INTERNATIONAL STANDARD

ISO 25539-4

First edition
2021-11

Cardiovascular implants — Endovascular devices —

Part 4: Application of ISO 17327-1 for coated endovascular devices

Reference number
ISO 25539-4:2021(E)

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword

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

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

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation 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 SC 2, *Cardiovascular implants and extracorporeal systems*.

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

ISO 17327-1 has a broad scope, including all non-active surgical implants, and thus only some of the requirements in ISO 17327-1 are applicable to coated endovascular devices. This document clarifies how ISO 12417-1, ISO/TS 17137, ISO 25539-1, ISO 25539-2, and ISO 25539-3 satisfy the requirements of ISO 17327-1. A device evaluation strategy is needed to identify the appropriate evaluation of specific coated devices.

It is recognized by this ISO committee that many coated endovascular devices have been shown to be safe and effective in clinical use. This document does not intend to require additional evaluation of these devices to comply with this document as the testing does not provide useful information regarding the expected clinical performance of the device. Manufacturers may rely on historical data gathered under the guidance of ISO 25539-1, ISO 25539-2, and ISO 25539-3. Similarly, for device modifications or changes in intended clinical use, this document does not intend to require additional evaluation of any aspects of the device that are not expected to change the clinical performance.

Cardiovascular implants — Endovascular devices —

Part 4: Application of ISO 17327-1 for coated endovascular devices

1 Scope

This document specifies the appropriate application of ISO 17327-1:2018 to coated endovascular prostheses, vascular stents, and vena cava filters. This document is intended to be used as a supplement to ISO 25539-1, ISO 25539-2, ISO 25539-3, ISO 12417-1 and ISO/TS 17137.

The following coatings are within the scope of ISO 17327-1 and addressed in this document for endovascular devices: drug coatings (eluting and non-eluting), non-drug coatings (absorbable and non-absorbable), and chemistry-related surface modifications (oxide, such as TiO_2, and non-oxide, such as amorphous silicon carbide and diamond-like carbon).

This document is not applicable to coated delivery systems or coated ancillary devices (e.g. guidewires), as these coatings are not within the scope of ISO 17327-1, which is specifically directed to implant coatings.

This document is not applicable to coverings of endovascular devices; however, if the covering of a device is coated, it is within the scope of this document.

This document does not address the requirements for, and the evaluation of, viable tissues and non-viable biologic materials used as implant coatings.

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 12417-1:2015, *Cardiovascular implants and extracorporeal systems — Vascular device-drug combination products — Part 1: General requirements*

ISO/TS 17137:2021, *Cardiovascular implants and extracorporeal systems — Cardiovascular absorbable implants*

ISO 17327-1:2018, *Non-active surgical implants — Implant coating — Part 1: General requirements*

ISO 25539-1:2017, *Cardiovascular implants — Endovascular devices — Part 1: Endovascular prostheses*

ISO 25539-2:2020, *Cardiovascular implants — Endovascular devices — Part 2: Vascular stents*

ISO 25539-3:2011, *Cardiovascular implants — Endovascular devices — Part 3: Vena cava filters*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 12417-1:2015, ISO/TS 17137:2021, ISO 17327-1:2018, ISO 25539-1:2017, ISO 25539-2:2020, ISO 25539-3:2011 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
implant coating
surface coating or surface modification

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]

4 Requirements for coating properties

4.1 General

Subclauses 4.2, 4.3, and 4.4 address the requirements as related to ISO 17327-1 for vascular stents, endovascular prostheses and vena cava filters, respectively. The coating types identified in Table 1 are addressed in this document. A device can have multiple coatings, each of which can be identified as different or multiple coating sub-types. For example, a drug eluting stent with an absorbable matrix can fit into eluting and absorbable coating sub-types.

Table 1 — Coating types addressed by this document

Coating category	Coating sub-type I	Coating sub-type II
Drug	Eluting	Non-eluting
Non-drug	Absorbable	Non-absorbable
Chemistry-related surface modifications	Oxide	Non-oxide

Evaluations identified in ISO 17327-1 will possibly not always be appropriate for all coated endovascular prostheses, vascular stents and vena cava filters. The device evaluation strategy described in ISO 25539-1 and ISO 25539-2 guides the development of the rationale for the testing selected to evaluate the endovascular device based on the requirements of the device design and potential failure modes. Evaluation of generic coating properties listed in ISO 17327-1 and identified as necessary by the device evaluation strategy shall be completed. Evaluation of coating properties listed in ISO 17327-1 deemed as not necessary by the device evaluation strategy do not need to be completed.

Due to the broad scope of ISO 17327-1, some terminology and associated requirements in that standard are appropriate for other types of nonactive surgical implants, but inconsistent with standard terminology and requirements for endovascular devices. In these cases, more relevant terminology and requirements are presented in this document and correlated to the requirements in ISO 17327-1. This includes the requirements for the consideration of adhesion strength and coating abrasion resistance. For the coatings and implants addressed in this document, these generic coating properties are evaluated by other tests. For example, adhesion strength is defined in ISO 17327-1:2018, as the "load per unit area required to separate the coating from the substrate." For the coatings and implants addressed in this document, coating adhesion is considered part of the assessment of maintenance of coating integrity which is evaluated through other means such as simulated use, durability, and particulate generation. Thus, the specific characterization of the adhesion strength (i.e. load per unit

area required to separate the coating from the substrate) is not required. Similarly, coating abrasion resistance is considered part of the assessment of maintenance of coating integrity.

For chemistry-related surface modifications on the devices within the scope of ISO 25539-1, ISO 25539-2, and ISO 25539-3, coating coverage integrity evaluation is addressed through corrosion testing, while corrosion resistance is not identified as a generic coating property in ISO 17327-1.

Evaluation of porosity and pore size, surface wettability, and surface texture are generally not applicable to coatings on endovascular devices. The potential need to evaluate these properties can be identified through the device evaluation strategy.

4.2 Vascular stents

In order to conform to the requirements of ISO 17327-1, the evaluation of drug coatings, non-drug coatings, and chemistry-related surface modifications of stents shall be conducted for the properties as outlined in Tables 3, 4, and 5, respectively. A description of column headings associated with Tables 3, 4, and 5 is provided in Table 2. The available test methods (non-mandatory) that can be of use in meeting the applicable requirements are provided in Tables 3, 4, and 5.

Table 2 — Description of Table 3, 4, and 5 column headings

ISO 17327-1:2018 generic coating property	Design attributes from other ISO standards corresponding to generic ISO 17327-1:2018 coating properties	Coating type			
		Coating sub-type I		Coating sub-type II	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Each generic coating property from ISO 17327-1 to be considered for characterization or evaluation.	Design attributes identified in the applicable ISO standards that correspond to the ISO 17327-1 generic coating property.	The requirements identified in the applicable ISO standard that correspond to the generic coating property or design attribute. Requirements that do not align with the ISO 17327-1 generic coating properties are not listed. Some requirements indicate the need to consider the evaluation of a property, while others indicate that the property shall be evaluated, as required by the applicable standard.	The available test methods that can be of use in meeting the applicable requirement. These test methods are not mandatory and are not limited to ISO standardized methods.	See column 3.	See column 4.

4.2.1 Drug coatings

Table 3 — Applicable requirements and informative test methods related to drug coatings

ISO 17327-1:2018 generic coating property	Design attributes from other ISO standards correlated to generic ISO 17327-1:2018 coating properties	Drug coating type			
		Eluting		Non-eluting	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Chemical composition	ISO 25539-2:2020, 6.8 Drug-eluting stent — Ability of the stent to consistently contain the desired type and amount of drug — Conformance of the residual drug quantity to design specifications for drug-eluting stents and not for drug containing stents — Freedom of the drug(s) from deleterious impurity and degradant levels at manufacture and with storage ISO 12417-1:2015, 5.2.2, d) Matrix Conformance of the matrix chemical properties to the design requirements ISO 12417-1:2015, 5.2.3, a) API Conformance of drug content, impurities, and degradants to the API specification on receipt and after storage and handling of the API during the vascular device-drug combination product (VDDCP) manufacturing process ISO 12417-1:2015, 5.2.3, d) API Conformance of drug content, drug impurities, and drug degradants to VDDCP specifications at the time of manufacture and after storage	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.3.4 Drug content ISO 12417-1:2015, 7.2.4.3.5 Drug distribution IO 12417-1:2011, 7.2.4.3.7 Drug identity and purity	Use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.3.4 Drug content ISO 12417-1:2015, 7.2.4.3.5 Drug distribution ISO 12417-1:2015, 7.2.4.3.7 Drug identity and purity	Use applicable standard(s) or other appropriate method.
Phase composition	N/A	N/A	N/A	N/A	N/A
Surface texture	N/A	N/A	N/A	N/A	N/A
Coating coverage integrity	ISO 12417-1:2015, 5.2.2, d) Matrix Conformance of other matrix parameters (e.g. distribution) to the design requirements ISO 12417-1:2015, 5.2.3, b) API Ability to reproducibly incorporate, as demonstrated by content uniformity, the desired drug and amount within the VDDCP	ISO 12417-1:2015, 7.2.4.3.5 Drug distribution	Use applicable standard(s) or other appropriate method.	ISO 12417-1:2015, 7.2.4.3.5 Drug distribution	Use applicable standard(s) or other appropriate method.

Table 3 *(continued)*

ISO 17327-1:2018 generic coating property	Design attributes from other ISO standards correlated to generic ISO 17327-1:2018 coating properties	Drug coating type			
		Eluting		Non-eluting	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Dissolvability	ISO 25539-2:2020, 6.7 Absorbable stent or coating Ability to degrade or absorb as designed over time ISO 25539-2:2020, 6.8 Drug-eluting stent Ability to release the desired amount of drug over the specified amount of time for drug-eluting stents and not for drug containing stents ISO 12417-1:2015, 5.2.1, e) General Ability of the drug-containing part of the VDDCP (DCP) to deliver or maintain the intended amount of drug safely at the target site in accordance with the specification of the VDDCP at product release and for the duration of the labelled shelf life ISO 12417-1:2015, 5.2.2, e) Matrix Ability of the matrix to control the release of drug	ISO 25539-2:2020, 8.1 Design evaluation — General ISO 12417-1:2015, 7.2.4.3.6 Drug release characterization ISO 12417-1:2015, 7.2.4.3.12 Degradable matrix	Use applicable standard(s) or other appropriate method.	N/A	N/A
Coating thickness	ISO 25539-2:2020, 6.5 Coating on delivery system or stent conformance of the coating dimensions ISO 12417-1:2015, 5.2.2, d) Matrix Conformance of the matrix dimensions to the design requirements	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.2 Testing the drug-containing part-related attributes of the VDDCP	Use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.2 Testing the drug-containing part-related attributes of the VDDCP	Use applicable standard(s) or other appropriate method.

Table 3 *(continued)*

ISO 17327-1:2018 generic coating property	Design attributes from other ISO standards correlated to generic ISO 17327-1:2018 coating properties	Drug coating type			
		Eluting		Non-eluting	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Adhesion strength and abrasion resistance	ISO 25539-2:2020, 6.5 Coating on delivery system or stent — Ability of the coating to maintain adequate integrity according to design specifications (e.g. freedom from significant delamination, flaps and bare spots) — Ability of the coating to maintain adequate resistance to unintended particulate generation ISO 12417-1:2015, 5.2.2, a) Matrix Ability of the matrix to maintain adequate integrity during procedural use and over time in accordance with the design specifications (e.g. freedom from significant delamination, flaps, and bare spots) ISO 12417-1:2015, 5.2.2, b) Matrix Ability of the matrix to maintain adequate resistance to unintended generation of particles NOTE 1 Adhesion strength as defined in ISO 17327-1 is not listed as a design attribute in ISO 25539-2 or ISO 12417-1. However, in this document, the general property of adhesion is considered to correlate with the ability of the coating to maintain adequate integrity attribute listed in each of these standards. NOTE 2 Particulate generation is not described in ISO 17327-1. However, for this document, it is considered related to abrasion resistance and adhesion strength.	ISO 25539-2:2020, 8.5.1.7 Simulated use ISO 25539-2:2020, 8.5.2.3 Fatigue and Durability – in vitro testing ISO 25539-2:2020, 8.5.1.5 Particulate generation ISO 12417-1:2015, 7.2.4.3.10 Durability	ISO 25539-2:2020, D.5.2.8 Simulated use ISO 25539-2:2020, D.5.3.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, D.5.2.6 Particulate generation ASTM F2743[1] Coating Inspection and Acute Particulate Characterization of Coated Drug-Eluting Vascular Stent Systems For chronic particulate generation, use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.5.1.7 Simulated use ISO 25539-2:2020, 8.5.2.3 Fatigue and Durability – in vitro testing ISO 25539-2:2020, 8.5.1.5 Particulate generation ISO 12417-1:2015, 7.2.4.3.10 Durability	ISO 25539-2:2020, D.5.2.8 Simulated use ISO 25539-2:2020, D.5.3.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, D.5.2.6 Particulate generation ASTM F2743[1] Coating Inspection and Acute Particulate Characterization of Coated Drug-Eluting Vascular Stent Systems NOTE While the scope of this document includes only drug-eluting vascular stents, the content can inform testing for non-eluting vascular stent systems. For chronic particulate generation, use applicable standard(s) or other appropriate method.
Porosity and pore size	ISO 25539-2:2020, 6.5 Coating on delivery system or stent Conformance of the other coating parameters (e.g. porosity) to the design requirements ISO 12417-1:2015 5.2.2, d) Matrix — Conformance of the other matrix — Parameters (e.g. porosity) to the design requirements	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.2 Testing the drug-containing part-related attributes of the VDDCP	Use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 12417-1:2015, 7.2.4.2 Testing the drug-containing part-related attributes of the VDDCP	Use applicable standard(s) or other appropriate method.
Surface wettability	N/A	N/A	N/A	N/A	N/A

4.2.2 Non-drug coatings

Table 4 — Applicable requirements and informative test methods related to non-drug coatings

ISO 17327-1:2018 generic coating property	Design attributes from other relevant ISO standards correlated to generic ISO 17327-1:2018 coating properties	Non-drug coatings			
		Absorbable		Non-absorbable	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Chemical composition	N/A NOTE ISO 25539-2:2020 has no requirement to determine chemical composition, rather ISO 25539-2:2020, 4.3 requires that materials be described by their generic or chemical names.	N/A	N/A	N/A	N/A
Phase composition	N/A	N/A	N/A	N/A	N/A
Surface texture	N/A	N/A	N/A	N/A	N/A
Coating coverage integrity	ISO 25539-2:2020, 6.5 Coating on delivery system or stent Conformance of other coating parameters (e.g. distribution) to the design requirements	ISO 25539-2:2020, 8.1 Design evaluation – General	Use applicable standard(s) or other appropriate method. NOTE This evaluation can be done as part of simulated use.	ISO 25539-2:2020, 8.1 Design Evaluation – General	Use applicable standard(s) or other appropriate method. NOTE This evaluation can be done as part of simulated use.
Dissolvability	ISO 25539-2:2020, 6.7 Absorbable stent or coating Ability to degrade or absorb as designed over time	ISO 25539-2:2020, 8.1 Design evaluation – General ISO/ TS 17137:2021, 5.1.2 General considerations	ISO/ TS 17137:2021, 5.3 in vitro degradation evaluation	N/A	N/A
Coating thickness	ISO 25539-2:2020, 6.5 Coating on delivery system or stent Conformance of the coating dimensions	ISO 25539-2:2020, 8.1 Design evaluation – General	Use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.1 Design evaluation – General	Use applicable standard(s) or other appropriate method.

Table 4 *(continued)*

ISO 17327-1:2018 generic coating property	Design attributes from other relevant ISO standards correlated to generic ISO 17327-1:2018 coating properties	Non-drug coatings			
		Absorbable		Non-absorbable	
		Applicable requirement	Applicable test method	Applicable requirement	Applicable test method
Adhesion strength and abrasion resistance	ISO 25539-2:2020, 6.5 Coating on delivery system or stent — Ability of the coating to maintain adequate integrity according to design specifications (e.g. freedom from significant delamination, flaps and bare spots) — Ability of the coating to maintain adequate resistance to unintended particulate generation ISO 25539-2:2020, 6.7 Absorbable stent or coating — Ability of the absorbable stent or absorbable coating to maintain adequate resistance to unintended particulate generation over time — Appropriate mechanical properties over time NOTE 1 Adhesion strength as defined in ISO 17327-1 is not listed as a design attribute in ISO 25539-2. However, in this document, the general property of adhesion is considered to correlate with the ability of the coating to maintain adequate integrity attribute listed in each of these standards. NOTE 2 Particulate generation is not described in ISO 17327-1. However, in this document, it is considered related to abrasion resistance and adhesion strength.	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 25539-2:2020, 8.5.1.7 Simulated use ISO 25539-2:2020, 8.5.2.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, 8.5.1.5 Particulate generation ISO/ TS 17137:2021, 5.1.2 General considerations	ISO 25539-2:2020, D.5.2.8 Simulated use ISO 25539-2:2020, D.5.3.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, D.5.2.6 Particulate generation For chronic particulate generation, use applicable standard(s) or other appropriate method. ISO/ TS 17137:2021, 5.3 in vitro degradation evaluation	ISO 25539-2:2020, 8.1 Design evaluation – General ISO 25539-2:2020, 8.5.1.7 Simulated use ISO 25539-2:2020, 8.5.2.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, 8.5.1.5 Particulate generation	ISO 25539-2:2020, D.5.2.8 Simulated use ISO 25539-2:2020, D.5.3.3 Fatigue and durability – in vitro testing ISO 25539-2:2020, D.5.2.6 Particulate generation For chronic particulate generation, use applicable standard(s) or other appropriate method.
Porosity and pore size	ISO 25539-2:2020, 6.5 Coating on delivery system or stent Conformance of the other coating parameters (e.g. porosity) to the design requirements	ISO 25539-2:2020, 8.1 Design evaluation – General ISO/ TS 17137:2021, 5.1.2 General considerations	Use applicable standard(s) or other appropriate method.	ISO 25539-2:2020, 8.1 Design evaluation – General	Use applicable standard(s) or other appropriate method.
Surface wettability	N/A	N/A	N/A	N/A	N/A