

This document is a preview generated by EVS

**Cardiovascular implants - Cardiac valve prostheses -  
Part 2: Surgically implanted heart valve substitutes  
(ISO 5840-2:2021 + ISO 5840-2:2021/Amd 1:2025)**

**EESTI STANDARDI EESSÕNA****NATIONAL FOREWORD**

See Eesti standard EVS-EN ISO 5840-2:2021+A1:2025 sisaldab Euroopa standardi EN ISO 5840-2:2021 ja selle muudatuse A1:2025 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 5840-2:2021+A1:2025 consists of the English text of the European standard EN ISO 5840-2:2021 and its amendment A1:2025.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas.  Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 03.02.2021, muudatus A1 19.03.2025.	This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation.  Date of Availability of the European standard is 03.02.2021, for A1 19.03.2025.
Muudatusega A1 lisatud või muudetud teksti algus ja lõpp on tekstis tähistatud sümbolitega $\boxed{A1}$ $\boxed{A1}$ .  Standard on kättesaadav Eesti Standardimis- ja Akrediteerimiskeskusest.	The start and finish of text introduced or altered by amendment A1 is indicated in the text by tags $\boxed{A1}$ $\boxed{A1}$ .  The standard is available from the Estonian Centre for Standardisation and Accreditation.

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile [standardiosakond@evs.ee](mailto:standardiosakond@evs.ee).

ICS 11.040.40

**Standardite reprodutseerimise ja levitamise õigus kuulub Eesti Standardimis- ja Akrediteerimiskeskusele**

Andmete paljundamine, taastekitamine, kopeerimine, salvestamine elektroonsesse süsteemi või edastamine ükskõik millises vormis või millisel teel ilma Eesti Standardimis- ja Akrediteerimiskeskuse kirjaliku loata on keelatud.

Kui Teil on küsimusi standardite autoriõiguse kaitse kohta, võtke palun ühendust Eesti Standardimis- ja Akrediteerimiskeskusega: Koduleht [www.evs.ee](http://www.evs.ee); telefon 605 5050; e-post [info@evs.ee](mailto:info@evs.ee)

**The right to reproduce and distribute standards belongs to the Estonian Centre for Standardisation and Accreditation**

No part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, without a written permission from the Estonian Centre for Standardisation and Accreditation.

If you have any questions about standards copyright protection, please contact the Estonian Centre for Standardisation and Accreditation:

Homepage [www.evs.ee](http://www.evs.ee); phone +372 605 5050; e-mail [info@evs.ee](mailto:info@evs.ee)

EUROPEAN STANDARD

**EN ISO 5840-2 + A1**

NORME EUROPÉENNE

EUROPÄISCHE NORM

February 2021, March 2025

ICS 11.040.40

Supersedes EN ISO 5840-2:2015

English Version

**Cardiovascular implants - Cardiac valve prostheses - Part  
2: Surgically implanted heart valve substitutes (ISO 5840-  
2:2021 + ISO 5840-2:2021/Amd 1:2025)**

Implants cardiovasculaires - Prothèses valvulaires -  
Partie 2: Prothèse valvulaires implantées  
chirurgicalement (ISO 5840-2:2021 + ISO 5840-  
2:2021/Amd 1:2025)

Herz- und Gefäßimplantate - Herzklappenprothesen -  
Teil 2: Chirurgisch implantierter Herzklappenersatz  
(ISO 5840-2:2021 + ISO 5840-2:2021/Amd 1:2025)

This European Standard was approved by CEN on 21 September 2020. Amendment A1 was approved by CEN on 12 March 2025.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard and its amendment the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard and its Amendment A1 exist in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and United Kingdom.



EUROPEAN COMMITTEE FOR STANDARDIZATION  
COMITÉ EUROPÉEN DE NORMALISATION  
EUROPÄISCHES KOMITEE FÜR NORMUNG

**CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels**

## European foreword

This document (EN ISO 5840-2:2021) has been prepared by Technical Committee ISO/TC 150 "Implants for surgery" in collaboration with Technical Committee CEN/TC 285 "Non-active surgical implants" the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by August 2021, and conflicting national standards shall be withdrawn at the latest by August 2021.

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

This document supersedes EN ISO 5840-2:2015.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

## Endorsement notice

The text of ISO 5840-2:2021 has been approved by CEN as EN ISO 5840-2:2021 without any modification.

## **A1** Amendment A1 European foreword

This document (EN ISO 5840-2:2021/A1:2025) has been prepared by Technical Committee ISO/TC 150 "Implants for surgery" in collaboration with Technical Committee CEN/TC 285 "Non-active surgical implants" the secretariat of which is held by DIN.

This Amendment to the European Standard EN ISO 5840-2:2021 shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by September 2025, and conflicting national standards shall be withdrawn at the latest by September 2025.

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

Any feedback and questions on this document should be directed to the users' national standards body/national committee. A complete listing of these bodies can be found on the CEN website.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and the United Kingdom.

### **Endorsement notice**

The text of ISO 5840-2:2021/Amd 1:2025 has been approved by CEN as EN ISO 5840-2:2021/A1:2025 without any modification. **A1**

This document is a preview generated by EVS

<b>Contents</b>	<b>Page</b>
<b>Foreword</b> .....	<b>v</b>
<b>[A1] Amendment A1 Foreword [A1]</b> .....	<b>vi</b>
<b>Introduction</b> .....	<b>vii</b>
<b>1 Scope</b> .....	<b>1</b>
<b>2 Normative references</b> .....	<b>1</b>
<b>3 Terms and definitions</b> .....	<b>2</b>
<b>4 Abbreviations</b> .....	<b>4</b>
<b>5 Fundamental requirements</b> .....	<b>4</b>
<b>6 Device description</b> .....	<b>4</b>
6.1 General.....	4
6.2 Intended use.....	4
6.3 Design inputs.....	4
6.3.1 Operational specifications .....	4
6.3.2 Performance specifications.....	4
6.3.3 Packaging, labelling, and sterilization.....	5
6.4 Design outputs.....	5
6.5 Design transfer (manufacturing verification/validation) .....	5
6.6 Risk management.....	5
<b>7 Design verification and validation</b> .....	<b>6</b>
7.1 General requirements.....	6
7.2 <i>In vitro</i> assessment .....	6
7.2.1 General.....	6
7.2.2 Test conditions, sample selection, and reporting requirements .....	6
7.2.3 Material property assessment.....	6
7.2.4 Hydrodynamic performance assessment.....	6
7.2.5 Structural performance assessment.....	7
7.2.6 Design- or procedure-specific testing.....	8
7.2.7 Device MRI compatibility .....	8
7.2.8 Simulated use .....	8
7.2.9 Human factors/usability assessment.....	8
7.2.10 Implant thrombogenic and haemolytic potential assessment.....	8
7.3 Preclinical <i>in vivo</i> evaluation .....	8
7.3.1 General.....	8
7.3.2 Overall requirements .....	8
7.3.3 Methods.....	9
7.3.4 Test report.....	10
7.4 Clinical investigations.....	11
7.4.1 General.....	11
7.4.2 Study considerations.....	12
7.4.3 Study endpoints .....	14
7.4.4 Ethical considerations .....	14
7.4.5 Pivotal studies: Distribution of subjects and investigators.....	15
7.4.6 Statistical considerations including sample size and duration .....	16
7.4.7 Patient selection criteria.....	17
7.4.8 Valve thrombosis prevention .....	18
7.4.9 Clinical data requirements.....	18
<b>Annex A (informative) Surgical heart valve substitute hazard analysis example</b> .....	<b>23</b>

<b>Annex B (informative) <i>In vitro</i> procedures for testing unstented or similar valves in compliant chambers</b> .....	25
<b>Annex C (informative) Preclinical <i>in vivo</i> evaluation</b> .....	27
<b>Annex D (informative) Description of the surgical heart valve substitute and system</b> .....	30
<b>Annex E (informative) Examples of components of some surgical heart valve substitutes and systems</b> .....	32
<b>Annex F (informative) Guidelines for verification of hydrodynamic performance — Pulsatile flow testing</b> .....	36
<b>Annex G (informative) Examples of design specific testing</b> .....	40
<b>Annex H (informative) Fatigue assessment</b> .....	42
<b>Annex I (normative) Methods of evaluating clinical data against objective performance criteria</b> .....	45
<b>Annex J (normative) Adverse event classification during clinical investigation</b> .....	46
<b>Bibliography</b> .....	51

## 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](http://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](http://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](http://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 5840-2:2015), which has been technically revised.

The main changes compared to the previous edition are as follows: the engineering and clinical requirements in the ISO 5840 series have been updated to current specifications and integrated and harmonized across all of its parts.

A list of all parts in the ISO 5840 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](http://www.iso.org/members.html).

## **A1** Amendment A1 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 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](http://www.iso.org/directives)).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at [www.iso.org/patents](http://www.iso.org/patents). ISO shall not be held responsible for identifying any or all such patent rights.

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](http://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).

A list of all parts in the ISO 5840 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](http://www.iso.org/members.html). **A1**

## Introduction

This document has been prepared for surgical heart valve substitutes with emphasis on providing guidance for *in vitro* testing, preclinical *in vivo* and clinical evaluations, reporting of all *in vitro*, preclinical *in vivo*, and clinical evaluations and labelling and packaging of the device. This process is intended to clarify the required procedures prior to market release and to enable prompt identification and management of any subsequent issues.

This document is used in conjunction with ISO 5840-1 and ISO 5840-3.

This document is a preview generated by EVS

This document is a preview generated by EVS

# Cardiovascular implants — Cardiac valve prostheses —

## Part 2: Surgically implanted heart valve substitutes

### 1 Scope

This document is applicable to heart valve substitutes intended for implantation in human hearts, generally requiring cardiopulmonary bypass and generally with direct visualization. See Annex E for examples of surgical heart valve substitutes and their components.

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

This document establishes an approach for verifying/validating the design and manufacture of a surgical heart valve substitute through risk management. The selection of appropriate qualification tests and methods are derived from the risk assessment. The tests can include those to assess the physical, chemical, biological, and mechanical properties of surgical heart valve substitutes and of their materials and components. The tests can also include those for pre-clinical *in vivo* evaluation and clinical evaluation of the finished surgical heart valve substitute.

This document defines operational conditions and performance requirements for surgical heart valve substitutes where adequate scientific and/or clinical evidence exists for their justification.

For some heart valve substitutes (e.g. sutureless), the requirements of both this document and ISO 5840-3:2021 can be relevant and are considered as applicable to the specific device design and are based on the results of the risk analysis.

### 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 5840-1:2021, *Cardiovascular implants — Cardiac valve prostheses — Part 1: General requirements*

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

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

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

ISO 14630, *Non-active surgical implants — General requirements*

ISO 16061, *Instrumentation for use in association with non-active surgical implants — General requirements*

ISO/PAS 7020:2023, *Sizing parameters of surgical valve prostheses: Requirements regarding the application of ISO 5840-2*