Australian Standard™

Biological evaluation of medical devices

Part 5: Tests for in vitro cytotoxicity

Standards Australia

This Australian Standard was prepared by Committee HE-012, Surgical Implants. It was approved on behalf of the Council of Standards Australia on 26 June 2002 and published on 28 June 2002.

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Australian Dental Association

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Part 5: Tests for in vitro cytotoxicity

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PREFACE

This Standard has been developed to assist in the process of implementation of the Australian Medical Device legislation.

After consultation with stakeholders in both countries, Standards Australia and Standards New Zealand decided to develop this Standard as an Australian, rather than an Australian/New Zealand Standard, through the Joint Standards Australia/Standards New Zealand Committee HE-012 on Surgical Implants.

This Standard is identical with and has been reproduced from ISO 10993-5:1999, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity.*

The objective of this Standard is to specify requirements for test methods to assess the in vitro cytotoxicity for biological evaluation of medical devices.

As this Standard is reproduced from an international Standard, the following applies:

(a) Its number does not appear on each page of text and its identity is shown only on the cover and title page.

(b) In the source text 'this International Standard' should read 'this Australian Standard'.

(c) A full point substitutes for a comma when referring to a decimal marker.

CONTENTS

INTRODUCTION

Due to the general applicability of *in vitro* cytotoxicity tests and their widespread use in evaluating a large range of medical 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 which advocate *in vitro* biological tests.

The numerous methods used and end-points measured in cytotoxicity determination can be grouped into categories of evaluation type:

a) assessments of cell damage by morphological means;

b) measurements of cell damage;

c) measurements of cell growth;

d) measurements of specific aspects of cellular metabolism.

There are, therefore, several alternative means of producing results in each of these four categories. The investigator should be aware of the categories of test and into which a particular technique fits, in order that comparisons may be made with other results on similar medical devices or materials, and in order that interlaboratory tests may be conducted.

AUSTRALIAN STANDARD

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 either directly or through diffusion

a) with extracts of a device, and/or

b) in contact with a device.

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

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 10993. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 10993 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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing.*

ISO 10993-12:1996, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials.*

3 Terms and definitions

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

3.1
negative control material
material which, when tested in accordance with this part of ISO 10993, does not produce a cytotoxic response

NOTE The purpose of the negative control is to demonstrate background response. For example, high-density polyethylene[1)], synthetic polymers, and aluminium oxide ceramic rods for dental material, have been used as negative controls.

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1) High-density polyethylene can be obtained from the U.S. Pharmacopeia (Rockville, Maryland, USA) and Food and Drug Safety Center, Hatano Research Institute (Ochiai 729-5, Hadanoshi, Kanagawa 257 - Japan). This information is given for the convenience of the user of this part of ISO 10993 and does not constitute an endorsement by ISO of these products.