



SLOVENSKI STANDARD
oSIST prEN ISO 5840-1:2019
01-marec-2019

Vsadki (implantati) za srce in ožilje - Proteze za srčno zaklopko - 1. del: Splošne zahteve (ISO/DIS 5840-1:2019)

Cardiovascular implants - Cardiac valve prostheses - Part 1: General requirements (ISO/DIS 5840-1:2019)

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Implants cardiovasculaires - Prothèses valvulaires - Partie 1: Exigences générales (ISO/DIS 5840-1:2019)

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Ta slovenski standard je istoveten z: prEN ISO 5840-1

ICS:

11.040.40	Implantanti za kirurgijo, protetiko in ortetiko	Implants for surgery, prosthetics and orthotics
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en

DRAFT INTERNATIONAL STANDARD

ISO/DIS 5840-1

ISO/TC 150/SC 2

Secretariat: ANSI

Voting begins on:
2019-01-14Voting terminates on:
2019-04-08

Cardiovascular implants — Cardiac valve prostheses —

Part 1: General requirements

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ISO/CEN PARALLEL PROCESSING



Reference number
ISO/DIS 5840-1:2019(E)

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Published in Switzerland

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 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).

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: [Foreword - Supplementary Information](#)

The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition of ISO 5840-1 cancels and replaces the first edition (ISO 5840-1:2015), which has been technically revised.

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

- *Part 1: General requirements*
- *Part 2: Surgically implanted heart valve substitutes*
- *Part 3: Heart valve substitutes implanted by transcatheter techniques*

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Introduction

There is, as yet, no heart valve substitute which can be regarded as ideal.

The ISO 5840-series has been prepared by a group well aware of the issues associated with heart valve substitutes and their development. In several areas, the provisions of the ISO 5840-series deliberately have not been specified to encourage development and innovation. It does specify the types of tests, provides guidance for test methods and test apparatuses and requires documentation of test methods and results. The areas with which the ISO 5840-series are concerned are those which will ensure that associated risks to the patient and other users of the device have been adequately mitigated, facilitate quality assurance, aid the clinician in choosing a heart valve substitute, and ensure that the device will be presented in convenient form. Emphasis has been placed on specifying types of *in vitro* testing, preclinical *in vivo* and clinical evaluations, reporting of all *in vitro*, preclinical *in vivo*, and clinical evaluations, and the labelling 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, the ISO 5840-series also covers important hydrodynamic and durability characteristics of heart valve substitutes and systems required for their implantation. The ISO 5840-series does not specify exact test methods for hydrodynamic and durability testing, but it offers guidelines for the test apparatus.

The ISO 5840-series is intended to be revised, updated, and/or 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 parts 2 and 3.

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Cardiovascular implants—Cardiac valve prostheses— Part 1: General requirements

1 Scope

This part of ISO 5840 is applicable to heart valve substitutes intended for implantation and provides general requirements. Subsequent parts of the ISO 5840 series provide specific requirements.

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

ISO 5840 outlines an approach for verifying/validating the design and manufacture of a heart valve substitute through risk management. The selection of appropriate qualification tests and methods are 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.

ISO 5840 defines operational conditions for heart valve substitutes.

ISO 5840 does not provide requirements specific to homografts, tissue engineered heart valves (e.g. valves intended to regenerate *in vivo*), and heart valve substitutes designed for implantation in circulatory support devices.

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

2 Normative references

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

ISO 5840-2, *Cardiovascular implants — Cardiac valve prostheses —Part 2: Surgically implanted heart valve substitutes*

ISO 5840-3, *Cardiovascular implants — Cardiac valve prostheses —Part 3: Heart valve substitutes implanted by transcatheter techniques*

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

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

ISO 11607 (all parts), *Packaging for terminally sterilized medical devices*

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

ISO 176651, *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/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, Medical Devices – Application of usability engineering to medical devices

ASTM F1830 – 97, Standard practice for selection of blood for in vitro evaluation of blood pumps

ASTM F2052, *Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment*

ASTM F2119, *Standard Test Method for Evaluation of MR Image Artifacts from Passive Implants*

ASTM F2182, *Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging*

ASTM F2213, *Standard Test Method for Measurement of Magnetically Induced Torque 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*

3 Terms and definitions

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

3.1

accessories

device-specific tools that are required to assist in the implantation of the *heart valve substitute* (3.33)

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

actuarial methods

statistical technique for calculating event rates over time

Note 1 to entry: Standard actuarial methods calculate the probability of freedom from events within pre-specified intervals of time. When the intervals approach zero width, the methods are called Kaplan-Meier methods.

3.4

arterial end diastolic pressure

minimum value of the arterial pressure during diastole

3.5

arterial peak systolic pressure

maximum value of the arterial pressure during *systole* (3.73)

3.6

back pressure

differential pressure across the valve during the closed phase

3.7

body surface area

BSA

total surface area (m²) of the human body

Note 1 to entry: This can be calculated (Mosteller's formula) as the square root of the product of the weight in kg times the height in cm divided by 3.600 (see Reference [7]).

3.8

cardiac index

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cardiac output (3.9) (L/min) divided by the *body surface area* (3.7) (m²) with units L/min/m²

3.9**cardiac output****CO**

stroke volume (3.69) times heart rate

3.10**closing volume**

portion of the *regurgitant volume* (3.53) that is associated with the dynamics of valve closure during a single cycle (3.15)

Note 1 to entry: See Figure 1.

3.11**coating**

thin-film material that is applied to an element of a *heart valve system* (3.34) to modify its physical or chemical properties

3.12**compliance**

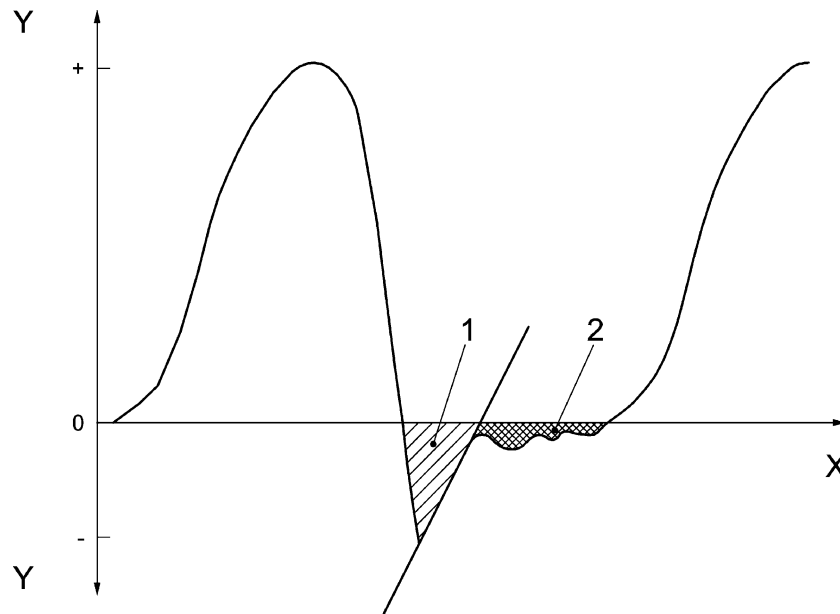
relationship between change in diameter and change in pressure of a deformable tubular structure (e.g. aorta, conduit) defined in ISO 5840 as

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

where

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- 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: Reference ISO 25539-1 [3].

**Key**

- X time
- Y flowrate
- 1 closing volume
- 2 leakage volume

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

3.13**component-joining material**

material such as a suture, adhesive, or welding compound used to assemble the components of a *heart valve system* (3.34)

3.14**cumulative incidence**

statistical technique where events other than death can be described by the occurrence of the event over time without including death of the subjects

Note 1 to entry: Cumulative incidence is also known as “actual” analysis.

3.15**cycle**

one complete sequence in the action of a *heart valve substitute* (3.33) under pulsatile-flow conditions

3.16**cycle rate**

number of complete *cycles* (3.15) per unit of time usually expressed as cycles per minute (cycles/min)

3.17**design verification**

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

3.18**design validation**

establishment by objective evidence that device specifications conform with user needs and *intended use(s)* (3.36)

3.19**device embolization**

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

3.20**device failure**

inability of a device to perform its intended function

3.21**device migration**

detectable movement or displacement of the *heart valve substitute* (3.33) from its original position within the *implant position* (3.35) and without *device embolization* (3.19)

3.22**effective orifice area****EOA**

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

For *in vitro* testing, EOA is defined as:

$$EOA = \frac{q_{v_{RMS}}}{51,6 \times \sqrt{\frac{\Delta p}{\rho}}}$$

where

EOA is the Effective Orifice Area (cm²);

$q_{v_{RMS}}$ is the *root mean square forward flow* (3.58) (ml/s) during the positive differential pressure period;

Δp is the mean pressure difference (measured during the positive differential pressure period) (mmHg);

ρ is the density of the test fluid (g/cm³).

3.23**end of diastole****ED**

end of forward flow (zero crossing of flow to negative) for mitral and tricuspid positions

3.24**end of leakage**

EL

Start of systole (SS) for aortic and pulmonary positions; start of diastole (SD) for mitral and tricuspid positions.

3.25**end of positive differential pressure****EPDP**

First crossing of aortic and left ventricular waveforms for aortic position; first crossing of pulmonary and right ventricular waveforms for pulmonary position; first crossing of atrial and ventricular waveforms for mitral and tricuspid position.

3.26**end of systole****ES**

End of forward flow (zero crossing of flow to negative) for aortic and pulmonary positions

3.27**end of closure****EC**

If no zero crossing of flow, use a linear extrapolation of highest slope of flow; if zero crossing, use the first zero crossing.

3.28**failure mode**

mechanism of *device failure* (3.20)

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

3.29**flexible surgical heart valve substitute**

surgical heart valve substitute (3.72) wherein the *occluder* (3.45) is flexible under physiological conditions (e.g. bioprostheses)

Note 1 to entry: The orifice ring may or may not be flexible.

3.30**follow-up**

continued assessment of patients who have received the *heart valve substitute* (3.33)

3.31**forward flow volume**

volume of flow ejected through the *heart valve substitute* (3.33) in the forward direction during one *cycle* (3.15)

3.32**fracture**

complete separation of any structural component of the *heart valve substitute* (3.33) that was previously intact

3.33**heart valve substitute**

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

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3.34

heart valve system

implantable device, *accessories* (3.1), packaging, labelling, and instructions

3.35

implant site/implant position

intended location of *heart valve substitute* (3.33) implantation or deployment

3.36

intended use

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

3.37

Kaplan-Meier methods

statistical approaches for calculating event rates over time when the actual dates of events for each person in the population are known

3.38

leakage volume

portion of the *regurgitant volume* (3.53) which is associated with leakage during the closed phase of a valve in a single *cycle* (3.15) and is the sum of the *transvalvular leakage volume* (3.76) and *paravalvular leakage volume* (3.48)

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).

3.39

linearized rate

total number of events divided by the total time under evaluation

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

3.40

major bleeding

any episode of major internal or external bleeding that causes death, hospitalization, or permanent injury (e.g. vision loss) or necessitates transfusion

3.41

major paravalvular leak

paravalvular leakage leading to or causing any of the following: death or reintervention; heart failure requiring additional medication; moderate or severe regurgitation; prosthesis “rocking” on investigation even in the apparent absence of symptoms; or haemolytic anaemia

3.42

mean arterial pressure

time-averaged arithmetic mean value of the arterial pressure during one *cycle* (3.15)

3.43

mean pressure difference/mean pressure gradient

time-averaged arithmetic mean value of the pressure difference across a *heart valve substitute* (3.33) during the positive differential pressure period of the *cycle* (3.15)

3.44**nonstructural valve dysfunction**

abnormality extrinsic to the *heart valve substitute* (3.33) that results in stenosis, regurgitation, and/or haemolytic anaemia

3.45**occluder/leaflet**

component that inhibits backflow

3.46**outflow tract profile height**

maximum distance that the *heart valve substitute* (3.33) extends axially into the outflow tract in the open or closed position, whichever is greater

3.47**pannus**

ingrowth of tissue onto the *heart valve substitute* (3.33) which can interfere with normal functioning

3.48**paravalvular leakage volume**

portion of the *leakage volume* (3.38) that is associated with leakage around the closed heart valve substitute during a single *cycle* (3.15)

3.49**profile height**

maximal axial dimension of a *heart valve substitute* (3.33) in the open or closed position, whichever is greater

3.50**prosthetic valve endocarditis**

any infection involving a prosthetic valve based on reoperation, autopsy, or the Duke Criteria for endocarditis

Note 1 to entry: See Reference [15]

3.51**reference valve**

heart valve substitute (3.33) with a known clinical experience used for comparative preclinical and clinical evaluations

3.52**regurgitant fraction**

regurgitant volume (3.53) expressed as a percentage of the *forward flow volume* (3.31)

3.53**regurgitant volume**

volume of fluid that flows through a *heart valve substitute* (3.33) in the reverse direction during one *cycle* (3.15) and is the sum of the *closing volume* (3.10) and the *leakage volume* (3.38)

NOTE 1 to entry: Clinically, it may only be possible to measure the leakage volume, and may not include the closing volume.