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Biological evaluation of medical devices - Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process (ISO 10993-1:2025)

EESTI STANDARDIMIS- JA AKREDITEERIMISKESKUS
ESTONIAN CENTRE FOR STANDARDISATION AND ACCREDITATION

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 10993-1:2026 sisaldab Euroopa standardi EN ISO 10993-1:2025 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 10993-1:2026 consists of the English text of the European standard EN ISO 10993-1:2025.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas.	This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation.
Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 24.12.2025.	Date of Availability of the European standard is 24.12.2025.
Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest.	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.

ICS 11.100, 11.100.20

EUROPEAN STANDARD

NORME EUROPÉENNE

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EN ISO 10993-1

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English Version

Biological evaluation of medical devices - Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process (ISO 10993-1:2025)

Évaluation biologique des dispositifs médicaux - Partie 1: Exigences et principes généraux pour l'évaluation de la sécurité biologique au sein d'un processus de gestion des risques (ISO 10993-1:2025)

Biologische Beurteilung von Medizinprodukten - Teil 1: Anforderungen und allgemeine Grundsätze für die Beurteilung der biologischen Sicherheit im Rahmen eines Risikomanagementsystems (ISO 10993-1:2025)

This European Standard was approved by CEN on 18 August 2025.

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This European Standard exists 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.

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

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

Ref. No. EN ISO 10993-1:2025 E

European foreword

This document (EN ISO 10993-1:2025) 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 June 2026, and conflicting national standards shall be withdrawn at the latest by June 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 10993-1:2020.

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 10993-1:2025 has been approved by CEN as EN ISO 10993-1:2025 without any modification.

International Standard

ISO 10993-1

Sixth edition
2025-11

Biological evaluation of medical devices —

Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process

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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 sixth edition cancels and replaces the fifth edition (ISO 10993-1:2018), which has been technically revised.

The main changes are as follows:

— this document has been completely reorganised and the title has been aligned with the risk management framework described in ISO 14971;

— content has been added to provide guidance and clarification of calculation of exposure duration;

— content has been added to provide guidance on characterization of the device and identification of biological hazards;

— the identification of biological effects (previously referred to as biological end points) has been modified;

— the term “externally communicating” has been replaced by language which reflects the specific tissue contact of device components;

— the term “effects after implantation” has been changed to “local effects after tissue contact” as some non-implanted devices also will need this type of assessment;

— Annex A has been revised to move most of the content to the main text and the remaining text in Annex A is now confined to the provision of guidance on materials characterization;

— Annex B has been added to explain the rationale for the changes to biological effects listed in Table 1 to Table 4.

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 aim of this document is to provide guidance and requirements for the biological evaluation of a medical device within a risk management process to protect humans from biological risks arising from the use of medical devices and the materials from which they are made. Biological risk evaluation compares the estimated biological risk against given risk criteria to determine the acceptability of the biological risk as part of the overall risk management.

Biological evaluation is primarily concerned with medical device biological safety, through consideration of risks associated with biological hazards. Nonetheless, some activities undertaken in the course of biological evaluation in addition to assessments of long-term safety can also generate information on device performance. For example, functional implant models can be used to assess long-term responses such as tissue ingrowth. Biological evaluation, as described in this document, is synonymous with biocompatibility evaluation.

Biological evaluation is conducted on the finished medical device. The principles and methods described can also be useful in the evaluation of candidate materials or prototype devices during a medical device development process, and data obtained from such evaluations can be of value in the assessment of the finished medical device.

Medical device design is wide-ranging, and, at one extreme, a medical device consists only of a single material, which can exist in more than one physical form, while at the other extreme, is a complex article consisting of numerous components made from multiple materials. Biological safety cannot be considered in isolation from the overall medical device design and can require the balancing of conflicting requirements. For example, the choice of the best material with respect to its biological safety can result in a less functional medical device.

The evaluation of biological safety is conducted in the context of the intended use of a particular medical device. Materials can be safe in one medical device and not in another. It is impossible to make generalized conclusions about the safety of a particular material for all medical applications. Biological responses that are regarded as adverse, caused by a material in one application, are not necessarily regarded as adverse in a different situation.

Physical and chemical information supports the overall biological evaluation and can be used to inform testing needs, if any. When biological testing is required, such testing is based upon in vitro, ex vivo or in vivo models. The interpretation of the results of biological tests requires caution because the inherent variability in biological responses between species and individuals means that the biological response observed in animal or cell culture models can differ from those observed in clinical use. Differences in response to the same material among individuals means that some individuals can have adverse reactions, even to well-established materials. Thus, biological evaluation is an exercise in risk management. When applied to the evaluation of candidate materials or prototype devices during a medical device development process, biological evaluation allows the informed and timely consideration of risk control measures such as use of alternative materials, manufacturing processes or designs.

The biological evaluation process described in this document draw on all available sources of information relevant to biological safety of the medical device, including post-market information. This approach allows a comprehensive review of the medical device, the identification of biological hazards and the biological harms which can arise and estimation of the associated risks. This comprehensive approach allows for the identification of any gaps in the existing data set and the consequent need for supplementary assessments (e.g. chemical analysis and hazard identification, biological testing to refine a biological risk estimate) to be conducted.

This document is supported by a wide range of test methods and guidance published in other documents in the ISO 10993 series, as well as other standards. Those who use this document can also consider more specific guidance contained in device-specific standards, where available. For some complex or novel materials or technologies, it can be difficult to use the established methods described in the ISO 10993 series. This document allows for the use of alternative procedures where scientifically justified.

The welfare of animals is very important and the selection of test methods and evolution of testing within the ISO 10993 framework is directed to continue to reduce, refine and, where possible, replace the use of animals for biological testing.

Biological evaluation of medical devices —

Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process

1 Scope

This document specifies the requirements and general principles governing the biological evaluation of medical devices within a risk management process according to ISO 14971.

This document applies to the biological evaluation of medical devices that have direct contact or indirect contact with either:

— a patient's body during intended use or reasonably foreseeable misuse; or

— the body of other users who are not patients, if the medical device is intended for personal protection (e.g. medical gloves, surgical masks).

Biological evaluation assesses the biological safety of the medical device by considering the biological risks associated with:

— constituents of a medical device; and

— tissue-device interactions (including physical effects).

The biological evaluation specified in this document can address the biological safety of the medical device, considering the life cycle from design and development through initial use of the finished medical device to final decommissioning or withdrawal from use. The biological evaluation considers both the biological safety of the finished device in first use, and the significance of any changes to the medical device which can occur throughout the life cycle. However, the evaluation of risks related to environmental impacts of decommissioning of medical devices are not within the scope of this document. This document does not mandate re-testing of medical devices that are already on the market and have established and acceptable safety profiles (see 6.6.2).

This document can be useful to support clinical or usability evaluations of medical devices. For example, a biological evaluation is a pre-requisite for conducting a clinical trial. This means that principles outlined in this document can be applied to the evaluation of prototype or development stage devices, as well as to finished medical devices.

Other parts of the ISO 10993 series cover specific aspects of biological evaluation, such as chemical characterization, biological testing, sample preparation, animal welfare and toxicological risk assessment.

For some types of medical devices, specific requirements from other standards (outside the ISO 10993 series) can be considered with a justification for the approach taken if there are differences between the requirements of the ISO 10993 series and those provided in other standards. For example, the ISO 18562 series provides specific requirements for biological evaluation of breathing gas pathway medical devices and ISO 7405 provides specific requirements for biological evaluation of dental devices.

The evaluation of risks related to infectious agents [e.g. bacteria, moulds, yeasts, viruses, transmissible spongiform encephalopathy (TSE) agents] is not within the scope of this document.

NOTE 1 The evaluation of bacterial endotoxins is addressed by ISO 11737-3.

NOTE 2 The evaluation of risks related to viruses, TSE agents and other pathogens originating from materials of animal origin is addressed by the ISO 22442 series.

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

ISO 10993-3, *Biological evaluation of medical devices — Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*

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

ISO 10993-5, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 10993-6, *Biological evaluation of medical devices — Part 6: Tests for local effects after implantation*

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO 10993-9:2019, *Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products*

ISO 10993-10, *Biological evaluation of medical devices — Part 10: Tests for skin sensitization*

ISO 10993-11, *Biological evaluation of medical devices — Part 11: Tests for systemic toxicity*

ISO 10993-12, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials*

ISO 10993-13, *Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices*

ISO 10993-14, *Biological evaluation of medical devices — Part 14: Identification and quantification of degradation products from ceramics*

ISO 10993-15, *Biological evaluation of medical devices — Part 15: Identification and quantification of degradation products from metals and alloys*

ISO 10993-16, *Biological evaluation of medical devices — Part 16: Toxicokinetic study design for degradation products and leachables*

ISO 10993-17:2023, *Biological evaluation of medical devices — Part 17: Toxicological risk assessment of medical device constituents*

ISO 10993-18:2020, *Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process*

ISO/TS 10993-19, *Biological evaluation of medical devices — Part 19: Physico-chemical, morphological and topographical characterization of materials*

ISO 10993-23, *Biological evaluation of medical devices — Part 23: Tests for irritation*

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

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