Meditsiinivahendite bioloogiline hindamine. Osa 5: Katsed tsütotoksilisuse hindamiseks - in vitro meetodid

Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity

EESTI STANDARDIKESKUS
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NATIONAL FOREWORD

Käesolev Eesti standard EVS-EN ISO 10993-5:2009 sisaldab Euroopa standardi EN ISO 10993-5:2009 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 10993-5:2009 consists of the English text of the European standard EN ISO 10993-5:2009.
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 01.06.2009.	Date of Availability of the European standard text 01.06.2009.
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Biologische Beurteilung von Medizinprodukten - Teil 5: Prüfungen auf In-vitro-Zytotoxizität (ISO 10993-5:2009)

This European Standard was approved by CEN on 17 April 2009.

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Foreword

This document (EN ISO 10993-5:2009) 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.

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of an identical text or by endorsement, at the latest by December 2009, and conflicting national standards shall be withdrawn at the latest by December 2009.

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 10993-5:1999.

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 Annex ZA and ZB, which are integral parts of this document.

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Endorsement notice

The text of ISO 10993-5:2009 has been approved by CEN as EN ISO 10993-5:2009 without any modifications.

Annex ZA
(informative)

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

This International 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 International Standard and Directive 93/42/EEC

Clause(s)/sub-clause(s) of this International Standard	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	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 International standard.

Annex ZB
(informative)

Relationship between this International Standard and the Essential Requirements of EU Directive 90/385/EEC

This International 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 90/385/EEC on active implantable 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 ZB.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 ZB.1 — Correspondence between this International Standard and Directive 90/385/EEC

Clause(s)/sub-clause(s) of this International Standard	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	Annex I: 9	

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

Contents

Page

Foreword ... iv
Introduction ... vi
1 Scope ... 1
2 Normative references ... 1
3 Terms and definitions ... 1
4 Sample and control preparation ... 2
4.1 General ... 2
4.2 Preparation of liquid extracts of material ... 3
4.3 Preparation of material for direct-contact tests ... 4
4.4 Preparation of controls ... 5
5 Cell lines ... 5
6 Culture medium ... 5
7 Preparation of cell stock culture ... 6
8 Test procedures ... 6
8.1 Number of replicates ... 6
8.2 Test on extracts ... 6
8.3 Test by direct contact ... 7
8.4 Test by indirect contact ... 7
8.5 Determination of cytotoxicity ... 9
9 Test report ... 10
10 Assessment of results ... 11
Annex A (informative) **Neutral red uptake (NRU) cytotoxicity test** ... 12
Annex B (informative) **Colony formation cytotoxicity test** ... 19
Annex C (informative) **MTT cytotoxicity test** ... 24
Annex D (informative) **XTT cytotoxicity test** ... 29
Bibliography ... 34

Introduction

Due to the general applicability of *in vitro* cytotoxicity tests and their widespread use in evaluating a large range of devices and materials, it is the purpose of this part of ISO 10993, rather than to specify a single test, to define a scheme for testing which requires decisions to be made in a series of steps. This should lead to the selection of the most appropriate test.

Three categories of test are listed: extract test, direct contact test, indirect contact test.

The choice of one or more of these categories depends upon the nature of the sample to be evaluated, the potential site of use and the nature of the use.

This choice then determines the details of the preparation of the samples to be tested, the preparation of the cultured cells, and the way in which the cells are exposed to the samples or their extracts.

At the end of the exposure time, the evaluation of the presence and extent of the cytotoxic effect is undertaken. It is the intention of this part of ISO 10993 to leave open the choice of type of evaluation. Such a strategy makes available a battery of tests, which reflects the approach of many groups that advocate *in vitro* biological tests.

The numerous methods used and endpoints measured in cytotoxicity determination can be grouped into the following categories of evaluation:

— assessments of cell damage by morphological means;

— measurements of cell damage;

— measurements of cell growth;

— measurements of specific aspects of cellular metabolism.

There are several means of producing results in each of these four categories. The investigator should be aware of the test categories and into which category a particular technique fits, in order that comparisons be able to be made with other results on similar devices or materials both at the intra- and interlaboratory level. Examples of quantitative test protocols are given in annexes. Guidance for the interpretation of the results is given in this part of ISO 10993.

Biological evaluation of medical devices —

Part 5:
Tests for *in vitro* cytotoxicity

1 Scope

This part of ISO 10993 describes test methods to assess the *in vitro* cytotoxicity of medical devices.

These methods specify the incubation of cultured cells in contact with a device and/or extracts of a device either directly or through diffusion.

These methods are designed to determine the biological response of mammalian cells *in vitro* using appropriate biological parameters.

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, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management system*

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