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STN	**Biologické hodnotenie zdravotníckych pomôcok Časť 18: Chemická charakterizácia materiálov zdravotníckych pomôcok v procese riadenia rizík (ISO 10993-18: 2020)**	**STN EN ISO 10993-18** 85 6510

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

Táto norma obsahuje anglickú verziu európskej normy.
This standard includes the English version of the European Standard.

Táto norma bola oznámená vo Vestníku ÚNMS SR č. 08/20

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English Version

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

Évaluation biologique des dispositifs médicaux - Partie 18: Caractérisation chimique des matériaux des dispositifs médicaux au sein d'un processus de gestion du risque (ISO 10993-18:2020)

Biologische Beurteilung von Medizinprodukten - Teil 18: Chemische Charakterisierung von Werkstoffen für Medizinprodukte im Rahmen eines Risikomanagementsystems (ISO 10993-18:2020)

This European Standard was approved by CEN on 21 July 2019.

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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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Ref. No. EN ISO 10993-18:2020 E

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European foreword

This document (EN ISO 10993-18:2020) 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of an identical text or by endorsement, at the latest by November 2020, and conflicting national standards shall be withdrawn at the latest by November 2020.

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 10993-18:2009.

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, ZB and ZC, which are an 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

Normative references as listed in Clause 2 of the ISO standard	**Equivalent dated standard**	
	EN	ISO or IEC
ISO 10993-1	EN ISO 10993-1:2020	ISO 10993-1:2018
ISO 10993-17	EN ISO 10993-17:2009	ISO 10993-17:2002
ISO 14971	EN ISO 14971:2020	ISO 14971:2020

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 10993-18:2020 has been approved by CEN as EN ISO 10993-18:2020 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 a Commission's standardisation request [Full reference to the request "M/xxx"] 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].

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 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.

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 This Annex ZA is based on normative references according to the table of references in the European Foreword, replacing the references in the core text.

NOTE 4 When a General Safety and Performance Requirement does not appear in Table ZC.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]

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
10.1 a), b) and h)	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including a qualitative characterization of the chemicals and materials used, a quantitative characterization of the amounts of chemicals and materials used and an evaluation of chemical release (leachable and extractable profile) in both the design and manufacturing processes. This chemical characterization can be used to define or confirm chemical specifications [10.1 h)] and evaluate the risk of toxicity [10.1 a) and b)] and biocompatibility [10.1 b)]. Flammability [10.1 a)] is not covered.* *For 10.1 b), ADME (absorption, distribution, metabolism, and excretion) is not covered. .* *For 10.1 h), physical specifications are not covered.*
10.2	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including an evaluation of the release of contaminants and residues (composition, leachable and extractable profile) in both the design and manufacturing processes. Packaging is not covered. Aspects of contaminants and residues during transport and storage are not covered.*
10.4.1 (First paragraph, first sentence)	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including an evaluation of chemical substances that may be released from the medical device (composition, leachable and extractable profile) in both the design and manufacturing processes.* *Particles and wear debris are not covered.*

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.

Annex ZB
(informative)

Relationship between this European Standard and the essential requirements of Directive 90/385/EEC [OJ L 189] aimed to be covered

This European Standard has been prepared under a Commission's joint standardization request M/BC/CEN/89/9 concerning harmonized standards relating to horizontal aspects in the field of medical devices to provide one voluntary means of conforming to essential requirements of Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices [OJ L 189].

Once this standard is cited in the Official Journal of the European Union under that Directive, compliance with the normative clauses of this standard given in Table ZB.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding essential requirements of that Directive and associated EFTA regulations.

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 Directive 90/385/EEC as amended by 2007/47/EC. This means that risks have to be reduced 'as far as possible', 'to a minimum', 'to the lowest possible level', 'minimized' or 'removed', according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer's policy for determining acceptable risk must be in compliance with Essential Requirements 1, 4, 5, 8, 9 and 10 of the Directive.

NOTE 3 This Annex ZB is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZB.1, it means that it is not addressed by this European Standard.

Table ZB.1 — Correspondence between this European Standard and Annex I of Directive 90/385/EEC [OJ L 189]

Essential Requirements of Directive 90/385/EEC	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
9 (only first and second indent)	5 and 6	*This standard provides requirements and recommendations for evaluating the chemical characterization of medical devices as part of a risk management process, including a qualitative characterization of the chemicals and materials used, a quantitative characterization of the amounts of chemicals and materials used and an evaluation of chemical release (leachable and extractable profile) in both the design and manufacturing processes. This chemical characterization can be used to evaluate the risk of toxicity (first indent) and biocompatibility (second indent).*

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

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 products falling within the scope of this standard.

Annex ZC
(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 a Commission's standardisation request [Full reference to the request "M/xxx"] 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].

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 ZC.1 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.

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 This Annex ZC is based on normative references according to the table of references in the European Foreword, replacing the references in the core text.

NOTE 4 When a General Safety and Performance Requirement does not appear in Table ZC.1, it means that it is not addressed by this European Standard.

Table ZC.1 — Correspondence between this European Standard and Annex I of Regulation (EU) 2017/745 [OJ L 117]

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s)/sub-clause(s) of this EN	Remarks/Notes
10.1 a), b) and h)	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including a qualitative characterization of the chemicals and materials used, a quantitative characterization of the amounts of chemicals and materials used and an evaluation of chemical release (leachable and extractable profile) in both the design and manufacturing processes. This chemical characterization can be used to define or confirm chemical specifications [10.1 h)] and evaluate the risk of toxicity [10.1 a) and b)] and biocompatibility [10.1 b)]. Flammability [10.1 a)] is not covered.* *For 10.1 b), ADME (absorption, distribution, metabolism, and excretion) is not covered. .* *For 10.1 h), physical specifications are not covered.*
10.2	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including an evaluation of the release of contaminants and residues (composition, leachable and extractable profile) in both the design and manufacturing processes. Packaging is not covered. Aspects of contaminants and residues during transport and storage are not covered.*
10.4.1 (First paragraph, first sentence)	5 and 6	*This standard provides requirements and recommendations for the chemical characterization of medical devices as part of a risk management process, including an evaluation of chemical substances that may be released from the medical device (composition, leachable and extractable profile) in both the design and manufacturing processes.* *Particles and wear debris are not covered.*

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

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 10993-18

Second edition
2020-01

Biological evaluation of medical devices —

Part 18: Chemical characterization of medical device materials within a risk management process

Évaluation biologique des dispositifs médicaux —

Partie 18: Caractérisation chimique des matériaux des dispositifs médicaux au sein d'un processus de gestion du risque

Reference number
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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 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 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.*

This second edition cancels and replaces the first edition (ISO 10993-18:2005), which has been technically revised. The main changes compared to the previous edition are as follows:

— greater integration and harmonization with ISO 10993-1, ISO 10993-12, and ISO 10993-17;

— a revised and expanded chemical characterization process flowchart;

— a strengthened explanation that analytical testing is not necessarily required;

— added a number of definitions (e.g. medical device configuration, materials of construction, and material composition);

— clarified testing approaches unique to chemical characterization (i.e. digestion and dissolution for hazard identification);

— added discussion of considerations related to analytical method qualification;

— added informative annexes on general principles, vehicle extraction considerations, and the analytical evaluation threshold (AET; concentration threshold below which extractables or leachables identification is unneeded).

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

ISO 10993-1 serves as a framework in which to plan a biological evaluation which, as scientific knowledge advances our understanding of the basic mechanisms of tissue responses, minimizes the number and exposure of test animals. Preference is given to the assessment of chemical/physical properties and testing with *in vitro* models in situations within a risk assessment process. These methods are used when the results yield equally relevant information to that obtained from *in vivo* models.

The characterization procedure and its associated flowchart is based on the principles in ISO 10993-1; specifically, that the biological evaluation and risk assessment process is most efficient and effective if it is based on the minimum amount of acceptable and necessary chemical information that can establish that a medical device presents an acceptable health risk.

ISO 10993-1:2018, 4.2 states that in the selection of materials to be used in medical device manufacture, the first consideration shall be fitness for purpose with regard to characteristics and properties of the material, which can include chemical, toxicological, physical, electrical, morphological and mechanical properties. Furthermore, ISO 10993-1:2018, 6.1 states that gathering physical and chemical information on the medical device or component is a crucial first step in the biological evaluation process and its associated process of material characterization.

Lastly, ISO 10993-1:2018, and by reference ISO 14971, points out that a biological risk analysis depends on what is known about the material formulation, what nonclinical and clinical safety and toxicological data exist, and on the nature and duration of body contact with the medical device.

The requirements specified in this document are intended to yield the following information, which will be of value in assessing the biological response to the materials as represented in the final product.

— The identities and quantities, as appropriate, of the materials of construction of the medical device (device configuration).

— The identities and quantities, as appropriate, of the chemical constituents in each material of construction (material composition).

— The identities and quantities, as appropriate, of chemical substances used in the medical device's manufacturing process, including processing aids and residues.

— The potential of the medical device and/or its materials of construction to release chemical substances to which a potentially affected individual could be exposed to during clinical conditions of use.

The composition of the materials of construction is mainly established by the suppliers of these materials. The composition can change during manufacture of a medical device. Other medical device characteristics are chiefly established by component suppliers or device manufacturers to address the performance and quality requirements to be met by the finished medical device as well as the production, storage and distribution processes experienced by the medical device.

INTERNATIONAL STANDARD ISO 10993-18:2020(E)

Biological evaluation of medical devices —

Part 18:
Chemical characterization of medical device materials within a risk management process

1 Scope

This document specifies a framework for the identification, and if necessary, quantification of constituents of a medical device, allowing the identification of biological hazards and the estimation and control of biological risks from material constituents, using a generally stepwise approach to the chemical characterization which can include one or more of the following:

— the identification of its materials of construction (medical device configuration);

— the characterization of the materials of construction via the identification and quantification of their chemical constituents (material composition);

— the characterization of the medical device for chemical substances that were introduced during manufacturing (e.g. mould release agents, process contaminants, sterilization residues);

— the estimation (using laboratory extraction conditions) of the potential of the medical device, or its materials of construction, to release chemical substances under clinical use conditions (extractables);

— the measurement of chemical substances released from a medical device under its clinical conditions of use (leachables).

This document can also be used for chemical characterization (e.g. the identification and/or quantification) of degradation products. Information on other aspects of degradation assessment are covered in ISO 10993-9, ISO 10993-13, ISO 10993-14 and ISO 10993-15.

The ISO 10993 series is applicable when the material or medical device has direct or indirect body contact (see ISO 10993-1 for categorization by nature of body contact).

This document is intended for suppliers of materials and manufacturers of medical devices, to support a biological evaluation.

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 10993-17, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

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