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Cardiovascular implants and extracorporeal systems — Cardiac valve repair devices

Implants cardiovasculaires et circuits extra-corporels — Dispositifs de réparation de valves cardiaques

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Foreword

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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).

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This document was prepared by ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition (ISO 5910:2018), which has been technically revised.

The main changes are as follows:

— requirements in 7.2.2.3 and an informative annex (Annex J) have been added for test platforms;

— requirements and the informative annex on functional performance assessment have been removed;

— fatigue and durability testing have been combined into integrated device assessment in 7.2.4 and Annex M;

— the description of the types of heart valve repair devices, including the added section on robotically-assisted systems, have been moved into Annex B;

— Annex G on hazard and failure modes and Annex R on clinical imaging have been extensively revised;

— pulsatile flow conditions for the paediatric population have been clarified in Annex H;

— Annex I on boundary conditions has been added;

— annexes on physical and material property definitions and material property testing have been removed;

— additional device design evaluation requirements have been included in Annex N;

— additional evaluation considerations for preclinical in vivo evaluations have been included in Annex P.

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.

Cardiovascular implants and extracorporeal systems — Cardiac valve repair devices

1 Scope

1.1 This document specifies an approach for verifying and validating the design and manufacture of a heart valve repair system through risk management. The selection of appropriate verification and validation tests and methods are derived from the risk assessment. The tests include assessments of the physical, chemical, biological and mechanical properties of components and materials of heart valve repair systems. The tests also include preclinical in vivo evaluation and clinical investigation of the finished heart valve repair system to assess the safety and effectiveness of the heart valve repair system.

NOTE For the purposes of this document, effectiveness end point includes clinical performance and benefits.

1.2 This document defines operational conditions and performance requirements for heart valve repair systems where adequate scientific and/or clinical evidence exists for their justification. It also describes the labels and packaging of the device.

1.3 This document applies to all heart valve repair systems that have an intended use to repair and/or improve the function of native human heart valves by acting either on the valve apparatus or on the adjacent anatomy (e.g. ventricle, coronary sinus).

1.4 This document does not apply to cardiac resynchronization therapy (CRT) devices, paravalvular leakage closure devices, systems that do not leave an implant in place (e.g. ablation, radio frequency annuloplasty), apical conduits and devices with components containing viable cells. This document also excludes materials not intended for repairing and/or improving the function of human heart valves according to its intended use (e.g. patch material and sutures used in general surgical practice).

NOTE A rationale for the provisions of this document is given in Annex A.

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 10993-4, *Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood*

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 11137-1, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11137-2, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

ISO 11137-3, *Sterilization of health care products — Radiation — Part 3: Guidance on dosimetric aspects of development, validation and routine control*

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

ISO 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

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

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

ISO 14160, *Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices*

ISO 14630, *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 15223-1, *Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements*

ISO 15223-2, *Medical devices — Symbols to be used with medical device labels, labelling, and information to be supplied — Part 2: Symbol development, selection and validation*

ISO 17664-1, *Processing of health care products — Information to be provided by the medical device manufacturer for the processing of medical devices — Part 1: Critical and semi-critical 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*

ISO/TS 17665-2, *Sterilization of health care products — Moist heat — Part 2: Guidance on the application of ISO 17665-1*

ISO/TS 17665-3, *Sterilization of health care products — Moist heat — Part 3: Guidance on the designation of a medical device to a product family and processing category for steam sterilization*

ISO 20417, *Medical devices — Information to be supplied by the manufacturer*

ISO 22442-1, *Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management*

ISO 22442-2, *Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling*

ISO 22442-3, *Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents*

ISO/TR 22442-4, *Medical devices utilizing animal tissues and their derivatives — Part 4: Principles for elimination and/or inactivation of transmissible spongiform encephalopathy (TSE) agents and validation assays for those processes*

IEC 62366-1, *Medical devices — Part 1: Application of usability engineering to medical devices*

ASTM F1830, *Standard Practice for Selection of Blood for In Vitro Evaluation of Blood Pumps*

3 Terms and definitions

For the purposes of this document, the following terms and definitions 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
accessory
device-specific tool that is required to assist in the implantation and/or adjustment of the *heart valve repair device* (3.25), excluding the *delivery system* (3.12)

3.2
active comparator
intervention (e.g. transcatheter or surgical valve repair or replacement) generally accepted as the standard of care for the intended valve device indication that can be used as a basis of comparison for the *safety* (3.45) and effectiveness of the *heart valve repair device* (3.25)

3.3
adverse event
AE
untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated

Note 1 to entry: This definition includes events related to the investigational medical device or the *active comparator* (3.2).

Note 2 to entry: This definition includes events related to the procedures involved.

Note 3 to entry: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

3.4
boundary condition
displacement, force, moment, pressure or constraint acting on an implanted valve repair device and/or surrounding tissue

3.5
cardiac output
CO
stroke volume [i.e. volume of blood pumped by a ventricle during *systolic duration* (3.53)] multiplied by the heart rate

3.6
coating
thin-film material that is applied to an element of a *heart valve repair system* (3.26) to modify its surface physical or chemical properties

3.7
compliance
C
relationship between the change in radius and the change in pressure of a deformable tubular structure (e.g. valve annulus, aorta, conduit), given as

$$C = \frac{(r_2 - r_1)\times 100}{r_1 \times (p_2 - p_1)} \times 100\,\%$$

where

p_1 is the diastolic pressure, in mmHg;

p_2 is the systolic pressure, in mmHg;

r_1 is the inner radius at p_1, in mm;

r_2 is the inner radius at p_2, in mm

Note 1 to entry: Compliance is expressed in percentage of radial change per 100 mmHg.

3.8
component-joining material
material, such as a suture, adhesive or welding compound, used to assemble the components of a *heart valve repair device* (3.25), thereby becoming part of the implanted device

3.9
cycle
complete sequence in the action of a native or repaired heart valve under pulsatile flow conditions

3.10
cycle rate
beat rate
number of complete *cycles* (3.9) per unit of time

Note 1 to entry: The cycle rate is usually expressed as cycles per minute or beats per minute.

3.11
delivery approach
anatomical access used to deliver the *implant* (3.28) to the *implant site* (3.29) (e.g. transfemoral, transapical, transseptal)

3.12
delivery system
catheter or other system used to deliver, deploy, attach or adjust the device in the *implant site* (3.29)

3.13
design validation
establishment by objective evidence that device specifications conform with user needs and *intended use(s)* (3.31)

3.14
design verification
establishment by objective evidence that the design output meets the design input requirements

3.15
device embolization
dislodgement from the intended and documented original position to an unintended and nontherapeutic location

3.16
device failure
inability of a device to perform its intended function

3.17
device migration
detectable movement or displacement of the *implant* (3.28) from its original position within the *implant site* (3.29), without *device embolization* (3.15)

3.18
failure mode
mechanism of *device failure* (3.16)

EXAMPLE *Support structure* (3.52) *fracture* (3.22), calcification and prolapse.

3.19
fatigue
process of progressive localized permanent structural change occurring in a material subjected to conditions that produces fluctuating stresses and strains at some point(s) and that can culminate in cracks or complete *fracture* (3.22) after a sufficient number of fluctuations

3.20
follow-up
continued assessment of subjects who have received the *heart valve repair device* (3.25)

3.21
forward flow volume
volume of flow ejected through the repaired heart valve in the forward direction

3.22
fracture
complete separation of any part of the *heart valve repair device* (3.25) that was previously intact

3.23
harm
injury or damage to the health of people, or damage to property or the environment

[SOURCE: ISO/IEC Guide 51:2014, 3.1]

3.24
hazard
potential source of *harm* (3.23)

[SOURCE: ISO/IEC Guide 51:2014, 3.2]

3.25
heart valve repair device
implant (3.28) intended to improve the function of native human heart valves by acting either on the valve apparatus or on the adjacent anatomy (e.g. ventricle, coronary sinus)

Note 1 to entry: See examples of heart valve repair devices in Annex B.

3.26
heart valve repair system
set of elements provided to repair the native heart valve, consisting of the *heart valve repair device* (3.25), *delivery system* (3.12), *accessories* (3.1) as applicable, packaging, labelling and instructions

3.27
imaging modality
method used to visualize and assess native anatomy and/or device position, geometry and/or function

3.28
implant
device placed surgically or non-surgically into the human body and intended to remain in place after the procedure

3.29
implant site
intended location of heart valve repair device (3.25) implantation or deployment

3.30
indication for use
clinical condition of the patient population that the *heart valve repair device* (3.25) is intended to treat or improve

3.31
intended use
use of a product or process according to the specifications, instructions and information provided by the manufacturer

3.32
linearized rate
total number of events divided by the total time under evaluation

Note 1 to entry: Generally, linearized rate is expressed in terms of percent per patient year.

3.33
loading
process to affix, attach or insert a repair device component onto or into a *delivery system* (3.12)

3.34
mean arterial pressure
time-averaged arithmetic mean value of the arterial pressure during one *cycle* (3.9)

3.35
non-structural dysfunction
abnormality extrinsic to the *heart valve repair device* (3.25) that results in abnormal function of the device or causes clinical symptoms

EXAMPLE Entrapment by *pannus* (3.36), tissue or suture; paravalvular leak; inappropriate sizing or positioning, residual leak or obstruction after implantation and clinically important haemolytic anaemia. This definition excludes infection or thrombosis of the heart valve repair device and intrinsic factors, which cause *structural native valve deterioration* (3.51).

3.36
pannus
ingrowth of tissue onto the *heart valve repair device* (3.25) which can interfere with normal functioning

3.37
pull-out testing
testing for a situation in which the suture or anchoring device remains structurally intact but tears through the tissue in which it is implanted

3.38
reference device
heart valve substitute or *heart valve repair device* (3.25) with known clinical history used for comparative preclinical and clinical evaluations

3.39
regurgitant volume
volume of fluid that flows through a repaired heart valve in the reverse direction during one *cycle* (3.9)

3.40
repositioning
intentional change of *implant* (3.28) position of a partially or fully deployed *heart valve repair device* (3.25) via a surgical or transcatheter technique, possibly requiring full or partial removal or recapturing of the device

3.41
retrieval
removal of a partially or fully deployed *heart valve repair device* (3.25) via a surgical or transcatheter technique

3.42
risk
combination of the probability of occurrence of *harm* (3.23) and the *severity* (3.48) of that harm

[SOURCE: ISO 14971:2019, 3.18]

3.43
risk analysis
systematic use of available information to identify *hazards* (3.24) and to estimate the associated *risks* (3.42)

[SOURCE: ISO 14971:2019, 3.19]

3.44
risk assessment
overall process comprising a *risk analysis* (3.43) and a *risk* (3.42) evaluation

[SOURCE: ISO 14971:2019, 3.20]

3.45
safety
freedom from unacceptable *risk* (3.42)

[SOURCE: ISO 14971:2019, 3.26]

3.46
serious adverse device effect
SADE
adverse effect of the device that has resulted in any of the consequences characteristic of a *serious adverse event* (3.47)

Note 1 to entry: Planned hospitalization for a pre-existing condition or a procedure required by the clinical investigation plan, without serious deterioration in health, is not considered a serious adverse event.

3.47
serious adverse event
SAE
adverse event (3.3) that leads to any of the following

a) death,

b) serious deterioration in the health of the subject, users or other persons, as defined by one or more of the following:

   1) a life-threatening illness or injury, or

   2) a permanent impairment of a body structure or a body function including chronic diseases, or

   3) in-patient or prolonged hospitalization, or

   4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,

c) foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment

3.48
severity
measure of the possible consequences of a *hazard* (3.24)

[SOURCE: ISO 14971:2019, 3.27]

3.49
sterility assurance level
SAL
probability of a single viable microorganism occurring on an item after *sterilization* (3.50)

Note 1 to entry: Sterility assurance level is expressed as the negative exponent to the base 10.

[SOURCE: ISO 11139:2018, 3.275]

3.50
sterilization
validated process used to render product free from viable microorganisms

Note 1 to entry: In a sterilization process, the nature of microbial inactivation is exponential and thus the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

[SOURCE: ISO 11139:2018, 3.277]

3.51
structural native valve dysfunction
structural native valve deterioration
dysfunction or deterioration intrinsic to the native valve, including calcification, leaflet fibrosis, leaflet tear or flail, resulting in stenosis or regurgitation

3.52
support structure
load bearing structural component of a *heart valve repair device* (3.25)

3.53
systolic duration
portion of cardiac *cycle* (3.9) time corresponding to ventricular contraction

Note 1 to entry: For in vitro testing, systolic duration corresponds to the duration of forward flow in a cardiac *cycle* (3.9).

3.54
thromboembolism
embolic event involving a clot(s) that occurs in the absence of infection

Note 1 to entry: Thromboembolism can be manifested by a neurological event or an embolic event to another organ or limb (e.g. ocular, coronary, mesenteric, femoral).

3.55
total product life cycle
period of time over which a product is developed, brought to market and eventually removed from the market

3.56
usability
characteristic of the user interface that facilitates use and thereby establishes effectiveness, efficiency, ease of user learning and user satisfaction in the *intended use* (3.31) environment

[SOURCE: IEC 62366-1:2015, 3.16]

3.57
use error
act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user

Note 1 to entry: Incorrect sizing, suboptimal positioning, structural distortion of the device.

Note 2 to entry: An unexpected physiological response of the patient is not by itself considered a use error.