Meditsiiniseadmete bioloogiline hindamine. Osa 15: Metallide ja sulamite lagusaaduste identifitseerimine ja kvantifitseerimine

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

EESTI STANDARDI EESSÕNA **NATIONAL FOREWORD**

Käesolev Eesti standard EVS-EN ISO 10993-15:2001 sisaldab Euroopa standardi EN ISO 10993-15:2000 ingliskeelset teksti. Käesolev dokument on jõustatud 18.05.2001 ja selle kohta on avaldatud teade Eesti standardiorganisatsiooni ametlikus väljaandes. Standard on kättesaadav Eesti standardiorganisatsioonist.	This Estonian standard EVS-EN ISO 10993-15:2001 consists of the English text of the European standard EN ISO 10993-15:2000. This document is endorsed on 18.05.2001 with the notification being published in the official publication of the Estonian national standardisation organisation. The standard is available from Estonian standardisation organisation.

Käsitlusala: This part of the standard provides guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding materials samples finished as ready for clinical use. It is applicable only those degradation products generated by chemical alteration of the finished metallic device in an in vitro accelerated degradation test.	**Scope:** This part of the standard provides guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding materials samples finished as ready for clinical use. It is applicable only those degradation products generated by chemical alteration of the finished metallic device in an in vitro accelerated degradation test.

ICS 11.100

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

EUROPEAN STANDARD
NORME EUROPÉENNE
EUROPÄISCHE NORM

EN ISO 10993-15

December 2000

ICS 11.100

English version

Biological evaluation of medical devices

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

(ISO 10993-15 : 2000)

Evaluation 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 2000-12-01.

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 Management Centre or to any CEN member.

The European Standards 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 Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

CEN

European Committee for Standardization
Comité Européen de Normalisation
Europäisches Komitee für Normung

Management Centre: rue de Stassart 36, B-1050 Brussels

Ref. No. EN ISO 10993-15 : 2000 E

Foreword

International Standard

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

which was prepared by ISO/TC 194 'Biological evaluation of medical devices' of the International Organization for Standardization, has been adopted by Technical Committee CEN/TC 206 'Biocompatibility of medical and dental materials and devices', the Secretariat of which is held by NEN, as a European Standard.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, and conflicting national standards withdrawn, by June 2001 at the latest.

In accordance with the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard:

Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

Endorsement notice

The text of the International Standard ISO 10993-15 : 2000 was approved by CEN as a European Standard without any modification.

NOTE: Normative references to international publications are listed in Annex ZA (normative).

Contents

Page

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.

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.*

3 Terms and definitions

For the purposes of this part of ISO 10993, the terms and definitions given in ISO 8044, ISO 10993-1, ISO 10993-9, ISO 10993-12 and the following apply.

3.1
alloy
material composed of a metallic element with one or more addition(s) of other metallic and/or non-metallic elements

3.2
electrolyte
solution containing ions with the capacity to conduct electric current

3.3
open-circuit potential
potential of an electrode measured with respect to a reference electrode or another electrode when no current flows to or from it

3.4
passive limit potential
E_a
electrode potential of the positive limit of the passive range

See Figure 1.

3.5
breakdown potential
E_p
critical electrode potential above which localized or transpassive corrosion is found to occur

See Figure 1.

4 Degradation test methods

4.1 General

To identify and quantify degradation products from metals and alloys in medical devices, a combination of two procedures is described. The choice of test procedure shall be justified according to the function of the medical device.

The first procedure described is a combination of a potentiodynamic test and a potentiostatic test. The second procedure described is an immersion test.

The potentiodynamic test is used to determine the general electrochemical behavior of the material under consideration and to determine certain specific points (E_a and E_p) on the potential/current density curve.