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Cardiovascular implants — Cardiac valve prostheses —

Part 3: Heart valve substitutes implanted by transcatheter techniques

Implants cardiovasculaires — Prothèses valvulaires —

Partie 3: Valves cardiaques de substitution implantées par des techniques transcathéter

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Foreword

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

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 5840-3 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

ISO 5840 consists of the following parts, under the general title *Cardiovascular implants — Cardiac valve prostheses*:

— *Part 3: Heart valve substitutes implanted by minimally invasive techniques*

Introduction

No heart valve substitute is ideal. Therefore, a group of engineers, scientists and clinicians well aware of the problems associated with heart valve substitutes and their development has prepared this part of ISO 5840. In several areas, the provisions of this part of ISO 5840 have been deliberately left partially defined so as not to inhibit development and innovation. This part of ISO 5840 specifies types of tests, test methods and requirements for test apparatus. It requires documentation of test methods and results. This part of ISO 5840 deals with those areas that will ensure adequate mitigation of device-associated risks for patients and other users of the device, facilitate quality assurance, aid the cardiac surgeon and cardiologist in choosing a heart valve substitute, and ensure that the device will be presented in a convenient form. This part of ISO 5840 emphasizes the need to specify types of *in vitro* testing, preclinical *in vivo* and clinical evaluations as well as to report all *in vitr*o, preclinical *in vivo* and clinical evaluations. It describes the labels and packaging of the device. Such a process involving *in vitro*, preclinical *in vivo* and clinical evaluations is intended to clarify the required procedures prior to market release and to enable prompt identification and management of any subsequent problems.

With regard to *in vitro* testing and reporting, apart from basic material testing for mechanical, physical, chemical and biocompatibility characteristics, this part of ISO 5840 also covers important hydrodynamic and durability characteristics of transcatheter heart valve substitutes and their delivery systems. This part of ISO 5840 does not specify exact test methods for hydrodynamic and durability testing but it offers guidelines for the test apparatus.

This part of ISO 5840 should be revised, updated and amended as knowledge and techniques in heart valve substitute technology improve.

This part of ISO 5840 is to be used in conjunction with ISO 5840:2005, which will be replaced by ISO 5840-1 in future.

Cardiovascular implants — Cardiac valve prostheses —

Part 3: Heart valve substitutes implanted by transcatheter techniques

1 Scope

This part of ISO 5840 outlines an approach for verifying/validating the design and manufacture of a transcatheter heart valve substitute through risk management. The selection of appropriate verification/validation tests and methods are to be derived from the risk assessment. The tests may include those to assess the physical, chemical, biological and mechanical properties of heart valve substitutes and of their materials and components. The tests can also include those for preclinical *in vivo* evaluation and clinical evaluation of the finished heart valve substitute.

This part of ISO 5840 defines operational conditions and performance requirements for transcatheter heart valve substitutes where adequate scientific and/or clinical evidence exists for their justification.

This part of ISO 5840 is applicable to all devices intended for implantation in human hearts as a transcatheter heart valve substitute.

This part of ISO 5840 is applicable to both newly developed and modified transcatheter heart valve substitutes and to the accessory devices, packaging and labelling required for their implantation and for determining the appropriate size of heart valve substitute to be implanted.

This part of ISO 5840 excludes heart valve substitutes designed for implantation in artificial hearts or heart assist devices.

This part of ISO 5840 excludes valve-in-valve configurations and homografts.

This part of ISO 5840 does not specifically address non-traditional surgically implanted heart valve substitutes (e.g. sutureless). For these devices, the requirements of both this part of ISO 5840 and ISO 5840:2005 might be relevant and can be considered.

NOTE A rationale for the provisions of this part of ISO 5840 is given in Annex A.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 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 11135-1, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO/TS 11135-2, *Sterilization of health care products — Ethylene oxide — Part 2: Guidance on the application of ISO 11135-1*

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*

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 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 14630:2012, *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*

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/IEC 17025, *General requirements for the competence of testing and calibration laboratories*

IEC 62366, *Medical devices — Application of usability engineering to medical devices*

ASTM F2052, *Standard test method for measurement of magnetically induced displacement force on medical devices in the magnetic resonance environment*

ASTM F2503, *Standard practice for marking medical devices and other items for safety in the magnetic resonance environment*

ASTM F2213, *Standard test method for measurement of magnetically induced torque on medical devices in the magnetic resonance environment*

ASTM F2182, *Standard test method for measurement of radio frequency induced heating near passive implants during magnetic resonance imaging*

ASTM F2119, *Standard test method for evaluation of MR image artifacts from passive implants*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

NOTE Additional definitions can be found in the informative annexes.

3.1
accessories
device-specific tools that are required to assist in the implantation of the transcatheter heart valve substitute

3.2
adverse event
AE
untoward medical occurrence in a study subject which does not necessarily have to have a causal relationship with study treatment

Note 1 to entry: An AE can be an unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease, temporary or permanent, whether or not related to the prosthetic valve implantation or procedure.

3.3
arterial end diastolic pressure
minimum value of the arterial pressure during diastole

3.4
arterial peak systolic pressure
maximum value of the arterial pressure during systole

3.5
back pressure
differential pressure applied across the valve during the closed phase

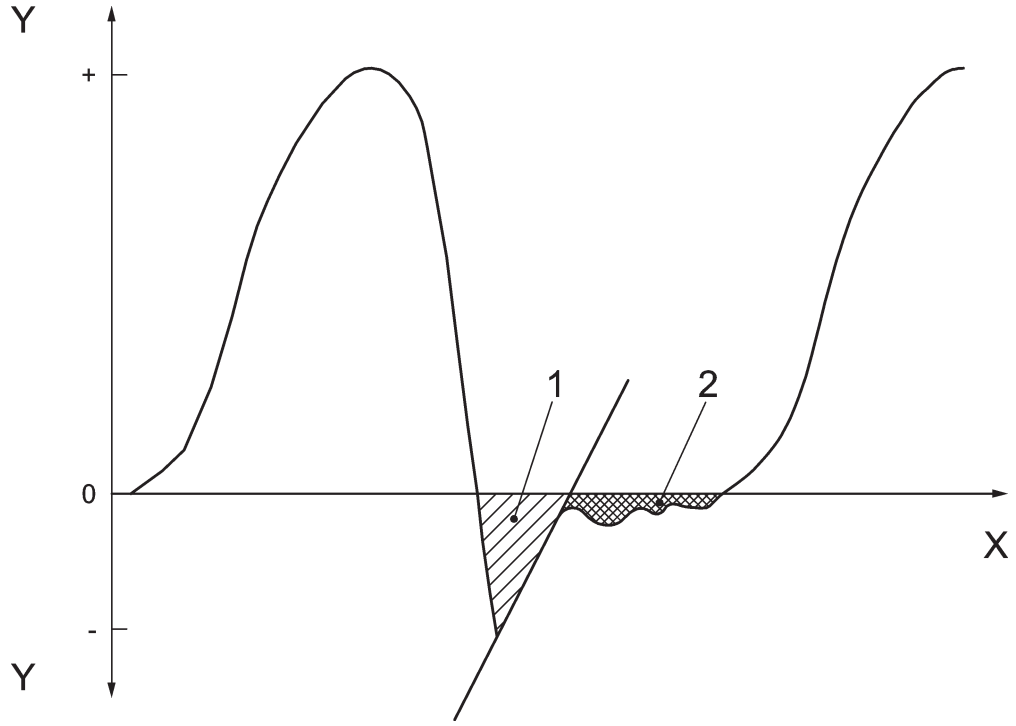
3.6
body surface area
A_{bs}
total surface area (m^2) of the human body

Note 1 to entry: This can be calculated (Mosteller's formula) as the square root of product of the weight in kg times the height in cm divided by 3 600 (see Reference [12]).

3.7
cardiac index
cardiac output (CO, l/min) divided by the body surface area (A_{bs}, m^2), in units l/min/m^2

3.8
closing volume
portion of the regurgitant volume that is associated with the dynamics of the valve closure during a single cycle

Note 1 to entry: See Figure 1.



Key

X time
Y flowrate
1 closing volume
2 leakage volume

Figure 1 — Schematic representation of flow waveform and regurgitant volumes for one cycle

3.9
coating
thin-film material that is applied to an element of a heart valve substitute to modify its physical or chemical properties

3.10
compliance
relationship between change in diameter and change in pressure of a deformable tubular structure (e.g. valve annulus, aorta, conduit), defined in this part of ISO 5840 as

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

where

C is the compliance in units of % radial change/100 mmHg;

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 millimetres;

r_2 is the inner radius at p_2, in millimetres.

Note 1 to entry: See ISO 25539-1.

3.11
component-joining material
material, such as a suture, adhesive or welding compound, used to assemble the components of a heart valve substitute, thereby becoming part of the implant device

Note 1 to entry: See examples in Annex B.

3.12
cycle
one complete sequence in the action of a heart valve substitute under pulsatile flow conditions

3.13
cycle rate
number of complete cycles per unit of time, usually expressed as cycles per minute (cycles/min)

3.14
delivery approach
anatomical access used to deliver the implant to the implant site (e.g. transfemoral, transapical, transeptal)

3.15
delivery system
catheter or other device-based system used to deliver the implant to the implant site

3.16
deployed valve diameter
outer diameter (mm) of the implantable device when deployed within the target implant site in an idealized circular configuration

3.17
device embolization
dislodgement from the intended and documented original position to an unintended and non-therapeutic location

3.18
device failure
inability of a device to perform its intended function sufficient to cause a hazard

3.19
device migration
detectable movement or displacement of the device from its original position within the implant site, without embolization

3.20
effective orifice area
EOA
orifice area that has been derived from flow and pressure or velocity data

3.21
failure mode
mechanism of device failure

Note 1 to entry: Catastrophic support structure fracture, calcification and prolapse are examples of failure modes.

3.22
follow-up
continued assessment of patients who have received the heart valve substitute

3.23
forward flow volume
volume of flow ejected through the test heart valve substitute in the forward direction during one cycle

3.24
fracture
disruption, under the action of applied stress or strain, of any part of the transcatheter heart valve substitute that was previously intact

3.25
heart valve substitute
device used to replace the function of a natural valve of the heart

Note 1 to entry: See examples in Annex B.

3.26
imaging modality
imaging method used to facilitate delivery and/or retrieval of the implant within the target implant site, as well as to assess valve performance after implantation

3.27
implant site
intended site of transcatheter heart valve substitute deployment

3.28
intended use
use of a product, process or service in accordance with the specifications, instructions and information provided by the manufacturer

3.29
leakage volume
component of the regurgitant volume that is associated with leakage during closed phase of a valve in a single cycle and is the sum of the transvalvular leakage volume and paravalvular leakage volume

Note 1 to entry: The point of separation between the closing and leakage volumes is obtained according to a defined and stated criterion (the linear extrapolation shown in Figure 1 is just an example).

Note 2 to entry: See Figure 1.

3.30
mean arterial pressure
time-averaged arithmetic mean value of the arterial pressure during one cycle

3.31
mean pressure difference
time-averaged arithmetic mean value of the pressure difference across a heart valve substitute during the forward flow phase of the cycle

3.32
non-structural valve dysfunction
abnormality extrinsic to the transcatheter heart valve substitute that results in valve dysfunction (stenosis, regurgitation or both)

3.33
occluder/leaflet
component that inhibits back flow

Note 1 to entry: See examples in Annex B.

3.34
paravalvular leakage volume
component of the leakage volume that is associated with leakage around the closed heart valve substitute during a single cycle

3.35
reference valve
heart valve substitute with a known clinical experience used for comparative preclinical and clinical evaluations

3.36
regurgitant fraction
regurgitant volume expressed as a percentage of the forward flow volume

3.37
regurgitant volume
volume of fluid that flows through a heart valve substitute in the reverse direction during one cycle and is the sum of the closing volume and the leakage volume

Note 1 to entry: See Figure 1.

3.38
repositioning
change in implant position of a partially or fully deployed transcatheter heart valve substitute via a transcatheter technique, possibly requiring full or partial recapturing of the device

3.39
retrieval
removal of a partially or fully deployed transcatheter heart valve substitute via a transcatheter technique

3.40
risk

combination of the probability of occurrence of harm and the severity of that harm

Note 1 to entry: Adapted from ISO 14971.

3.41
risk analysis
systematic use of available information to identify hazards and to estimate the associated risks

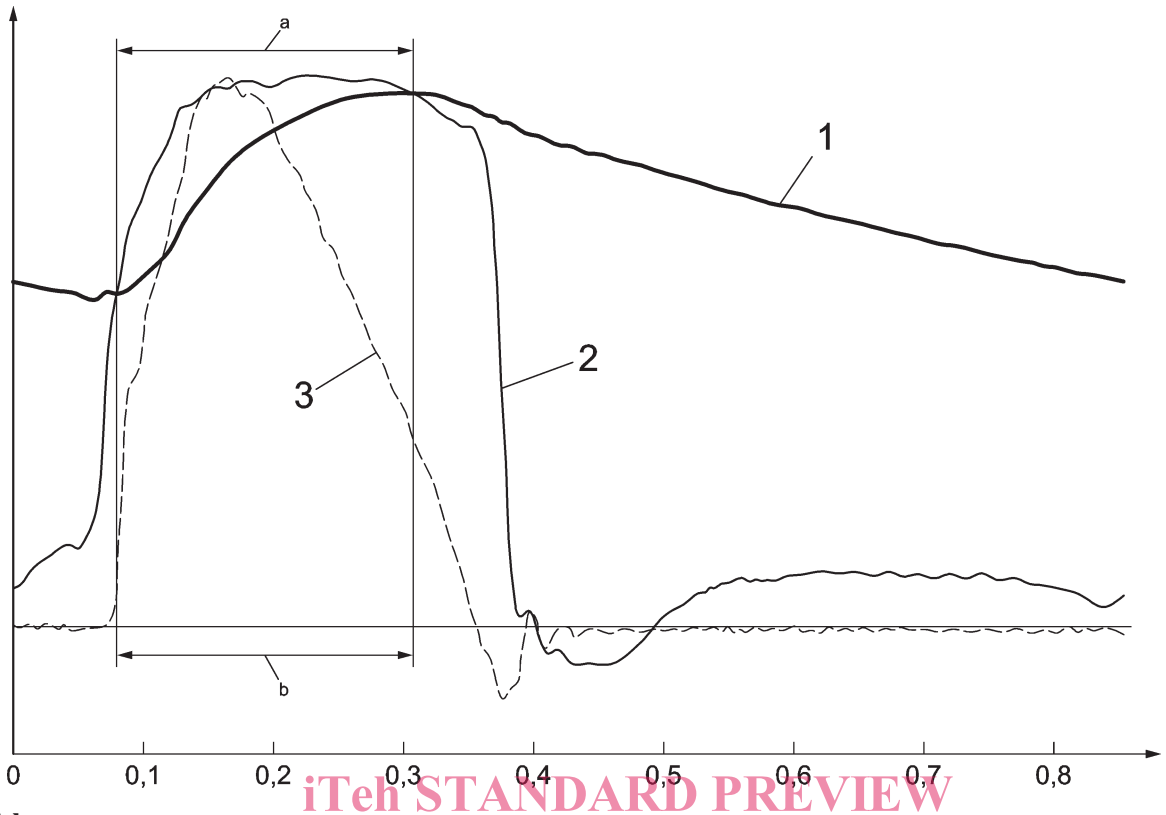
Note 1 to entry: Adapted from ISO 14971.

3.42
risk assessment
overall process comprising a risk analysis and a risk evaluation

Note 1 to entry: Adapted from ISO 14971.

3.43
root mean square forward flow
RMS forward flow
square root of the integral of the volume flow rate waveform squared during the positive differential pressure interval of the forward flow phase used to calculate EOA

Note 1 to entry: See Figure 2.



Key title

1 aortic pressure

2 left ventricular pressure

3 aortic flow rate

a Positive pressure range.

b Q_{rms} range.

Figure 2 — Schematic representation of the positive pressure period of an aortic forward flow interval

3.44
safety
freedom from unacceptable risk

Note 1 to entry: Adapted from ISO 14971.

3.45
severity
measure of the possible consequences of a hazard

Note 1 to entry: Adapted from ISO 14971.

3.46
special processes
processes for which the product cannot be fully verified by inspection or test

3.47
sterility assurance level
SAL
probability of a single viable microorganism occurring on an item after sterilization

Note 1 to entry: The term SAL takes a quantitative value, generally 10^{-6} or 10^{-3}. When applying this quantitative value to assurance of sterility, an SAL of 10^{-6} has a lower value but provides a greater assurance of sterility than an SAL of 10^{-3}.

[ISO/TS 11139, definition 2.46]

3.48
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.

Note 2 to entry: See **sterility assurance level** (3. 47).

Note 3 to entry: Adapted from ISO/TS 11139.

3.49
structural component failure
degradation of structural integrity of the support structure (e.g. strut fractures) that results in the functional performance of the implant no longer being acceptable and/or that results in adverse events

3.50
structural valve dysfunction
structural abnormality intrinsic to the transcatheter heart valve substitute that results in valve dysfunction (stenosis and/or transvalvular and/or paravalvular regurgitation)

3.51
support structure
portion of the transcatheter heart valve substitute that transfers loads between occluder and implant site and anchors the device within the implant site

3.52
surgically implanted heart valve substitute
heart valve substitute generally requiring direct visualization and cardiopulmonary bypass for implantation

3.53
transcatheter heart valve substitute
heart valve substitute implanted in a manner generally not involving direct visualization, and generally involving a beating heart

3.54
transcatheter heart valve system
implantable device, delivery system, accessories, packaging, labelling and instructions

3.55
transvalvular leakage volume
component of the leakage volume that is associated with leakage through the closed valve during a single cycle

3.56
usability
characteristic of the user interface that establishes effectiveness, efficiency, ease of user learning and user satisfaction