filters. Additional testing is appropriate for optional filters.

If the convertible filter can be used as a permanent filter, testing appropriate for a permanent filter system shall be conducted. If part of the convertible filter is retrieved, testing appropriate for an optional filter system shall be conducted. If the convertible filter is intended to function as a stent after conversion, the requirements of ISO 25539-2 are applicable after conversion. If the convertible filter is not intended to function as a stent after conversion, additional testing addressing the risks associated with the remaining implant can be appropriate.

The requirements and testing described in ISO 10555-1 and ISO 10555-3 can apply to the design evaluation of a delivery system, retrieval system or conversion system.

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

- device description (e.g. physical description, materials of construction), what the device key design features are intended to do and how the key design features accomplish the intended objective;
- intended clinical use (see [4.4](#));
- device implantation procedures;
- conditions of use/intended in vivo environment;
- minimum design life of the device.

A device evaluation strategy shall be created. A device evaluation strategy provides the rationale for the testing selected to evaluate the filter system, retrieval system or conversion system, based on the requirements of the device design and potential failure modes. The device evaluation strategy may be communicated in a table (device evaluation strategy table) as described in [Annex A](#). Alternative methods for presenting the device evaluation strategy may be used (e.g. a non-tabular presentation of the rationale for the testing based on the potential risks and benefits of the various systems for the intended clinical use).

Emerging-technologies associated with the intended clinical use should be evaluated following the requirements of this document, where appropriate. The device evaluation strategy should identify testing needed beyond the scope of this document to characterize these systems.

NOTE 1 All testing in this document are not necessarily appropriate for all within scope systems or intended clinical uses.

Whenever changes are made in materials, construction, configuration, intended clinical use or processing methods, an appropriate analysis of the potential impact of the change on the potential failure modes and performance of the system shall be performed. This evaluation may be communicated using appropriate tables as described in [Clause A.2](#). Appropriate testing shall be conducted as deemed necessary, considering the potential impact on device performance of the change.

The use of a comparator device may be considered in the evaluation of certain design attributes, particularly for design iterations.

The device design evaluation should be appropriate for the conditions of use described in the design concept and in the IFU. Though not required for the design evaluation, testing beyond these limits may be considered to characterize the changes in device performance (e.g. durability, proper positioning, orientation) as a function of use outside of the recommended conditions (e.g. sizing). Information obtained from such testing can be useful in establishing acceptance criteria and in identifying appropriate warnings or precautions in the IFU for physician users.

Testing to establish the labelled shelf-life shall be conducted by repeating appropriate tests after aged conditions, where applicable. Justification for the selection of tests shall be provided. Generally, this will not include long-term durability testing, unless the materials of construction are susceptible to degradation that cannot be evaluated through shorter-term testing, or other tests that measure parameters that are not expected to be affected by aging (e.g. MRI safety testing, corrosion testing).

NOTE 2 Additional information regarding shelf-life can be found in ASTM F2914.

8.2 Sampling

A sampling plan shall be utilized which ensures adequate representation of the design has been obtained for each characteristic measured. It should be verified that the design attributes of the filter system, retrieval system or conversion system are representative of the devices to be released for distribution including all sizes, configurations and components.

The sampling shall fully represent the range of device sizes and does not necessarily require testing of each size. It can be necessary to conduct an analysis to identify the size(s) of the device with the greatest potential for failure.

Multiple approaches to sample selection should be considered, depending on whether there are differences in relevant attributes of different device sizes (e.g. strut thickness, length, diameter) and the parameter under test (e.g. radial force).

The samples selected for each test shall represent adequately challenging case(s). Consideration shall be given to filter size and orientation, delivery system sizes (diameter and length) and implant conditions (e.g. intended vena cava size and shape). It can be necessary to conduct an analysis to identify the samples with the greatest potential for failure under specified implant conditions.

A rationale should be provided for sample selection. For all tests, the number of samples should be justified.

8.3 Conditioning of test samples

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

Samples should be subjected to conditions that are normally encountered that can affect the performance of the device and test results. Examples of conditioning are preparation of the filter system, loading of the filter inside the delivery system, tracking of the filter system through relevant simulated tortuous vasculature and deployment of the filter.

8.4 Reporting

For the purposes of this document, reporting refers to submission to a national regulatory authority.

The design evaluation report should include an appropriate table of contents and four main sections: a background, an executive summary, individual test summaries and appendices that include the device evaluation strategy and the detailed reports. Pages should be numbered sequentially throughout the document (including appendices).

- a) The background section should describe the device design concept.
- b) The executive summary should include:
 - a description of the bench testing and analyses that have been performed;
 - a summary of the device evaluation strategy, including justification for the omission of tests identified in this document;
 - a table to summarize the testing completed, with the following columns: name of test, test purpose, test sample description, number of samples, acceptance criteria, summary of results and conclusions, and cross references to the test summary and full test report;
 - a summary conclusion statement.
- c) Individual test summaries should include:
 - a brief summary of the purpose, methods and results;
 - the significance of the test results:
 - for tests with acceptance criteria, justification for the criteria; or
 - for characterization tests, an explanation of the relevance of the results.
- d) Individual test reports should include the following information:
 - purpose: state the purpose of the test as it corresponds to this document;

- materials: list significant materials (e.g. test articles with lot/serial numbers or other appropriate means of traceability, critical equipment) used in performing the test, using figures and diagrams as appropriate;
- sampling: state the sampling plan, including the basis for and the number of samples tested; selection of test articles shall be justified (e.g. sizes, conditioning);
- acceptance criteria, if applicable: state the criteria for the test results, including justification and/or clinical relevance; clinical applicability of the acceptance criteria shall take into consideration the anatomical and physiological conditions of the intended use;
- test method: describe in detail the method used to perform the test, including any prospectively defined inspection procedures, and provide a justification for relevant test parameters;
- protocol deviations: describe any deviations and their potential significance on the interpretation of the results;
- expression of results: report testing results expressed in units as indicated in the test method;
- discussion, if applicable: include a discussion on the potential clinical significance of the results;
- conclusions: state conclusions, based on comparing results to acceptance criteria or provide an explanation of the relevance of the results for characterization tests.

8.5 Bench and analytical tests

8.5.1 General

Testing of the filter system, the filter, the filter retrieval system and the filter conversion system shall be conducted to evaluate the design attributes in [Clause 6](#), as applicable. The appropriate tests to evaluate each design attribute are based on the potential associated failure modes, device effects of failure and clinical effects of failure. The rationale for the requirements specified in this document for the bench tests and analytical analyses to assess device performance is described in [Annex A](#).

8.5.2 Filter system

8.5.2.1 General

The ability of the filter system to permit safe and consistent delivery, deployment and withdrawal shall be assessed.

The associated device/procedure related functions, potential failure modes and potential device effects of failure and clinical effects of failure to be considered are listed in [Table A.3](#).

Testing shall include the items listed in [8.5.2.2](#) to [8.5.2.6](#), as appropriate to the design of the filter system.

8.5.2.2 Dimensional verification and component dimensional compatibility

Determine the filter system dimensions, including the usable or working length, profile, and all other appropriate dimensions, for conformance with design specifications, and determine the dimensions for compatibility with the dimensions of recommended accessories.

8.5.2.3 Force to deploy

Determine the force to deploy the filter under simulated anatomical conditions. All applicable steps of the deployment process (e.g. filter release, delivery system retraction) as specified in the IFU should be evaluated.

NOTE The force to deploy can be used to help establish relevant tensile strength acceptance criteria.

8.5.2.4 Simulated use

8.5.2.4.1 General

Evaluate the performance of the filter system with accessory devices specified in the IFU and using a model(s) that simulate(s) the intended use conditions.

8.5.2.4.2 Ability to deliver

Evaluate the ability of the filter system to be advanced through the introducer sheath. Torquability shall be assessed for designs that require significant rotational control.

8.5.2.4.3 Ability to deploy

8.5.2.4.3.1 General

Evaluate the ability of the filter system to deploy the filter.

8.5.2.4.3.2 Deployment accuracy

Evaluate the accuracy of the filter deployment in relation to the intended target site.

8.5.2.4.3.3 Deployed configuration

Evaluate the ability of the filter to take the proper configuration and orientation (e.g. without unacceptable tilting) following deployment from the filter system.

8.5.2.4.4 Ability to withdraw

Evaluate the ability of the filter system to be withdrawn from the anatomical model(s), post filter deployment.

8.5.2.4.5 Compatibility

Evaluate the compatibility of the filter system with accessory devices.

8.5.2.4.6 Contrast injection

Evaluate the ability to perform a contrast injection via the delivery system, as applicable.

8.5.2.5 Tensile bond strength

Determine the tensile bond strength of the joints and/or fixed connections of the filter system. Evaluate the strength of the segments adjacent to the bonds of the filter system separately or concurrently with the bond strength determination.

The acceptance criteria for the bond strength(s) should take into consideration the expected forces applied to the filter system during clinical use [e.g. tracking (access and withdrawal) and deployment].

NOTE The force to deploy can be used to help establish relevant bond strength acceptance criteria.

8.5.2.6 Torsional bond strength

Evaluate the torsional strength of the joints and/or fixed connections in the segments of the filter system that are subjected to torsion during clinical use, or provide justification if torsion is not applicable based on the intended clinical use. Evaluate the torsional strength of the segments adjacent to the bonds of the filter system separately or concurrently with the torsional bond strength evaluation. The results shall be evaluated in relation to the torque necessary to access, deploy and withdraw the system, if applicable based on the intended clinical use.

8.5.3 Vena cava filter

8.5.3.1 General

The ability of the implant to filter blood for clots without causing caval occlusion shall be assessed.

The associated device/procedure related functions, potential failure modes and potential device and clinical effects of failure to be considered are listed in [Table A.4](#).

Testing shall include the items listed in [8.5.3](#) to [8.5.5](#), as appropriate to the design of the filter. The tests are grouped based on similarities in the objectives of the testing; however, tests are not repeated within multiple categories. Refer to [Annex A](#) for a complete listing of the test applicable to each design attribute.

8.5.3.2 Clot trapping

Determine the ability of the filter to capture clots, demonstrating that the device can capture clinically significant emboli, yet still permit sufficient blood flow around trapped emboli without caval occlusion. Clinically significant emboli, usually described as the numbers of clots at various sizes (e.g. diameters and lengths), shall be determined and justified by the manufacturer. The clot-trapping ability of the filter shall also be challenged in non-optimal positions (e.g. tilted) to determine the sensitivity of the design. Refer to References [\[48\]](#), [\[52\]](#), [\[73\]](#), [\[75\]](#), [\[80\]](#), [\[82\]](#) to [\[86\]](#) and [\[104\]](#) to [\[106\]](#) for more information on clot trapping.

8.5.3.3 Corrosion

Evaluate the susceptibility of a filter with metallic materials to corrosion.

The corrosion mechanisms can include pitting, fretting, crevice and galvanic corrosion. Each corrosion mechanism should be evaluated for specific filter designs, as appropriate.

In cases where different metals can be in contact by virtue of the device design or IFU, galvanic corrosion shall be assessed (e.g. radiopaque markers). Corrosion assessment includes, but is not limited to, the evaluation of test results, the review of literature and the consideration of the historical clinical performance of the material(s) under assessment. Guidance on corrosion assessment is given in a variety of sources (e.g. literature, textbooks, standards, regulatory guidance documents).

NOTE 1 Additional guidance is given in ISO 17475, ASTM F746, ASTM F2129, ASTM G5, ASTM G71, ASTM G102 and ASTM F3044.

Depending on the surface finish and the corrosion testing results, the potential detrimental clinical effect of ion release should also be considered. Guidance on ion release is given in a variety of sources (e.g. literature, textbooks, standards, regulatory guidance documents).

NOTE 2 Additional guidance is given ASTM F3306.

8.5.3.4 Fatigue and durability — Computational analyses

Calculate the magnitude and location of the maximum stresses and/or strains for each appropriate loading scenario based upon the intended clinical application and device design. Appropriate computational analysis tools, such as finite element analysis (FEA), can be used to calculate the stresses and/or strains. The stresses and/or strains can be compared to material characteristics to calculate the fatigue safety factor.

Computational analyses may also be used to establish appropriate test conditions and to select test articles for fatigue and durability testing.

8.5.3.5 Fatigue and durability — In vitro testing

8.5.3.5.1 General

Evaluate the long-term structural integrity of the filter under cyclic loading conditions that represent the in vivo environment (this can require several different test configurations).

Potential integrity failures to be assessed can include fracture and component separation. Relevant in vivo loads (e.g. compression resulting from respiration and Valsalva manoeuvre) shall be considered when evaluating fatigue and durability.

In vitro fatigue testing of the filter or the appropriately justified test article shall be performed to demonstrate durability for an appropriate and justified duration. For example, in vitro testing representing a minimum of 10 years should be conducted for permanent implants. If the intended implant duration is less than 10 years, then shorter duration fatigue testing is more appropriate, with justification.

If fatigue testing is performed to compare the durability of one filter to another filter that has clinically demonstrated durability or clinically known problems with durability, the duration of the test shall be justified.

Consideration shall be given specifically to convertible filters in both filtering and converted states.

8.5.3.5.2 General considerations

In identifying the appropriate durability tests, developing test methods and establishing acceptance criteria, consideration of the device design (e.g. geometry, material selection) and intended clinical use (e.g. implant location, disease state) is necessary. Compressive loading associated with normal respiration, Valsalva or an interaction with other native anatomy in the vicinity of the vena cava should be considered. The loading modes, magnitudes and numbers of cycles should be justified.

8.5.3.5.3 Compression fatigue and durability

Evaluated the long-term structural integrity of the filter when subjected to cyclic compressive loading conditions perpendicular to the filter axis (e.g. compression along the entire length, local compression), if applicable.

8.5.3.6 Dimensional verification of the filter

Determine the appropriate dimensions of the deployed filter for verification to design specifications.

8.5.3.7 Filter tensile strength

Determine the tensile strength of relevant components, including bond joints and/or fixed connections of the filter.

8.5.3.8 Migration resistance

Determine the pressure gradient necessary to cause a clot-loaded filter or the force necessary to cause a non-loaded filter to migrate in the cephalad direction. Also, consider determining migration resistance in the caudal direction depending upon the device design.

8.5.3.9 Magnetic resonance imaging

Using clinically relevant magnetic resonance (MR) environments (e.g. appropriate static magnetic field and spatial magnetic gradient field), evaluate the potential for

- a) magnetically induced displacement force and torque, and
- b) radiofrequency-induced (RF) heating of the filter.

Determine the appropriate MR safety term (i.e. MR safe, MR conditional or MR unsafe) as defined in ASTM F2503.

Characterize the MR image artefact produced by the filter. Describe the location and extent of the image artefact effect on the ability to visualize the device and adjacent anatomy.

NOTE 1 No acceptance criterion is needed for image artefact as the effect of the MR artefact on the usefulness of the image depends on the MR environment and the anatomical region being imaged with respect to the location of the filter. For example, although image artefact associated with an abdominal filter can affect the ability to image the lumbar spine, it would not affect the ability to image the head and neck.

NOTE 2 The MRI artefact caused by some filters can compromise the effectiveness and limit the use of MRI in patients with the implants.

Test methods for evaluating magnetically induced displacement, torque, RF heating and imaging artefact can be found in:

- ASTM F2052;
- ASTM F2213;
- ASTM F2182;
- ASTM F2119.

8.5.3.10 Radial force

Determine the force exerted on the surrounding tissue by a vena cava filter as a function of the filter diameter.

8.5.4 Optional filter

8.5.4.1 General

In addition to the attributes listed in [8.5.3.1](#), the ability of the optional filter to be safely, consistently and accurately retrieved shall be assessed.

The associated device/procedure related functions, potential failure modes and potential device and clinical effects of failure to be considered are listed in [Table A.5](#).

Testing shall include the items listed in [8.5.4.2](#) to [8.5.4.4](#), as appropriate to the design of the optional filter.

8.5.4.2 Filter tensile strength

Determine the tensile strength of relevant components, including bond joints and/or fixed connections of the filter.

8.5.4.3 Force to retrieve

Determine the force to retrieve the vena cava filter in an anatomical model, using the retrieval system as specified in the IFU, if applicable.

8.5.4.4 Simulated use

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

Evaluate the ability to be engaged during retrieval and the ability to be retrieved using an anatomical model(s) that is (are) representative of the anatomical variation in the intended patient population.

8.5.5 Convertible filter

8.5.5.1 General

In addition to the attributes listed in [8.5.2.1](#), the ability of the convertible filter to be safely, consistently and accurately converted shall be assessed, including the use of the conversion system as specified in the IFU, as applicable. The associated device/procedure related functions, potential failure modes and potential device and clinical effects of failure to be considered are listed in [Table A.6](#).

Testing shall include the items listed in [8.5.4.2](#) to [8.5.4.4](#), as appropriate to the design of the convertible filter.

8.5.5.2 Filter tensile strength

Determine the tensile strength of relevant components, including bond joints and/or fixed connections of the filter.

8.5.5.3 Force to convert

Determine the force to convert the vena cava filter in an anatomical model, using the conversion system as specified in the IFU, as applicable.

8.5.5.4 Simulated use

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

Evaluate the ability to be engaged during conversion and the ability to be converted to the proper configuration, using an anatomical model(s) that is (are) representative of the anatomical variation in the intended patient population.

8.5.6 Retrieval system

8.5.6.1 General

The ability of the retrieval system to permit safe and consistent retrieval of the filter shall be assessed.

The associated device/procedure related functions, potential failure modes and potential device effects of failure and clinical effects of failure to be considered are listed in [Table A.7](#).

Testing shall include the items listed in [8.5.6.2](#) to [8.5.6.6](#), as appropriate to the design of the retrieval system.

8.5.6.2 Dimensional verification and component dimensional compatibility

Determine the retrieval system dimensions, including the usable or working length, profile and all other appropriate dimensions, for conformance with design specifications and determine the dimensions for compatibility with the dimensions of recommended accessories.

8.5.6.3 Force to retrieve

Determine the force to retrieve the filter in an anatomical model using the retrieval system as specified in the IFU.

8.5.6.4 Simulated use

8.5.6.4.1 General

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

Evaluate the ability to be advanced through the introducer sheath, engage the filter, retrieve the filter and withdraw the retrieval system (including filter, if applicable) using an anatomical model(s) that is (are)

representative of the anatomical variation in the intended patient population. Evaluate the compatibility of the retrieval system with accessory devices.

8.5.6.4.2 Contrast injection

Evaluate the ability to perform a contrast injection via the retrieval system, as applicable.

8.5.6.5 Torsional bond strength

Evaluate the torsional strength of the joints and/or fixed connections in the segments of the retrieval system that are subjected to torsion during clinical use. Evaluate the torsional strength of the segments adjacent to the bonds of the retrieval system separately or concurrently with the torsional bond strength evaluation. The results shall be evaluated in relation to the torque necessary to access, retrieve and withdraw the system. Alternatively, provide justification if torsion is not applicable based on the intended clinical use.

8.5.6.6 Tensile bond strength

Determine the tensile bond strength of the joints and/or fixed connections of the retrieval system. Evaluate the strength of the segments adjacent to the bonds of the retrieval system separately or concurrently with the bond strength determination.

The acceptance criteria for the bond strength(s) should take into consideration the expected forces applied to the retrieval system during clinical use [e.g. tracking (access and withdrawal) and retrieval].

NOTE The force to retrieve can be used to help establish relevant bond strength acceptance criteria.

8.5.7 Conversion system

8.5.7.1 General

The ability of the conversion system to permit safe and consistent conversion of the filter shall be assessed.

The associated device/procedure related functions, potential failure modes and potential device effects of failure and clinical effects of failure to be considered are listed in [Table A.8](#).

Testing shall include the items listed in [8.5.6.2](#) to [8.5.6.6](#), as appropriate to the design of the conversion system.

8.5.7.2 Dimensional verification and component dimensional compatibility

Determine the conversion system dimensions, including the usable or working length, profile and all other appropriate dimensions, for conformance with design specifications and determine the dimensions for compatibility with the dimensions of recommended accessories.

8.5.7.3 Force to convert

Determine the force to convert the filter in an anatomical model using the conversion system as specified in the IFU, if applicable.

8.5.7.4 Simulated use

8.5.7.4.1 General

Evaluate conversion using a model(s) that simulate(s) the intended conditions.

As applicable, evaluate the ability of the conversion system to be advanced, to engage the filter, to convert the filter and to be withdrawn using an anatomical model(s) that is (are) representative of the anatomical variation in the intended patient population. Evaluate the ability to perform a contrast injection with the filter system in place, as applicable. Evaluate the compatibility of the conversion system with accessory devices.

8.5.7.4.2 Contrast injection

Evaluate the ability to perform a contrast injection via the conversion system, as applicable.

8.5.7.5 Torsional bond strength

Evaluate the torsional strength of the joints and/or fixed connections in the segments of the conversion system that are subjected to torsion during clinical use. Evaluate the torsional strength of the segments adjacent to the bonds of the conversion system separately or concurrently with the torsional bond strength evaluation. The results shall be evaluated in relation to the torque necessary to access, convert and withdraw the system. Alternatively, provide justification if torsion is not applicable based on the intended clinical use.

8.5.7.6 Tensile bond strength

Determine the tensile bond strength of the joints and/or fixed connections of the conversion system. Evaluate the strength of the segments adjacent to the bonds of the conversion system separately or concurrently with the bond strength determination.

The acceptance criteria for the bond strength(s) should take into consideration the expected forces applied to the conversion system during clinical use [e.g. tracking (access and withdrawal) and conversion].

NOTE The force to convert can be used to help establish relevant bond strength acceptance criteria.

8.5.8 Filter system, retrieval system and conversion system

8.5.8.1 General

The associated device/procedure related functions, potential failure modes and potential device effects of failure and clinical effects of failure to be considered are listed in [Table A.9](#).

Testing shall include the items listed in [8.5.7.1](#) and [8.5.7.5](#), as appropriate to the design of all device components.

8.5.8.2 Visibility

Evaluate the ability to visualize filter and/or system radiopaque components (e.g. markers) using the imaging techniques specified in the IFU.

8.5.8.3 Biocompatibility

The biocompatibility of the filter system, the retrieval system and the conversion systems shall be evaluated in accordance with ISO 10993-1 and appropriate other parts of the ISO 10993 series. The filter should generally be tested separately from the delivery system. However, there can be some tests (e.g. thrombogenicity, implantation) where the filter and delivery system are used or tested together for at least part of the test, and these should be appropriately justified.

8.5.8.4 Sterilization assurance

Sterilization shall be ensured in accordance with appropriate international standards.

8.5.8.5 Haemostasis

Evaluate the ability of haemostatic seals or valves in the filter system, the retrieval system and the conversion system to minimize leakage of blood. This requirement is not applicable to systems that do not contain haemostatic seals or valves.

8.5.8.6 Particulate generation

8.5.8.6.1 General

Consider the potential for particulate generation and likely clinical significance that can be associated with the filter system through a risk assessment. The risk assessment should consider the potential for occurrence of adverse clinical events associated with particulate generation (e.g. stroke, pulmonary embolism) based on several factors, including the tolerance for ischemia of the end organ. The risk assessment should consider whether there are device design features that are susceptible to particulate generation (e.g. presence of an absorbable coating, hydrophilic coating) or if there is an observation during testing to indicate that there can be a higher risk of having significant particulates generated in either size or quantity (e.g. generation of visible particles during simulated use, observation of particulates or particle effects in downstream tissue beds during in vivo studies).

Document the risk assessment. If the risk assessment indicates that either acute and/or chronic particulate generation does not require further evaluation based on the level of risk, the risk assessment documentation is sufficient to address the particulate generation requirement. If the risk assessment indicates that the potential for acute and/or chronic particulate generation and likely clinical significance exists, acute and/or chronic testing shall be conducted, as applicable. It is not expected that particulates will always need to be characterized beyond size and quantity. Depending on the quantified particulate test results and associated clinical risk, additional particulate characterization (e.g. chemical identification, crystallinity, morphology) and identification of the particulate source can be appropriate.

8.5.8.6.2 Acute particulate generation

Characterize the particles generated acutely from the filter system, the retrieval system and the conversion system that can be associated with advancement, deployment, retrieval, conversion and withdrawal.

8.5.8.6.3 Chronic particulate generation

Characterize the particles generated over time from the filter that can be associated with designs that are susceptible to particulate generation over time (e.g. absorbable, coated).

8.5.9 Coating on the delivery system, the retrieval system, the conversion system or the filter

Based on the potential associated failure modes, device effects of failure and clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with a coating on a delivery system or filter and conduct testing to address the risks identified in the assessment. Testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

Selection of the appropriate tests for a filter coating (i.e. an implant coating such as a surface coating or surface modification) should take into account the overall requirements described herein as well as the potentially relevant evaluations described in ISO 25539-4, which describes numerous coating varieties and methods of characterization that should be selected based on their relevance to both the utilized coating process and this intended filter application. Although ISO 25539-4 considers an oxide layer to be a coating, it is expected that the testing described in this document would be adequate to fulfil the requirements described in ISO 25539-4 for a filter with an oxide layer.

8.5.10 Absorbable filter or coating

Based on the potential associated failure modes, the device effects of failure and the clinical effects of failure, identify the appropriate testing to evaluate the specific design attributes associated with an absorbable filter or a filter containing an absorbable coating and conduct testing to address the risks identified in the assessment. Testing shall be identified as part of the device evaluation strategy and shall include an assessment of shelf-life.

Not all testing parameters described in this document are applicable to absorbable filters. Selection of the appropriate tests should take into account this document and ISO/TS 17137 which includes requirements and testing applicable to absorbable implants.

8.6 Preclinical in vivo evaluation

8.6.1 Purpose

The purpose of preclinical in vivo testing is to evaluate the deployment of the filter, the biological response of the host to the filter, the effect of the implant environment on the filter, and the retrieval or conversion of the filter. Preclinical in vivo testing should provide data pertaining to safety. If the objective of an animal study can be met through alternative means (e.g. through reference to previously conducted animal and/or clinical studies), the use of previously obtained data or other supportive information shall be justified. The justification should include comment on the relevance of any differences between the subject device and the device used in the previous study and the relevance of any differences in the intended uses. Multiple studies may be conducted to address all the relevant specific aims for a particular filter system, a retrieval system and/or a conversion system.

8.6.2 Specific aims

Specific aims of the study shall be stated in the protocol. More than one study may be used to address these aims which can include the following:

- a) to evaluate the ability to access the target location with the filter system;
- b) to evaluate the handling, the ease of use, the visualization of the filter system, the visualization of the filter and the visualization of caval perforation/penetration;
- c) to evaluate the deliverability of the filter to the intended implant location;
- d) to evaluate the accuracy of deployment including adequate fixation;
- e) to evaluate the ability to withdraw the delivery system;
- f) to evaluate the position, patency and structural integrity of the filter acutely and at explant;
- g) to evaluate the ability to access the intended retrieval or conversion location with the retrieval system or the conversion system (if applicable);
- h) to evaluate the handling, the ease of use and the visualization of the retrieval system or the conversion system (if applicable);
- i) to evaluate the ability and ease of retrieving or converting the filter (if applicable);
- j) to evaluate the ability to withdraw the retrieval system or conversion system, with any removed previously implanted components following retrieval or conversion (if applicable);
- k) to evaluate the functional haemostasis of the delivery system, the retrieval system or the conversion system, as applicable;
- l) to conduct gross and histopathological evaluation of explants and pertinent tissues/organs including the following:
 - evaluate local effects after implantation (e.g. caval wall response, thrombogenicity, haemorrhage, filter extending outside cava wall);
 - evaluate regional effects after implantation (e.g. clinical perforation/penetration, potential downstream effects in lungs);
 - evaluate systemic effects after implantation (e.g. necropsy);
- m) to consider the end points that can be used to help address the requirements of the ISO 10993 series;
- n) to record failure modes, device and clinical effects of failure (see [Annexes A, B and C](#) for potential failure modes and effects of failure) and adverse events.

Although the evaluation of failure modes such as structural failure of the filter is not always a specific aim of an animal study, recording and addressing the associated observations is appropriate.

8.6.3 Protocol considerations

Each filter system, retrieval system and/or conversion system shall be tested by implantation of the filter at the intended, or an analogous, vena cava site in a reasonable number of animals for an adequate duration of time (e.g. 12 weeks) to accomplish the specific aims of the study. A control can be appropriate for comparison purposes. For retrievability, an appropriate duration prior to filter retrieval shall be justified. Similarly, for conversion studies, an appropriate duration prior to conversion shall be justified. 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 should be of clinical quality and size and of the design intended for clinical use.

Interpretation of animal study results can be enhanced by the use of at least a small number of control animals or control devices for comparison purposes. A rationale should be provided if a control is not used in the study.

All animals in the study shall be regularly examined. Histological and pathological assessment of explants and appropriate tissues/organs shall be completed. If an animal either dies or must be sacrificed prior to scheduled termination, it shall be subjected to immediate post-mortem examination. The cause of death or illness, and the extent to which the implant was implicated shall be documented. Information for all animals implanted with either test or control filter, including those excluded from the final analyses, shall be recorded and included in the test report.

The design of the preclinical in vivo testing, including the experimental protocol, measurement methods and data analysis, shall be documented. In addition, the choice of animal model, such as species, gender, age, weight, shall be justified and shall be consistent with the study objectives. Implantation, and as applicable retrieval or conversion, shall be consistent with the instructions for use, as far as permitted by the limitations of the animal model. In particular, the filter sizing with respect to the IVC should be as close to the indicated sizing as possible in order to realistically simulate implantation conditions.

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

8.6.4 Data acquisition

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

- a) identification data:
 - 1) species;
 - 2) source of animal;
 - 3) animal identification;
 - 4) sex;
 - 5) approximate age;
 - 6) mass;
- b) pre-operative data:
 - 1) the verification of satisfactory health status;
 - 2) medication (e.g. prophylactic antibodies);
- c) operative data:
 - 1) the date of procedure;

- 2) the name of person(s) performing procedure;
- 3) the implant and procedure information including:
 - i) the identification of filter system, retrieval system and/or conversion system;
 - ii) the identification of accessory devices;
 - iii) the filter identification number;
 - iv) the diameter(s) of recipient vessel(s), including major and minor axes before and after implant;
 - v) the use of any medications;
 - vi) the implant location;
 - vii) the access site;
 - viii) the use of systemic antiplatelet/anticoagulant therapy;
- 4) the assessment of parameters specified in the protocol, such as:
 - i) the ability to access the target site with the filter system (e.g. pushability, flexibility, torquability, trackability as applicable);
 - ii) the ease and ability to accurately deploy the filter, including adequate fixation;
 - iii) the ability to visualize the delivery system, the filter and the retrieval or conversion system as applicable;
 - iv) the ability to withdraw the delivery system;
 - v) the compatibility with accessory devices;
 - vi) blood loss (e.g. amount and location);
 - vii) functional haemostasis of the delivery system and the retrieval or conversion system as applicable;
 - viii) position (e.g. location, tilt), patency, integrity and absence of abnormalities (e.g. filter damage) at pre-specified intervals;
 - ix) the ability to access the intended retrieval and conversion location with the retrieval system and conversion system (if applicable);
 - x) handling and visualization of the retrieval system and conversion system (if applicable);
 - xi) the ability to retrieve or convert filter (if applicable);
 - xii) the ability to withdraw the retrieval system and conversion system, with any removed previously implanted components following retrieval or conversion (if applicable);
 - xiii) the observed device and clinical effects of failure and adverse perioperative events, including severity, management and outcome;
 - xiv) any significant deviation from the proposed deployment instructions or protocol;
- 5) description of the explant procedure including:
 - i) the identification of retrieval system, conversion system and accessory devices (if applicable);
 - ii) the filter identification number;
 - iii) the diameter(s) of the recipient vessel(s);

- iv) the description of filter formation;
 - v) the location of filter prior to explant;
 - vi) the access site for retrieval or conversion (if applicable);
- d) post-operative and follow-up data:
- 1) post-operative duration at the time of follow-up;
 - 2) medications, including those that affect coagulation;
 - 3) the assessments of structural integrity, the position of the filter (e.g. location, tilt, caval perforation/penetration), including the method and date of visualization;
 - 4) the observed device and clinical effects of failure and adverse events (e.g. clinical perforation/penetration, including date of occurrence, severity, management and outcome);
 - 5) the assessment of other parameters specified in the protocol;
 - 6) any significant deviation from protocol;
- e) termination data:
- 1) the date of sacrifice;
 - 2) the reason for early termination or death (if applicable);
 - 3) the name of person(s) performing procedures and assessments;
 - 4) the assessments of structural integrity, patency and position of filter, including the method of visualization;
 - 5) the assessment of other parameters specified in the protocol;
 - 6) the gross alteration in the dimensional and physical properties of the filter;
 - 7) the gross and histopathological assessment of explants and appropriate surrounding and distal tissues/organs.

8.6.5 Test report and additional information

Results of all animals enrolled in the protocol shall be recorded and reported, even if excluded from the final analysis.

The test report shall include the following:

- a) the study protocol;
- b) the rationale for selection of the following:
 - 1) animal model, including species, gender, age and weight;
 - 2) implantation site;
 - 3) the control for comparison or rationale for not using a control group (if applicable);
 - 4) implantation periods;
 - 5) methods of assessment;
 - 6) intervals of observation;

- 7) sample size (i.e. number of animals and implants);
- c) results:
- 1) animal accountability, including rationale for exclusion of data from the primary analysis;
 - 2) the number of filters successfully implanted and the number of filters unsuccessfully implanted;
 - 3) the number of filters successfully retrieved or converted, and the number of filters not successfully retrieved or converted, as applicable;
 - 4) the operator's assessment of ease of deployment, visualization and handling;
 - 5) the discussion of sizing and potential impact on study results;
 - 6) a summary of any changes in position, structural and material integrity and patency of the filter;
 - 7) a summary of device and clinical effects of failure and adverse events;
 - 8) a summary of unexpected deaths or early terminations, with discussion of post-mortem pathological evaluation, suspected aetiology and the potential for the death to be related to the device;
 - 9) a summary of animal health including scheduled examinations, clinical observations, clinical pathology values and weight gain or loss;
 - 10) a summary of gross pathology evaluation and histopathology of explants and appropriate tissues/organs, including gross photographs, radiographs of explants and representative photomicrographs;
 - 11) a summary of other information required by the protocol;
 - 12) significant and/or relevant deviations from protocol;
 - 13) a comparison of outcomes for test and control groups (if applicable);
 - 14) conclusions from the study;
 - 15) a summary of quality assurance and data auditing procedures.

8.7 Clinical evaluation

8.7.1 Purpose

The purpose of clinical evaluation is to assess the safety and effectiveness of the filter system, the retrieval system and/or the conversion system. An investigation shall be carried out for each new filter or new clinical application of a filter using the principles given in ISO 14155 or an equivalent reference. Significant design changes that can impact safety and performance shall require clinical evaluation if determined to be necessary based on an appropriate risk assessment. This evaluation may follow the requirements described in this document or the abbreviated requirements as appropriate to address the identified risks. Additional filter sizes outside the previously evaluated range can require clinical evaluation but does not always require assessment consistent with all requirements (e.g. multicenter study, statistically powered sample size).

If an objective of a clinical study can be met through alternative means (e.g. through reference to previously conducted clinical studies), the use of previously obtained data or other supportive information shall be justified. The justification should include comment on the relevance of any differences between the subject device and the device used in the previous study and the relevance of any differences in the intended uses.

The principles of [8.7](#) may be applied for the clinical evaluation of filters for uses other than in the inferior vena cava. Additional specific aims, end points and reporting requirements can be needed to define an appropriate study.

8.7.2 Specific aims

Specific aims of the study shall be based on an appropriate risk assessment for the filter system, the retrieval system and/or the conversion system stated in the protocol. The specific aims may include the following:

- a) to evaluate the performance of the filter system, the retrieval system or the conversion system, such as:
 - 1) the ability to access the target location with the filter system;
 - 2) the handling and visualization of the filter system and visualization of the filter and caval perforation/penetration;
 - 3) the accuracy of deployment, including adequate fixation;
 - 4) the ability to withdraw the delivery system;
 - 5) the position, patency and structural integrity of the filter acutely and over time;
 - 6) the appropriateness of filter sizing;
 - 7) the ability to access the intended retrieval or conversion location with the retrieval system or conversion system (if applicable);
 - 8) the handling and visualization of the retrieval system or conversion system (if applicable);
 - 9) the ability to retrieve or convert the filter (if applicable);
 - 10) the ability to withdraw the retrieval system or conversion system, with any removed previously implanted components following retrieval or conversion (if applicable);
 - 11) the device effects of failure (see [Annex C](#) for potential effects of failure);
- b) to evaluate the safety of the filter system, the retrieval system or the conversion system, such as:
 - 1) the clinical effects of failure (see [Annex B](#) for potential clinical effects of failure);
 - 2) adverse events.

8.7.3 Protocol considerations

A multicenter study shall be performed at a minimum of three investigational sites. A justification for the number of investigational sites shall be provided.

A specific question or set of questions (i.e. hypotheses) shall be defined prospectively. These questions shall delineate the appropriate safety (e.g. freedom from major adverse events), effectiveness (e.g. technical success in absence of serious device related events) or combined safety and effectiveness end points to be measured. Definitions of success and failure for each end point and the duration of follow-up needed to assess each end point shall be specified. A definition for the study success shall also be specified (e.g. meeting both the safety and effectiveness primary end points).

A statistical justification for the number of patients studied shall be provided based upon the primary hypotheses. Preferably no investigational site should enroll more than 35 % of the total number of study subjects.

The duration of the patient follow-up shall be determined in relation to the objectives of the clinical investigation. Patient follow-up intervals shall include a minimum of an assessment at discharge and at the specified study duration. A justification will be required for follow-up intervals. All patients enrolled in the study, including those excluded from the primary end point analyses, shall be recorded and reported. The final report may be completed when the required number of patients to test the hypotheses have reached the specified study duration. The report shall include current follow-up data on all patients. Longer-term patient follow-up (e.g. 2 years to 5 years after the filter has been implanted) can be appropriate for the post-market clinical assessment of device designs with a limited history of clinical use.