Meditsiiniseadmete bioloogilise sobivuse hindamine. Osa 15: Metallide ja sulamite laguproduktide kindlaksmääramine ja koguseline tuvastamine

Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys

EESTI STANDARDIKESKUS
ESTONIAN CENTRE FOR STANDARDISATION

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

Käesolev Eesti standard EVS-EN ISO 10993-15:2009 sisaldab Euroopa standardi EN ISO 10993-15:2009 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 10993-15:2009 consists of the English text of the European standard EN ISO 10993-15:2009.
Standard on kinnitatud Eesti Standardikeskuse 31.07.2009 käskkirjaga ja jõustub sellekohase teate avaldamisel EVS Teatajas.	This standard is ratified with the order of Estonian Centre for Standardisation dated 31.07.2009 and is endorsed with the notification published in the official bulletin of the Estonian national standardisation organisation.
Euroopa standardimisorganisatsioonide poolt rahvuslikele liikmetele Euroopa standardi teksti kättesaadavaks tegemise kuupäev on 10.06.2009.	Date of Availability of the European standard text 10.06.2009.
Standard on kättesaadav Eesti standardiorganisatsioonist.	The standard is available from Estonian standardisation organisation.

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Võtmesõnad: alloys, bioassay, decomposition, decomposition products, deterioration, determination, evaluations, identification, medical products, metals, quantification, toxicological testing

EUROPEAN STANDARD

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English Version

Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys (ISO 10993-15:2000)

Évaluation biologique des dispositifs médicaux - Partie 15: Identification et quantification des produits de dégradation issus des métaux et alliages (ISO 10993-15:2000)

Biologische Beurteilung von Medizinprodukten - Teil 15: Qualitativer und quantitativer Nachweis von Abbauprodukten aus Metallen und Legierungen (ISO 10993-15:2000)

This European Standard was approved by CEN on 23 May 2009.

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 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 Management Centre has the same status as the official versions.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
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EUROPÄISCHES KOMITEE FÜR NORMUNG

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Ref. No. EN ISO 10993-15:2009: E

Foreword

The text of ISO 10993-15:2000 has been prepared by Technical Committee ISO/TC 194 “Biological evaluation of medical devices” of the International Organization for Standardization (ISO) and has been taken over as EN ISO 10993-15:2009 by Technical Committee CEN/TC 206 “Biological evaluation of medical devices” the secretariat of which is held by NEN.

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 2009, and conflicting national standards shall be withdrawn at the latest by March 2010.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN ISO 10993-15:2000.

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 93/42/EEC on Medical Devices.

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

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, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 10993-15:2000 has been approved by CEN as a EN ISO 10993-15:2009 without any modification.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Communities under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in table ZA 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.

Table ZA — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9	Annex I: 7.1, 7.2, 7.5	

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

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Introduction

One of the potential health hazards resulting from medical devices may be due to the interactions of their electrochemically-induced degradation products with the biological system. Therefore, the evaluation of potential degradation products from metallic materials by methods suitable for testing the electrochemical behavior of these materials is a necessary step in the biological performance testing of materials.

The body environment typically contains cations of sodium, potassium, calcium and magnesium and anions of chloride, bicarbonate, phosphate and organic acids generally in concentrations between 2×10^{-3} mol and 150×10^{-3} mol. A range of organic molecules such as proteins, enzymes and lipoproteins is also present, but their concentrations may vary to a great extent. Earlier studies assumed that organic molecules did not exert a significant influence on the degradation of metallic implants, but newer investigations indicate that implant — protein interactions should be taken into account. Depending on a particular product or application, altering the pH of the testing environment may also need to be considered.

In such biological environments, metallic materials may undergo a certain degradation and the different degradation products may interact with the biological system in different ways. Therefore, the identification and quantification of these degradation products is an important step in evaluating the biological performance of medical devices.

Biological evaluation of medical devices —

Part 15: Identification and quantification of degradation products from metals and alloys

1 Scope

This part of ISO 10993 provides guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding material samples finished as ready for clinical use. It is applicable only to those degradation products generated by chemical alteration of the finished metallic device in an *in vitro* accelerated degradation test. Because of the accelerated nature of these tests, the test results may not reflect the implant or material behavior in the body. The described chemical methodologies are a means to generate degradation products for further assessments.

This part of ISO 10993 is not applicable to degradation products induced by applied mechanical stress.

NOTE Mechanically induced degradation, such as wear, may be covered in the appropriate product-specific standard. Where product-group standards provide applicable product-specific methodologies for the identification and quantification of degradation products, those standards should be considered.

Because of the wide range of metallic materials used in medical devices, no specific analytical techniques are identified for quantifying the degradation products. The identification of trace elements ($< 10^{-6}$) contained in the specific metal or alloy is not addressed in this part of ISO 10993, nor are specific requirements for acceptable levels of degradation products provided in this part of ISO 10993.

This part of ISO 10993 does not address the biological activity of the degradation products; see instead the applicable clauses of ISO 10993-1 and ISO 10993-17.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 3585, *Borosilicate glass 3.3 — Properties*.

ISO 3696, *Water for analytical laboratory use — Specification and test methods*.

ISO 8044, *Corrosion of metals and alloys — Basic terms and definitions*.

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing*.

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

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