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

Implants cardiovasculaires et circuits extra-corporels — Produits de combinaison médicament-dispositif vasculaire — Partie 1~~:~~: Exigences générales

Second edition

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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 ~~documents~~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).

Field Code Changed

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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 SC 2, *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).

This second edition cancels and replaces the first edition (ISO 12417-1:2015), which has been technically revised.

The main changes are as follows:

~~— xxx xxxxxxx xxx xxxx~~

— the text regarding ethylene oxide sterilization limits has been revised,

— references have been updated, and

— terms and definitions have been revised.

A list of all parts in the ISO 12417 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

Vascular device-drug combination products (VDDCPs) are medical devices with various clinical indications for use in the human vascular blood system. A VDDCP incorporates, as an integral part, substance(s) which, if used separately, can be considered to be a medicinal substance or product (drug substance, drug product) but the action of the medicinal substance is ancillary to that of the device and supports the primary mode of action (PMOA) of the device.

Many vascular device-drug combination products have been shown to be safe and effective in clinical use. This revision is not intended to require additional evaluation of these products as the testing would not provide useful information regarding the expected clinical performance of the product. Manufacturers can rely on historical data gathered ~~under the specifications of~~ in the previous edition~~.~~ of this document (i.e. ISO 12417-1:2015). Similarly, for product modifications or changes in intended clinical use, this ~~revision~~edition of this document (i.e. ISO 12417-1:202X) is not intended to require additional evaluation of any aspects of the product that are not expected to change clinical performance.

When developing this document, it was impossible~~, when writing this part of ISO 12417,~~ to ~~take into consideration~~consider all future and emerging technologies. VDDCPs using such technologies ~~will~~ need to be evaluated following the basic requirements of this ~~International Standard.~~document. Testing beyond the scope of this ~~part of ISO 12417~~document can also be necessary to characterize these future and emerging device systems~~. Consideration shall be given to the failure modes of the VDDCP and their effects on the performance in deciding what testing will be appropriate.~~

~~For issues related to the primary mode of action (PMOA) of the vascular VDDCP, a number of International Standards given in the Bibliography can be consulted.~~

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

1 Scope

This document ~~ISO 12417~~ specifies requirements for vascular device-drug combination products (VDDCPs~~) based upon current technical and medical knowledge.~~).

With regard to safety, this ~~part of ISO 12417~~document outlines requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization, packaging~~,~~ and information supplied by the manufacturer.

For implanted products, this ~~International Standard should~~document is intended to be ~~considered~~used as a supplement to ISO 14630, which specifies general requirements for the performance of non-active surgical implants. This ~~International Standard should also~~document is intended to be ~~considered~~used as a supplement to relevant device-specific standards, such as the ISO 25539 series specifying requirements for endovascular devices. Requirements listed in this ~~part of ISO 12417~~document also address VDDCPs that are not permanent implants.

NOTE 1 Due to variations in the design of combination products covered by this ~~part of ISO 12417~~document and due to the relatively recent development of some of these combination products, acceptable standardized in vitro test results and clinical study results are not always available. As further scientific and clinical data become available, appropriate revision of this ~~part of ISO 12417~~document can be necessary.

This document applies to delivery systems or parts of the delivery system ~~if they comprise~~ that are an integral component of the vascular device and ~~if they~~that are drug-covered (e.g. drug-covered balloon catheters and drug-covered guidewires).

This document does not apply to devices whose PMOA provide a conduit for delivery of a drug (e.g. infusion catheters), unless they contain a drug component that is intended to have an ancillary action to the device part (e.g. antimicrobial coated infusion catheter).

This document does not apply to procedures and devices used prior to and following the introduction of the VDDCP (e.g. balloon angioplasty devices) ~~are excluded from the scope of this part of ISO 12417 if they~~that do not affect the drug-related aspects of the device.

This ~~part of ISO 12417~~document does not provide a comprehensive pharmacological evaluation of VDDCPs.

NOTE 2 Some information about the requirements of ~~different~~certain national and regional authorities is given in Annex B.

The connection of absorbable components of VDDCPs (e.g. coatings) ~~are addressed by this part of ISO 12417 in their connection~~ with drug-related aspects of the device are addressed in this document. This document does not provide an exhaustive list of the degradation and other time-dependent aspects of absorbable implants and coatings.

NOTE ~~See also ISO/TS 17137 and ASTM F3036-13.~~ 3 For more information on absorbable coatings, refer to ISO/TS 17137 and ASTM F3036-13.

This ~~part of ISO 12417~~document does not address issues associated with viable or non-viable biological materials such as tissues, cells~~,~~ or proteins.

This ~~part of ISO 12417~~document does not address issues associated with active surgical implants (i.e. implants that require power not generated by the human body or gravity).

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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-2, *Biological evaluation of medical devices — Part 2: Animal welfare requirements*

ISO 10993-7~~:2021/AMD 1:2019~~, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO 11070, *Sterile single-use intravascular introducers, dilators and guidewires*

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

ISO 14155, *Clinical investigation of medical devices for human subjects — Good clinical practice*

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 14971:2019, *Medical devices — Application of risk management to medical devices*

ISO 15223-1, *Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements*

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

~~NOTE See the Bibliography for additional device-specific and regional information about standards and guidance documents.~~

43 Terms and definitions

For the purposes of this document, the terms and definitions provided 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
active pharmaceutical ingredient
API
drug substance
pharmacologically active (drug or medicinal) substance used as a raw material, which is coated on, bound to or incorporated into the device to achieve an ancillary device function (e.g. minimizing vascular restenosis)

3.2

batch
quantity of ~~VDDCP~~*vascular device-drug combination product* (3.27) at the final stage or pre-final stage of manufacture which has undergone the same manufacturing cycle, using the same components (e.g. same coating solution, same device size~~),~~) and meets the same specifications

3.3
change
alteration to an activity or to the ~~VDDCP~~*vascular device-drug combination product* (3.27) to improve or maintain the composition or performance of a ~~VDDCP~~vascular device-drug combination product

Note 1 to entry: ~~This include~~Certain local regional authorities require that changes are reported, including small alterations to a ~~VDDCP~~vascular device-drug combination product, a manufacturing process~~,~~ or a test procedure, even if it is not necessarily captured by a corrective action/preventative action (CAPA) system~~, and can require reporting to local regional authorities~~.

3.4
clinical event
complication, failure~~,~~ or device-related observation that can be observed with clinical use of a ~~VDDCP~~*vascular device-drug combination product* (3.27)

Note 1 to entry: It is possible events will not have clinical significance and ~~can not~~cannot be attributable to the ~~VDDCP~~vascular device-drug combination product.

3.5
compendial pharmaceutical reference standard
~~general term covering~~ reference ~~substances~~substance, reference ~~preparations, and~~preparation or reference ~~spectra that are~~spectrum recognized by a national pharmacopoeia

3.6
device part of the vascular device-drug combination product
device part of the VDDCP
device part
DP
part of the ~~VDDCP~~*vascular device-drug combination product* (3.27) intended ~~to treat~~that treats vascular disease by temporary or long-term intervention or implantation that does not achieve its ~~PMOA~~primary mode of action in or on the human body by pharmacological, immunological~~,~~ or metabolic means, but that can be assisted in its function by such means

3.7
assay
biological or chemical method to determine the activity or potency of a substance

3.8
drug product
medicinal product
~~API,~~*active pharmaceutical ingredient* (3.1), in its final form for administration to the patient (e.g. tablet, solution, spray), that is intended to prevent, diagnose~~,~~ or treat disease and that achieves its principal intended action in or on the body by pharmacological, immunological or metabolic means

3.9
drug-containing part of the ~~VDDCP~~vascular device-drug combination product
drug-containing part
DCP
part of the ~~VDDCP~~*vascular device-drug combination product* (3.27) that consists of the ~~API~~*active pharmaceutical ingredient* (3.1) or *matrix* (3.21) and associated device interfaces intended to assist in

the ~~PMOA~~primary mode of action of the device by diminishing or ameliorating, potential unintended effects that placement of the *device part* (3.6) can potentially stimulate

Note 1 to entry: Some ~~VDDCPs~~vascular device-drug combination product can incorporate medicinal or drug substances that are primarily intended to optimize the DP properties of the ~~VDDCP~~vascular device-drug combination product.

3.10
DCP interface
drug-containing part interface
~~**DCP interface**~~
common boundary or interconnection between the various components of the *device part*(*s*) (3.6) and the *drug-containing part*(s) (3.9) of a ~~VDDCP~~*vascular device-drug combination product* (3.27)

~~EXAMPLES~~

~~a) the~~ EXAMPLE 1 Interface between the *matrix* (3.21) containing the ~~API~~*active pharmaceutical ingredient* (3.1) and packaging materials with direct ~~DCP~~drug-containing part contact~~;~~.

~~b) the~~ EXAMPLE 2 Device surface(s~~);~~).

~~c) the~~ EXAMPLE 3 Interface between the matrix and the ~~API~~active pharmaceutical ingredient.

3.11
delivery system
transport device that physically or mechanically positions the ~~VDDCP~~*vascular device-drug combination product* (3.27) and/or the ~~DCP~~*drug-containing part* (3.9) at the intended anatomic location

EXAMPLE~~:~~ The delivery system of a drug-coated balloon~~,~~ would position the balloon in the lumen of the lesion intended to be treated.

3.12
drug content
total labelled amount of ~~API in a VDDCP~~*active pharmaceutical ingredient* (3.1) in a *vascular device-drug combination product* (3.27)

Note 1 to entry: Drug content ~~may~~can be expressed as µg~~/DCP~~ per *drug-containing part* (3.9) of a certain size.

3.13
drug delivery
local interaction between the ~~VDDCP~~*vascular device-drug combination product* (3.27) drug and the in vivo environment, whether the drug is released from, eluted from, or remains bound to the ~~VDDCP~~vascular device-drug combination product

3.14
drug-related ~~impurities~~impurity
substance in the ~~DCP~~*drug-containing part* (3.9) of a ~~VDDCP~~*vascular device-drug combination product* (3.27) that is not the ~~API~~*active pharmaceutical ingredient* (3.1) or an *excipient* (3.19)

Note 1 to entry: Drug-related impurities can include drug degradation products or degradants, drug-synthesis-related impurities, isomers of the drug, residual drug solvents~~,~~ or biological contaminants (e.g. occurring with drugs derived from biological systems).

3.15
drug release characterization

in vitro characterization of the ~~API~~*active pharmaceutical ingredient* (3.1) released from the ~~DCP~~*drug-containing part* (3.9) of a ~~VDDCP~~*vascular device-drug combination product* (3.27) over time

EXAMPLE~~:~~ The release ~~may~~can be determined by a drug elution test~~,~~ and ~~may~~can include a curve shape (or profile), a drug release rate, or both.

3.16
durability
ability to maintain adequate integrity and robustness during procedural (i.e. access, deployment, withdrawal), post-procedural~~,~~ and long-term use (i.e. over time) ~~in accordance with the~~according to design specifications

3.17
efficacy
effectiveness
ability of the ~~VDDCP~~*vascular device-drug combination product* (3.27) to achieve the planned and desired physiological result

3.18
evaluate, verb
~~appraise or~~ analyse qualitatively

3.19
excipient
additional material(s), other than the ~~API,~~*active pharmaceutical ingredient* (3.1), that are intentional components of the *drug-containing part* ~~of a VDDCP~~(3.9) of a *vascular device-drug combination product* (3.27)

~~EXAMPLES:~~EXAMPLE Filler, extender, diluent, wetting agent, solvent, colorant, stabilizer, antioxidant, preservative, pH maintainer, polymers, adhesives.

3.20
functionality
ability of the ~~VDDCP~~*vascular device-drug combination product* (3.27) to perform physically, chemically, and/or mechanically, as designed

Note 1 to entry: Functionality does not include the physiological response to the ~~VDDCP (~~vascular device-drug combination product [i.e. *efficacy*~~).~~ (3.17)].

3.21
matrix
~~any~~ organic or inorganic material, other than living cells, intentionally applied by a manufacturer to a vascular device and designed for the purpose of drug storage, local drug activity at the surface and/or enabling, retarding, delaying~~,~~ or modifying drug release

Note 1 to entry: The matrix can:

— be permanent or temporary (dissolvable, absorbable or degradable);

— include surface treatments such as primers;

— be a coating with or without an ~~API,~~*active pharmaceutical ingredient* (3.1), or ~~consist~~consisting of multiple *excipients* (3.19) and/or multiple ~~APIs~~active pharmaceutical ingredients.

3.22
particulate

particle
mobile matter, other than gas bubbles, present on, or arising from the use of the ~~VDDCP~~*vascular device-drug combination product* (3.27)

3.23
pharmacokinetics
absorption, distribution, metabolism~~,~~ and elimination of a drug in vivo

3.24
procedural fluid
blood and serum, saline, and contrast media that come into contact with a ~~VDDCP~~*vascular device-drug combination product* (3.27)

3.25
stability testing
tests undertaken according to a prescribed stability protocol to establish, support~~,~~ or confirm the shelf life of a ~~VDDCP~~*vascular device-drug combination product* (3.27)

Note 1 to entry: Additional guidance on the drug-related aspects of the *drug-containing part* (3.9) of the ~~VDDCP~~vascular device-drug combination product can be found in ~~International Conference on Harmonization Guideline~~ ICH Q1A.

3.26
~~**Uniformity of drug content**~~
content uniformity
uniformity of drug content
comparison of the uniformity of the *drug content* (3.12) between individual ~~VDDCPs~~*vascular device-drug combination products* (3.27) within each *batch* (3.2) as compared to the labelled claim

3.27
vascular device-drug combination product
VDDCP
vascular medical device that incorporates one or more ~~APIs~~*active pharmaceutical ingredients* (3.1) as an integral part ~~(ancillary mode of action) to that~~ of the device~~, but~~ that is not necessarily ~~to the VDDCP PMOA~~part of the device's primary mode of action(i.e. ancillary mode of action)

Note 1 to entry: The ~~VDDCP~~vascular device-drug combination product can be permanently deployed (~~i~~.e. ~~it can be~~. an implant like a drug-eluting stent) or temporarily deployed (~~i~~.e. ~~it can be~~. a drug-eluting balloon).

3.28
vascular device-drug combination product deployment
VDDCP deployment
physical or mechanical positioning of the ~~VDDCP~~*vascular device-drug combination product* (3.27) so that the *drug-containing part* (3.9) is in contact with the intended anatomic treatment site

Note 1 to entry: The ~~VDDCP~~vascular device-drug combination product may be permanently deployed (e.g. a drug-eluting stent) or temporarily deployed (e.g. a drug-eluting balloon).

3.29
vascular device-drug combination product specification
VDDCP specification
list of required ~~list of~~ test procedures and appropriate acceptance criteria which are numerical limits, ranges~~,~~ or other criteria for the tests described

Note 1 to entry: A specification is a critical quality standard. It establishes the set of criteria to which a ~~VDDCP~~*vascular device-drug combination product* (3.27) has to conform.