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Standards

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Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008)

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Biological evaluation of medical devices - Part 7: Ethylene oxide
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Évaluation biologique des dispositifs
médicaux - Partie 7: Résidus de
stérilisation à l'oxyde d'éthylène -
Rectificatif technique 1 (ISO 10993-
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Ce corrigendum prendra effet le 15 novembre 2009 pour incorporation dans les trois versions linguistiques officielles de la EN.

Die Berichtigung tritt am 15. November 2009 zur Einarbeitung in die drei offiziellen Sprachfassungen der EN in Kraft.



EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Ref. No.: EN ISO 10993-7:2008/AC:2009 D/E/F

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Foreword

This document (EN ISO 10993-7:2008/AC:2009) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 "Biological evaluation of medical devices" the secretariat of which is held by NEN.

Endorsement notice

The text of ISO 10993-7:2008/Cor 1:2009 has been approved by CEN as a EN ISO 10993-7:2008/AC:2009 without any modification.

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I.S. EN ISO 10993-7:2008/AC:2009
INTERNATIONAL STANDARD ISO 10993-7:2008
TECHNICAL CORRIGENDUM 1

Published 2009-11-15

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Biological evaluation of medical devices —
Part 7:
Ethylene oxide sterilization residuals

TECHNICAL CORRIGENDUM 1

Évaluation biologique des dispositifs médicaux —
Partie 7: Résidus de stérilisation à l'oxyde d'éthylène

RECTIFICATIF TECHNIQUE 1

Technical Corrigendum 1 to ISO 10993-7:2008 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

Page iv, Foreword

Correct the title of Part 1 to read as follows:

— *Part 1: Evaluation and testing within a risk management process*

Page 10, 5.3 Procedure for product release using residue dissipation curves

Second paragraph, second sentence should read:

Dissipation of EO from most materials and devices follows first-order kinetics, i.e. $(\ln[\text{EO}]) \propto$ (time after sterilization).

Page 13

Equation (A.5) should read as follows:

$$\sigma^2 = \frac{\left(\sum y^2 - \frac{(\sum y)^2}{n} \right) - S \times \left(\sum xy - \frac{(\sum x \sum y)}{n} \right)}{n - 2} \quad (\text{A.5})$$

Equation (A.6) should read as follows:

$$\lambda = \frac{\sum y}{n} \quad (\text{A.6})$$

Page 29, F.2.2 Intraocular lens limits

First paragraph, third sentence should read as follows:

This is necessary to prevent documented irritation responses of EO to ocular tissue (see References [44], [117], [118], [119] and [167]).

Second paragraph, third sentence should read as follows:

In such cases, References [44], [117], [118] and [119] indicate that the level of ECH that results in ocular toxicity is about four times greater than the corresponding EO level.

Page 30, F.2.5 Devices used in cardiopulmonary bypass procedures

First paragraph, delete the following sentences:

At this UTF, the allowable limit would increase to 21 mg EO. The EO limit reflects manufacturers' current ability to remove EO from these rather large devices.

Page 63, J.1.1

Footnote 9) should read as follows:

1 mmHg = 133,322 Pa or 760 mmHg = 101,325 kPa.

English Version

Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008)

Évaluation biologique des dispositifs médicaux - Partie 7:
Résidus de stérilisation à l'oxyde d'éthylène (ISO 10993-
7:2008)

Biologische Beurteilung von Medizinprodukten - Teil 7:
Ethylenoxid- Sterilisationsrückstände (ISO 10993-7:2008)

This European Standard was approved by CEN on 23 September 2008.

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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COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Annex ZB (informative) Relationship between this International Standard and the Essential Requirements of EU Directive 90/385/EEC on Active Implantable Medical Devices5

Foreword

This document (EN ISO 10993-7:2008) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with 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 April 2009, and conflicting national standards shall be withdrawn at the latest by October 2011.

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 10993-7:1995.

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 EC Directives.

For relationship with EC Directives, see informative Annexes ZA and ZB, which are an integral part of this document.

NOTE : The Essential Requirements of the Medical Devices Directives require that risks be reduced or eliminated as far as possible and, specifically, that risks posed by residues be minimized and risks posed by substances leaking from a device be reduced to a minimum. It is inherent in these Essential Requirements that, within the maximum limits specified by this standard, exposure to a genotoxic carcinogen should be reduced to levels as low as reasonably practicable, taking account of the generally acknowledged state of the art, the technological level existing at the time of design and technical and economic considerations compatible with a high level of health and safety.

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 10993-7:2008 has been approved by CEN as a EN ISO 10993-7:2008 without any modification.

I.S. EN ISO 10993-7:2008
**INTERNATIONAL
STANDARD**

**ISO
10993-7**

Second edition
2008-10-15

**Biological evaluation of medical
devices —**

Part 7:
Ethylene oxide sterilization residuals

Évaluation biologique des dispositifs médicaux —

Partie 7: Résidus de stérilisation à l'oxyde d'éthylène



Reference number
ISO 10993-7:2008(E)

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 10993-7 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This second edition cancels and replaces the first edition (ISO 10993-7:1995) which has been technically revised.

ISO 10993 consists of the following parts, under the general title *Biological evaluation of medical devices*:

- *Part 1: Evaluation and testing within a risk management system*
- *Part 2: Animal welfare requirements*
- *Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*
- *Part 4: Selection of tests for interactions with blood*
- *Part 5: Tests for in vitro cytotoxicity*
- *Part 6: Tests for local effects after implantation*
- *Part 7: Ethylene oxide sterilization residuals*
- *Part 9: Framework for identification and quantification of potential degradation products*
- *Part 10: Tests for irritation and skin sensitization*
- *Part 11: Tests for systemic toxicity*
- *Part 12: Sample preparation and reference materials*
- *Part 13: Identification and quantification of degradation products from polymeric medical devices*
- *Part 14: Identification and quantification of degradation products from ceramics*
- *Part 15: Identification and quantification of degradation products from metals and alloys*

- *Part 16: Toxicokinetic study design for degradation products and leachables*
- *Part 17: Establishment of allowable limits for leachable substances*
- *Part 18: Chemical characterization of materials*
- *Part 19: Physico-chemical, morphological and topographical characterization of materials* [Technical Specification]
- *Part 20: Principles and methods for immunotoxicology testing of medical devices* [Technical Specification]

Introduction

Requirements for the development, validation and routine control of an ethylene oxide sterilization process for medical devices are given in International Standards developed by ISO/TC 198. Certain requirements relating to medical devices for biological testing, selection of tests, and the allocation of devices to categories are dealt with in a variety of International Standards developed by ISO/TC 194. The specific requirement for ethylene oxide and other sterilization process residuals was referred to ISO/TC 194. Other International Standards delineate particular requirements for biological testing for specific products.

As noted in the introduction to ISO 11135-1:2007, when determining the suitability of ethylene oxide (EO) for sterilization of medical devices, it is important to ensure that the levels of residual EO, ethylene chlorohydrin (ECH) and ethylene glycol (EG) pose a minimal risk to the patient in normal product use. Therefore, it is important that the use of alternative materials and sterilization processes be considered during product design and development. EO is known to exhibit a number of biological effects. In the development of this part of ISO 10993, consideration was given to these effects, which include irritation, organ damage, mutagenicity and carcinogenicity in humans and animals, and reproductive effects in animals. Similar consideration was given to the harmful effects of ECH and EG. In practice, for most devices, exposure to EO and ECH is considerably lower than the maximum values specified in this part of ISO 10993.

Moreover, when the choice for EO sterilization has been made, irrespective of the provisions of this part of ISO 10993, exposure to EO residues should be minimized. Requirements herein are in addition to the biological evaluation and testing requirements for each individually designed medical device as indicated in ISO 10993-1. The biological evaluation and testing requirements, combined with the EO-sterilization process residue limits, form the justification that an EO-sterilized device is acceptable for use. Maximum allowable residues for ethylene chlorohydrin (ECH), when ECH has been found to be present in medical devices sterilized with EO, are also specified. Local effects (e.g., irritation) have been considered and are incorporated in the tolerable contact limit (TCL) as given in 4.3.5.2 and Annex G for EO, and in 4.3.5.3 and Annex H for ECH.

Biological evaluation of medical devices —

Part 7: Ethylene oxide sterilization residuals

1 Scope

This part of ISO 10993 specifies allowable limits for residual ethylene oxide (EO) and ethylene chlorohydrin (ECH) in individual EO-sterilized medical devices, procedures for the measurement of EO and ECH, and methods for determining compliance so that devices may be released. Additional background, including guidance and a flowchart showing how this document is applied, are also included in the informative annexes.

EO-sterilized devices that have no patient contact (e.g., *in vitro* diagnostic devices) are not covered by this part of ISO 10993.

NOTE This part of ISO 10993 does not specify limits for ethylene glycol (EG).

2 Normative references

The following referenced documents are indispensable for the application 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:—¹⁾, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-3, *Biological evaluation of medical devices — Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*

ISO 10993-10, *Biological evaluation of medical devices — Part 10: Tests for irritation and delayed-type hypersensitivity*

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

ISO 10993-17:2002, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 10993-1, ISO 10993-17 and the following apply.

3.1

simulated-use extraction

extraction to demonstrate compliance with the requirements of this part of ISO 10993, by evaluating residue levels available to the patient or user from devices during the routine use of a device with water extraction to simulate product use

1) To be published. (Revision of ISO 10993-1:2003)

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