



SLOVENSKI STANDARD
oSIST prEN 10993-9:2018
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Biološko ovrednotenje medicinskih pripomočkov - 9. del: Okvirni sistem za prepoznavanje in ugotavljanje količine morebitnih razgradnih produktov (ISO/DIS 10993-9:2018)

Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products (ISO/DIS 10993-9:2018)

Biologische Beurteilung von Medizinprodukten - Teil 9: Rahmen zur Identifizierung und Quantifizierung von möglichen Abbauprodukten (ISO/DIS 10993-9:2018)

Évaluation biologique des dispositifs médicaux - Partie 9: Cadre pour l'identification et la quantification des produits potentiels de dégradation (ISO/DIS 10993-9:2018)

Ta slovenski standard je istoveten z: prEN ISO 10993-9

ICS:

11.100.20	Biološko ovrednotenje medicinskih pripomočkov	Biological evaluation of medical devices
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Biological evaluation of medical devices —

Part 9: Framework for identification and quantification of potential degradation products

*Évaluation biologique des dispositifs médicaux —**Partie 9: Cadre pour l'identification et la quantification des produits potentiels de dégradation*

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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 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 third edition cancels and replaces the second edition (ISO 10993-9:2009), which has been technically revised.

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

- a) biodegradation changed to degradation;
- b) information on test methods amended to consider nanomaterials and relevant material specific standards;

A list of all parts in the ISO 10993- series can be found on the ISO website.

Introduction

This document is intended to present the general principles on which the specific material investigations to identify and quantify degradation products described in ISO 10993-13 (polymers), ISO 10993-14 (ceramics) and ISO 10993-15 (metals and alloys) are based.

Information obtained from these studies is intended to be used in the biological evaluations described in the remaining parts of ISO 10993.

The materials used to construct medical devices can form degradation products when exposed to the biological environment, and in the body these products might behave differently to the bulk material.

Mechanical wear, which is not in scope of this standard, causes mostly particulate debris, whereas the release of substances from surfaces due to leaching, chemical breakdown of structures or corrosion can lead to free ions or to different kinds of reaction products in the form of organic or inorganic compounds.

The degradation products can be either reactive or stable and without biochemical reaction with their environment. Accumulations of substantial quantities of stable degradation products can, however, have physical effects on the surrounding tissues. Degradation products might remain at the location of their generation or might be transported within the biological environment by various mechanisms.

The level of biological tolerability of degradation products depends on their nature and concentration, and should be primarily assessed through clinical experience and focused studies. For theoretically possible, new and/or unknown degradation products, relevant testing is necessary. For well-described and clinically accepted degradation products, further investigation need not be necessary.

Note that the safety and efficacy of a medical device can be compromised as a result of any unintended or premature degradation, which should be considered in the risk management of the device.

This document can be applied to the degradation of materials used in any kind of product that falls within the definition of "medical device" in ISO 10993-1, even if such products are subject to different regulations from those applying to medical devices, e.g. the scaffold in a tissue engineered medical product, or a carrier matrix to deliver drugs or biologics.

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Biological evaluation of medical devices —

Part 9:

Framework for identification and quantification of potential degradation products

1 Scope

This document provides general principles for the systematic evaluation of the potential and observed degradation of medical devices through the design and performance of in vitro degradation studies. Information obtained from these studies can be used in the biological evaluation described in the ISO 10993- series.

This document considers both materials designed to degrade in the body as well as materials that are not intended to degrade.

This document is not applicable to:

- a) evaluation of degradation which occurs by purely mechanical processes; methodologies for the production of this type of degradation product are described in specific product standards, where available;

NOTE Purely mechanical degradation causes mostly particulate matter. Although this is excluded from the scope of this document, such degradation products can evoke a biological response and thus need to undergo biological evaluation as described in other parts of ISO 10993.

- b) leachable components which are not degradation products;
- c) medical devices or components that do not contact the patient's body directly or indirectly.

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 10993-13, *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 13781, *Implants for surgery — Homopolymers, copolymers and blends on poly(lactide) — In vitro degradation testing*

ISO/TR 10993-22, *Biological evaluation of medical devices — Part 22: Guidance on nanomaterials*

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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 terminological databases for use in standardization at the following addresses:

IEC Electropedia: available at <http://www.electropedia.org/>

ISO Online browsing platform: available at <https://www.iso.org/obp>

3.1

degradation

decomposition of a material

3.2

absorb

action of a non-endogenous (foreign) material or substance passing through or being assimilated by cells and/or tissue over time

3.3

leachable

substances that can be released from a medical device or material during clinical use

3.4

corrosion

attack on metallic materials by chemical or electrochemical reactions

Note 1 to entry: The term is sometimes used in a general sense for the deterioration of other materials but is in this part of ISO 10993 reserved for metallic materials.

3.5

substance

single chemical element or compound, or a complex structure of compounds

3.6

device component

one of the different parts of which a device is composed

3.7

degradation product

particle or chemical compound that is derived from the chemical breakdown of the original material

3.8

service environment

anatomical location for the intended use of the device including surrounding fluids, tissues and biomolecules

4 Principles for design of degradation studies

4.1 General

The approach to the assessment of degradation varies with the nature of the material under investigation, the medical device and the anatomical location of the specific device. The *in vitro* degradation models chosen for evaluation shall be representative of these factors. The studies to be conducted do not require a biological environment, but one that simulates the conditions of the intended clinical use.

Experience has shown that in some degradation processes, *in vitro* models do not reflect all aspects of the service environment, e.g. mechanical processes can influence degradation, and should be taken into account when defining the model service environment.

Experience has also shown that material property changes during degradation can result in different biological responses. The user is urged to be aware of those property changes and apply the relevant material specific standards (e.g. crystallization of polymers).

Materials-specific or product-specific degradation standards that address identification and quantification of degradation products should be considered in the design of degradation studies. ISO 10993-13 (for polymers), ISO 10993-14 (for ceramics) or ISO 10993-15 (for metals and alloys) shall apply if no suitable material-specific standard exists. Devices composed of two or more material types should consider all relevant degradation standards.

ISO 10993-13, ISO 10993-14 and ISO 10993-15 consider only those degradation products generated by a chemical alteration of the finished device. They are not applicable to degradation of the device induced during its intended use by mechanical stress, wear or electromagnetic radiation. For such degradation other methods should be considered.

4.2 Preliminary considerations

Careful consideration of the potential for intended or unintended degradation of a material is essential to the evaluation of the biological safety of a device. Part of this consideration is an assessment of the chemical characteristics and known degradation mechanisms, followed by an assessment of the need for, and design of, experimental degradation studies.

It is neither necessary nor practical to conduct degradation studies for all medical devices. Consideration of the need for degradation studies is provided in [Annex A](#). The assessment of the need for experimental degradation studies shall include a review of the literature and/or documented clinical experience. Guidance on proper reviewing of the literature can be found in ISO 10993-1. Such an assessment can potentially result in the conclusion that no further testing is needed.

Guidance on the biological evaluation of leachables including degradation products is given in ISO 10993-1, ISO 10993-16 and ISO 10993-17. See ISO 10993-12 for guidance on the extraction of leachables from medical devices and ISO 10993-18 for guidance on the chemical characterization of materials and their leachables used in medical devices. See ISO/TS 10993-19 for guidance on the physico-chemical, morphological and topographical characterization of materials. Consideration of these standards prior to conducting degradation studies can prove helpful in distinguishing degradation products from other leachables.

NOTE Despite the difference between degradation products and other leachables, it might be possible to combine a study on degradation products with a study on other leachable components. Distinguishing between degradation products and other types of leachables need not be necessary for further biological evaluation studies. However, when a reduction of the level of leachable components is deemed necessary as a risk control measure, this information is important. Additionally, some degradation products can not leach from the device, but still impact the properties of the device.

4.3 Study design

A degradation study plan complete with the purpose of the study shall be designed and documented to address the issues identified in [4.1](#). The approved study plan shall define the analytical methods by which the following characteristics of degradation products are to be investigated:

- a) chemical properties;
- b) physicochemical properties;
- c) physical morphology (as applicable).

The approved study plan shall also describe the methods used to generate degradation products. The methods should be optimized for detection of degradable substances and justified.