Meditsiiniseadmete bioloogiline hindamine. Osa 3: Testid geenitoksiliste, kantserogeensete ja reproduktiivsete toksiinide määramiseks

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

EESTI STANDARDIKESKUS
ESTONIAN CENTRE FOR STANDARDISATION

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

Käesolev Eesti standard EVS-EN ISO 10993-3:2009 sisaldab Euroopa standardi EN ISO 10993-3:2009 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 10993-3:2009 consists of the English text of the European standard EN ISO 10993-3:2009.
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 20.05.2009.	Date of Availability of the European standard text 20.05.2009.
Standard on kättesaadav Eesti standardiorganisatsioonist.	The standard is available from Estonian standardisation organisation.

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English Version

Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity (ISO 10993-3:2003)

Évaluation biologique des dispositifs médicaux - Partie 3: Essais concernant la génotoxicité, la cancérogénicité et la toxicité sur la reproduction (ISO 10993-3:2003)

Biologische Beurteilung von Medizinprodukten - Teil 3: Prüfungen auf Gentoxizität, Karzinogenität und Reproduktionstoxizität (ISO 10993-3:2003)

This European Standard was approved by CEN on 28 April 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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Ref. No. EN ISO 10993-3:2009: E

Foreword

The text of ISO 10993-3:2003 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 10993-3:2009 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 November 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 10993-3:2003.

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 Directive.

For relationship with EC 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 10993-3:2003 has been approved by CEN as a EN ISO 10993-3:2009 without any modification.

Annex ZA
(Informative)

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

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.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.

Table ZA.1 – Correspondence between this European Standard and EU Directives

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7	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.

Contents

Page

Introduction

The basis for biological evaluation of medical devices is often empirical and driven by the relevant concerns for human safety. The risk of serious and irreversible effects, such as cancer or second-generation abnormalities, is of particular public concern. It is inherent in the provision of safe medical devices that such risks be minimized to the greatest extent feasible. The assessment of mutagenic, carcinogenic and reproductive hazards is an essential component of the control of these risks. Not all test methods for the assessment of genotoxicity, carcinogenicity or reproductive toxicity are equally well developed, nor is their validity well established for the testing of medical devices.

Significant issues in test sample size and preparation, scientific understanding of disease processes and test validation can be cited as limitations of available methods. For example, the biological significance of solid state carcinogenesis is poorly understood. It is expected that ongoing scientific and medical advances will alter our understanding of and approaches to these important toxicity test methods. At the time this part of ISO 10993 was prepared, the test methods proposed were those most acceptable. Scientifically sound alternatives to the proposed testing may be acceptable insofar as they address relevant matters of safety assessment.

In the selection of tests needed to evaluate a particular medical device, there is no substitute for a careful assessment of expected human uses and potential interactions of the medical device with various biological systems. These considerations will be particularly important in such areas as reproductive and developmental toxicology.

This part of ISO 10993 presents test methods for the detection of specific biological hazards, and strategies for the selection of tests, where appropriate, that will assist in hazard identification. Testing is not always necessary or helpful in hazard identification but, where it is appropriate, it is important that maximum test sensitivity be achieved. Most tests included in this part of ISO 10993 refer to Guidelines for Testing of Chemicals, prepared by the Organization for Economic Cooperation and Development (OECD).

The interpretation of findings and their implications for human health effects are beyond the scope of this part of ISO 10993. Because of the multitude of possible outcomes and the importance of factors such as extent of exposure, species differences and mechanical or physical considerations, risk assessment has to be performed on a case-by-case basis.

Biological evaluation of medical devices —

Part 3:
Tests for genotoxicity, carcinogenicity and reproductive toxicity

1 Scope

This part of ISO 10993 specifies strategies for hazard identification and tests on medical devices for the following biological aspects:

— genotoxicity,

— carcinogenicity, and

— reproductive and developmental toxicity.

This part of ISO 10993 is applicable for evaluation of a medical device whose potential for genotoxicity, carcinogenicity or reproductive toxicity has been identified.

NOTE Guidance on selection of tests is provided in ISO 10993-1.

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 10993-1:1997, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

ISO 10993-2:1992, *Biological evaluation of medical devices — Part 2: Animal welfare requirements*

ISO 10993-6:1994, *Biological evaluation of medical devices — Part 6: Tests for local effects after implantation*

ISO 10993-12:2002, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials*

ISO 10993-18, *Biological evaluation of medical devices — Part 18: Chemical characterization of materials*.

OECD 414[1)], *Prenatal Development Toxicity Study*

OECD 415, *One-Generation Reproduction Toxicity Study*

OECD 416, *Two-Generation Reproduction Toxicity*

1) Organization for Economic Cooperation and Development.

OECD 421, *Reproduction/Developmental Toxicity Screening Test*

OECD 451, *Carcinogenicity Studies*

OECD 453, *Combined Chronic Toxicity/Carcinogenicity Studies*

OECD 471, *Bacterial Reverse Mutation Test*

OECD 473, *In vitro Mammalian Chromosome Aberration Test*

OECD 476, *In vitro Mammalian Cell Gene Mutation Test*