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**MEDITSIINISEADMETE BIOLOOGILINE HINDAMINE.
OSA 12: PROOVI ETTEVALMISTAMINE JA ETALONAINED**

**Biological evaluation of medical devices -
Part 12: Sample preparation and reference materials
(ISO 10993-12:2021 + ISO 10993 12:2021/Amd 1:2025)**

EESTI STANDARDI EESSÕNA**NATIONAL FOREWORD**

See Eesti standard EVS-EN ISO 10993-12:2021+A1:2025 sisaldab Euroopa standardi EN ISO 10993-12:2021 ja selle muudatuse A1:2025 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 10993-12:2021+A1:2025 consists of the English text of the European standard EN ISO 10993-12:2021 and its amendment A1:2025.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas. Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 16.06.2021, muudatus A1 24.09.2025.	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 16.06.2021, for A1 24.05.2025.
Muudatusega A1 lisatud või muudetud teksti algus ja lõpp on tekstis tähistatud sümboolidega $\boxed{A1}$ $\langle A1 \rangle$. 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 $\boxed{A1}$ $\langle A1 \rangle$. 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 11.100.20

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EUROPEAN STANDARD

EN ISO 10993-12 + A1

NORME EUROPÉENNE

EUROPÄISCHE NORM

June 2021, September 2025

ICS 11.100.20

Supersedes EN ISO 10993-12:2012

English Version

Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021 + ISO 10993 12:2021/Amd 1:2025)

Évaluation biologique des dispositifs médicaux - Partie 12: Préparation des échantillons et matériaux de référence (ISO 10993-12:2021 + ISO 10993 12:2021/Amd 1:2025)

Biologische Beurteilung von Medizinprodukten - Teil 12: Probenvorbereitung und Referenzmaterialien (ISO 10993-12:2021 + ISO 10993 12:2021/Amd 1:2025)

This European Standard was approved by CEN on 15 September 2020. Amendment A1 was approved by CEN on 24 August 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 10993-12:2021) 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 December 2021, and conflicting national standards shall be withdrawn at the latest by December 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 10993-12:2012.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For the relationship with EU Directive(s) see informative Annex ZA, which is integral part of this document.

The following referenced documents are indispensable for the application of this document. For undated references, the latest edition of the referenced document (including any amendments) applies. For dated references, only the edition cited applies. However, for any use of this standard 'within the meaning of Annex ZA, the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this shall be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard, as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table — Correlations between undated normative references and dated EN and ISO standards

References as listed in the ISO standard	Equivalent dated standard	
	EN	ISO or IEC
ISO 10993-1	EN ISO 10993-1:2020 ^a	ISO 10993-1:2018
ISO 10993-5	EN ISO 10993-5:2009	ISO 10993-5:2009
ISO 10993-17	EN ISO 10993-17:2009	ISO 10993-17:2002
ISO 10993-18	EN ISO 10993-18:2020 ^a	ISO 10993-18:2020
^a Under preparation at European level.		

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 10993-12:2021 has been approved by CEN as EN ISO 10993-12:2021 without any modification.

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A1 Amendment A1 European foreword

This document (EN ISO 10993-12:2021/A1:2025) 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 Amendment to the European Standard EN ISO 10993-12:2021 shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by March 2026, and conflicting national standards shall be withdrawn at the latest by March 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 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 10993-12:2021/Amd 1:2025 has been approved by CEN as EN ISO 10993-12:2021/A1:2025 without any modification. **A1**

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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 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).

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).

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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 fifth edition cancels and replaces the fourth edition (ISO 10993-12:2012), which has been technically revised.

The main changes compared to the previous edition are as follows:

- change of scope to cover extractions only for biological evaluation tests;
- harmonization of definitions with ISO 10993-18;
- revision of 10.3.1 extraction condition table and Annex D regarding exhaustive extraction.

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.

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.

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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.

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Introduction

It is important that sample preparation methods be appropriate for both the biological evaluation methods and the materials being evaluated. Each biological test method requires the selection of materials, extraction solvents and conditions.

This document is based on existing national and international standards and regulations, wherever possible.

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Biological evaluation of medical devices —

Part 12:

Sample preparation and reference materials

1 Scope

This document specifies requirements and gives guidance on the procedures in the preparation of samples and the selection of reference materials for medical device testing primarily in biological test systems primarily in accordance with one or more parts of the ISO 10993 series.

Specifically, this document addresses the following:

- test sample selection;
- selection of representative portions from a medical device;
- test sample preparation;
- experimental controls;
- selection of, and requirements for, reference materials;
- preparation of extracts.

This document is not applicable to live cells but can be relevant to the material or medical device components of combination products containing live cells.

Extractions for chemical characterization are covered in ISO 10993-18. Clause 7, 8, 9, 10 [with the exception of 10.3.5 and 10.3.11 b)], and 11 can apply to extractions for chemical characterization. Information given in C.1 to C.4 can also be relevant.

2 Normative references

A1 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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-18, *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 14971, *Medical devices — Application of risk management to medical devices* **A1**