



SLOVENSKI STANDARD
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01-maj-2023

Nadomešča:

SIST EN ISO 10993-10:2013

Biološko ovrednotenje medicinskih pripomočkov - 10. del: Preskusi preobčutljivosti kože (ISO 10993-10:2021)

Biological evaluation of medical devices - Part 10: Tests for skin sensitization (ISO 10993-10:2021)

Biologische Beurteilung von Medizinprodukten - Teil 10: Prüfungen auf Hautsensibilisierung (ISO 10993-10:2021)

Évaluation biologique des dispositifs médicaux - Partie 10: Essais de sensibilisation cutanée (ISO 10993-10:2021)

Ta slovenski standard je istoveten z: EN ISO 10993-10:2023

ICS:

11.100.20	Biološko ovrednotenje medicinskih pripomočkov	Biological evaluation of medical devices
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NORME EUROPÉENNE

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February 2023

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Biological evaluation of medical devices - Part 10: Tests for skin sensitization (ISO 10993-10:2021)

Évaluation biologique des dispositifs médicaux - Partie
10: Essais de sensibilisation cutanée (ISO 10993-
10:2021)

Biologische Beurteilung von Medizinprodukten - Teil
10: Prüfungen auf Hautsensibilisierung (ISO 10993-
10:2021)

This European Standard was approved by CEN on 13 September 2021.

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.

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

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European foreword

This document (EN ISO 10993-10:2023) 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 August 2023, and conflicting national standards shall be withdrawn at the latest by August 2023.

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 10993-10:2010.

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

For the relationship with EU Directive(s) / Regulation(s), 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 10993-10:2021 has been approved by CEN as EN ISO 10993-10:2023 without any modification.

Annex ZA (informative)

Relationship between this European standard and 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 [O] 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 standard differs from a definition of the same term set out in Regulation (EU) 2017/745, the differences shall be indicated in this 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 standard 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)/sub-clause(s) of this EN	Remarks/Notes
10.1 [(a) and (b)]	4, 5, 6 and 7	ER 10.1 [(a) and (b)] are only partly covered by this document, since the standard does not provide requirements on design and manufacture and packaging. However, this standard provides a means to assess skin sensitization to substances used in the manufacture of medical devices. Other forms of toxicity and flammability are not covered.
10.2	4, 5, 6 and 7	ER 10.2 is only partly covered by this document, since the standard does not provide requirements on design and manufacture. However, this standard provides a means to assess skin sensitization to substances leaking from medical devices
10.4.1 (First paragraph)	4, 5, 6 and 7	ER 10.4.1 (first paragraph) is only partly covered by this document, since the standard does not provide requirements on design and manufacture. However, this standard provides a means to assess skin sensitization to substances used in the manufacture of medical devices. Other forms of toxicity are not covered.

NOTE This part of EN ISO 10993 refers to ISO 10993-1 which itself refers to ISO 14971. In Europe, it should be assumed that the reference to ISO 14971 is to EN ISO 14971:2020.

General Note: Presumption of conformity depends on also complying with the relevant parts of the ISO 10993 series.

Table ZA.2 — Applicable Standards to confer presumption of conformity as described in this Annex ZA

Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
ISO 10993-1	ISO 10993-1:2018	<i>Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process</i>	EN ISO 10993-1:2020
ISO 10993-2	ISO 10993-2:2006	<i>Biological evaluation of medical devices — Part 2: Animal welfare requirements</i>	EN ISO 10993-2:2006
ISO 10993-12	ISO 10993-12:2021	<i>Biological evaluation of medical devices - Part 12: Sample preparation and reference materials</i>	EN ISO 10993-12:2021
ISO 10993-18	ISO 10993-18:2020	<i>Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process</i>	EN ISO 10993-18:2020

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
10993-10

Fourth edition
2021-11

**Biological evaluation of medical
devices —**

**Part 10:
Tests for skin sensitization**

*Évaluation biologique des dispositifs médicaux —
Partie 10: Essais de sensibilisation cutanée*

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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).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on 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 the following URL: 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 10993-10:2010), which has been technically revised.

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

- this document now contains a description of skin sensitization testing only;
- [Annex C](#) on non-animal methods for skin sensitization (formerly [Annex D](#)) has been updated;
- the testing for irritation is now described in ISO 10993-23.

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.

ISO 10993-10:2021(E)

Introduction

This document assesses possible contact hazards from chemicals released from medical devices, which may produce skin sensitization.

Some materials that are included in medical devices have been tested, and their skin sensitization potential has been documented. Especially for dental materials, sensitizing properties were reported —see Reference [51]. Other materials and their chemical components have not been tested and may induce adverse effects when in contact with human tissue. The manufacturer is thus obliged to evaluate each device for potential adverse effects prior to marketing.

Traditionally, small animal tests are performed prior to testing on humans to help predict human response (background information is provided in [Annex D](#)). Since 2015, several in chemico and in vitro assays have been validated and Organization for Economic Co-operation and Development (OECD) test guidelines released to assess the skin sensitization potential of chemicals.[75][79][104] An overview of available alternative skin sensitization tests for neat chemicals is given in [Annex C](#). These test methods, each developed to address a specific key event, can possibly not be sufficient alone to conclude on the presence or absence of skin sensitization potential of chemicals and should be considered in the context of integrated approaches such as integrated approaches to testing and assessment (IATA), combining them with other complementary information. Note that the in vitro and in chemico tests for skin sensitization in [Annex C](#) have thus far been validated only for neat chemicals and not for medical devices. To confirm that they are applicable for evaluation of the skin sensitization potential of medical devices, their assays need to be assessed and validated.

Where appropriate, the preliminary use of in vitro methods is encouraged for screening purposes prior to animal testing. To reduce the number of animals used, this document presents a step-wise approach, with review and analysis of test results at each stage. It is intended that, for regulatory submission, skin sensitization studies be conducted using GLP or ISO/IEC 17025 as applicable to the respective country and comply with regulations related to animal welfare. Statistical analyses of data are recommended and used whenever appropriate. This document includes important tools for the development of safe products and is intended for use by professionals, appropriately qualified by training and experience, who can interpret its requirements and judge the outcomes of the evaluation for each medical device, taking into consideration all the factors relevant to the device, its intended use and the current knowledge of the medical device provided by review of the scientific literature and previous clinical experience.

This document is based on numerous standards and guidelines, including OECD Guidelines, US Pharmacopoeia and the European Pharmacopoeia. It is intended to be the basic document for the selection and conduct of tests enabling the evaluation of dermal sensitization responses relevant to the safety of medical materials and devices.

Biological evaluation of medical devices —

Part 10: Tests for skin sensitization

1 Scope

This document specifies the procedure for the assessment of medical devices and their constituent materials with regard to their potential to induce skin sensitization.

This document includes:

- details of in vivo skin sensitization test procedures;
- key factors for the interpretation of the results.

NOTE Instructions for the preparation of materials specifically in relation to the above tests are given in [Annex A](#).

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

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

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

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

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 10993-1 and the following 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>
- IEC Electropedia: available at <https://www.electropedia.org/>

3.1

allergen sensitizer

substance or material that is capable of inducing a specific hypersensitivity reaction upon repeated contact with that substance or material