SLOVENSKI STANDARD
SIST EN ISO 10993-6:2026

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Biološko ovrednotenje medicinskih pripomočkov - 6. del: Preskusi, povezani z lokalnimi učinki po implantaciji (ISO 10993-6:2026)

Biological evaluation of medical devices - Part 6: Tests for local effects after implantation (ISO 10993-6:2026)

Biologische Beurteilung von Medizinprodukten - Teil 6: Prüfungen auf lokale Effekte nach Implantationen (ISO 10993-6:2026)

Évaluation biologique des dispositifs médicaux - Partie 6: Essais concernant les effets locaux après implantation (ISO 10993-6:2026)

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11.100.20	Biološko ovrednotenje medicinskih pripomočkov	Biological evaluation of medical devices

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Biologische Beurteilung von Medizinprodukten - Teil 6: Prüfungen auf lokale Effekte nach Implantation (ISO 10993-6:2026)

This European Standard was approved by CEN on 22 January 2026.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard 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.

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COMITÉ EUROPÉEN DE NORMALISATION
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CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

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European foreword

This document (EN ISO 10993-6:2026) has been prepared by Technical Committee ISO/TC 194 "Biological and clinical evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 “Biological and clinical evaluation of medical devices” 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of an identical text or by endorsement, at the latest by November 2026, and conflicting national standards shall be withdrawn at the latest by November 2026.

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 10993-6:2016.

This document has been prepared under a standardization request addressed to CEN by the European Commission. The Standing Committee of the EFTA States subsequently approves these requests for its Member States.

For the relationship with EU Legislation, see informative Annex ZA, which is an integral part of this document.

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 10993-6:2026 has been approved by CEN as EN ISO 10993-6:2026 without any modification.

Annex ZA
(informative)

Relationship between this European Standard the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered

This European standard has been prepared under M/575 to provide one voluntary means of conforming to the General Safety and Performance Requirements of Regulation (EU) 2017/745 of 5 April 2017 concerning medical devices [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up.

Once this standard is cited in the Official Journal of the European Union under that Regulation, compliance with the normative clauses of this standard given in Table ZA.1 and application of the edition of the normatively referenced standards as given in Table ZA.2 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding General Safety and Performance Requirements of that Regulation, and associated EFTA Regulations.

Where a definition in this harmonised standard differs from a definition of the same term set out in Regulation (EU) 2017/745, the differences shall be indicated in the Annex Z. For the purpose of using this standard in support of the requirements set out in Regulation (EU) 2017/745, the definitions set out in this Regulation prevail.

Where the European standard is an adoption of an International Standard, the scope of this document can differ from the scope of the European Regulation that it supports. As the scope of the applicable regulatory requirements differ from nation to nation and region to region the standard can only support European regulatory requirements to the extent of the scope of the European Regulation for medical devices ((EU) 2017/745).

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Regulation (EU) 2017/745. This means that risks have to be ‘reduced as far as possible’, ‘reduced to the lowest possible level’, ‘reduced as far as possible and appropriate’, ‘removed or reduced as far as possible’, ‘eliminated or reduced as far as possible’, ’removed or minimized as far as possible’, or ‘minimized’, according to the wording of the corresponding General Safety and Performance Requirement.

NOTE 2 The manufacturer’s policy for determining **acceptable risk** must be in compliance with General Safety and Performance Requirements 1, 2, 3, 4, 5, 8, 9, 10, 11, 14, 16, 17, 18, 19, 20, 21 and 22 of the Regulation.

NOTE 3 When a General Safety and Performance Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZA.1 — Correspondence between this European Standard and Annex I of Regulation (EU) 2017/745 [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
10.1 [(a), (b), (c), (d) and (g)]	4, 5 and 6, and Annex A, Annex B, Annex C, Annex D	GSPR 10.1 [(a), (b), (c), (d) and (g)] is partly covered by this document, since the standard does not provide requirements on design and manufacture. However, this standard provides a means to assess interactions of medical devices with tissue after implantation. Toxicity as systemic effect is covered only when the study is designed accordingly. Performance of the medical device in terms of mechanical loading or functional performance is not covered. Flammability is not covered. Selection and applicability of relevant Annex should be performed according to 5.1.1.
10.2	4, 5 and 6, and Annex A, Annex B, Annex C, Annex D	GSPR 10.2 is partly covered by this document, since the standard does not provide requirements on design, manufacture and packaging. However, this standard provides a means to assess interactions of contaminants and residues from medical devices with the tissue. Selection and applicability of relevant Annex should be performed according to 5.1.1.
10.4.1 (first paragraph)	4, 5 and 6, and Annex A, Annex B, Annex C, Annex D	GSPR 10.4.1 (first paragraph) is partly covered by this document, since the standard does not provide requirements on design and manufacture. However, this standard provides a means to assess interactions of contaminants and residues from medical devices with the tissue. Selection and applicability of relevant Annex should be performed according to 5.1.1.

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s)/subclause(s) of this EN	Remarks/Notes
10.6	4, 5 and 6, and Annex A, Annex B, Annex C, Annex D	GSPR 10.6 is partly covered by this document, since the standard does not provide requirements on design and manufacture. However, this standard provides a means to assess the properties of particles which are or can be released into the patient's body. No guidance on size determination and nanomaterials is provided. Selection and applicability of relevant Annex should be performed according to 5.1.1.

Table ZA.2 — Normative references from clause 2 of this document and their corresponding European publications

Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
ISO 10993-1	ISO 10993-1:2025	Biological evaluation of medical devices — Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process	EN ISO 10993-1:2025
ISO 10993-2	ISO 10993-2:2022	Biological evaluation of medical devices — Part 2: Animal welfare requirements	EN ISO 10993-2:2022
ISO 10993-4	ISO 10993-4:2017 ISO 10993-4:2017/Amd 1:2025	Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood	EN ISO 10993-4:2017 EN ISO 10993-4:2017/A1:2025
ISO 10993-9	ISO 10993-9: 2019	Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products	EN ISO 10993-9:2021
ISO 10993-11	ISO 10993-11:2017	Biological evaluation of medical devices — Part 11: Tests for systemic toxicity	EN ISO 10993-11:2018
ISO 10993-12:2021	ISO 10993-12:2021 ISO 10993-12:2021/Amd 1:2025	Biological evaluation of medical devices — Part 12: Sample preparation and reference materials	EN ISO 10993-12:2021 EN ISO 10993-12:2021/A1:2025
ISO 10993-16	ISO 10993-16:2017	Biological evaluation of medical devices — Part 16: Toxicokinetic	EN ISO 10993-16:2017

Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
		study design for degradation products and leachables	

The documents listed in the Column 1 of Table ZA.2, in whole or in part, are normatively referenced in this document, i.e. are indispensable for its application. The achievement of the presumption of conformity is subject to the application of the edition of Standards as listed in Column 4 or, if no European Standard Edition exists, the International Standard Edition given in Column 2 of Table ZA.2.

WARNING 1 — Presumption of conformity stays valid only as long as a reference to this European standard is maintained in the list published in the Official Journal of the European Union. Users of this standard should consult frequently the latest list published in the Official Journal of the European Union.

WARNING 2 — Other Union legislation may be applicable to the product(s) falling within the scope of this standard.

International Standard

ISO 10993-6

Biological evaluation of medical devices —

Part 6: Tests for local effects after implantation

Évaluation biologique des dispositifs médicaux —

Partie 6: Essais concernant les effets locaux après implantation

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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 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).

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. 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.

This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 206, *Biological and clinical evaluation of medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This fourth edition cancels and replaces the third edition (ISO 10993-6:2016), which has been technically revised.

The main changes are as follows:

— new definitions for “comparative control”, “coupon”, “euthanasia”, “local effect”, “location marker”, “steady-state” and “reference control” have been added to Clause 3;

— a new paragraph on the use of smaller compositionally representative samples or coupons has been added to 4.2.2;

— a new subclause 4.3 “Selection of control materials” has been added;

— the discussion of assessment of lymph nodes for certain materials has been expanded;

— a new Annex E “Test methods for devices contacting peripheral nerve tissue” and Annex G “Microscopic evaluation of tissue responses to implanted materials” have been added;

— tissue and pathological terminology has been updated throughout this document;

— bibliographical entries have been updated.

A list of all parts in the ISO 10993 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

The objective of the implantation test methods is to characterize the local tissue response after implantation of a medical device or material (test sample) including integration, degradation, or absorption in an appropriate animal model.

The test sample is implanted into an anatomical site appropriate for the evaluation of the local effects of the medical device (or portion of) in an animal.

The medical device or material local effects are evaluated by a comparison of the tissue response caused by a test sample to that caused by comparative or reference control samples used in medical devices whose clinical acceptability and biocompatibility characteristics have been established.

Careful study design can include other relevant biological effects to reduce the number of animals used to evaluate safety and efficacy while accomplishing all study objectives. Additionally, a long-term systemic toxicity study that is designed to incorporate the methods, biological effects, additional timepoints and outcomes of implantation testing can satisfy the requirements of this document and ISO 10993-11.