AS ISO 10993.3—2002
ISO 10993-3:1992

Australian Standard™

Biological evaluation of medical devices

Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity

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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This Standard was issued in draft form for comment as DR 02214.

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First published as AS ISO 10993.3—2002.

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Published by Standards Australia International Ltd
GPO Box 5420, Sydney, NSW 2001, Australia

ISBN 0 7337 4714 0

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 10993-3:1992, *Biological evaluation of medical devices — Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity.*

The objective of this Standard is to specify the requirements for tests of genotoxicity, carcinogenicity and reproductive toxicity 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.

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INTRODUCTION

The basis for biocompatibility evaluation of medical devices is often empirical and driven by the relevant concerns for human safety. 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 and approaches to these important toxicity test methods. At the time the document was prepared, the test methods proposed were those most acceptable. Sound scientific alternatives to the proposed testing should be acceptable insofar as they address relevant matters of safety assessment.

In the selection of tests needed to evaluate a particular device, there is no substitute for a careful assessment of expected human uses and potential interactions of the 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 therefore maximum test sensitivity is required. The interpretation of findings and 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 such factors as extent of exposure, species differences and mechanical or physical considerations, risk assessment has to be performed on a case-by-case basis.

AUSTRALIAN STANDARD

Biological evaluation of medical devices

Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity

1 Scope

This part of ISO 10993 specifies tests for the following biological aspects:

— genotoxicity,

— carcinogenicity, and

— reproductive and developmental toxicity.

These are relevant in the biological evaluation of some categories of medical devices (see note 1). Guidance on selection of tests is provided in ISO 10993-1. Where the need for the evaluation of the potential for genotoxicity, carcinogenicity or reproductive toxicity has been identified, they should be evaluated in accordance with this part of ISO 10993.

Most tests included in this part of the International Standard refer to the OECD guidelines for testing of chemicals. Reference to these tests is made by the term "OECD guideline(s)" followed by the appropriate test number(s).

At the time of testing, these tests are to be performed according to current OECD guidelines.

NOTE 1 The term "devices" corresponds to the definition given in ISO 10993-1 and covers materials, as well as dental materials and devices. The definition is in accordance with the CEN standard document.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 10993-1:1992, *Biological evaluation of medical devices — Part 1: Guidance on selection of tests.*

ISO 10993-2:—[1], *Biological evaluation of medical devices — Part 2: Animal welfare requirements.*

***OECD Guidelines for testing of chemicals* — Selected assays**

— *In vitro* genotoxicity tests

471 *Genetic Toxicology:* Salmonella typhimurium, *Reverse Mutation Assay.*

472 *Genetic Toxicology:* Escherichia coli, *Reverse Mutation Assay.*

473 *Genetic Toxicology:* In vitro *Mammalian Cytogenetic Test.*

476 *Genetic Toxicology:* In vitro *Mammalian Cell Gene Mutation Test.*

479 *Genetic Toxicology:* In vitro *Sister Chromatid Exchange Assay in Mammalian Cells.*

480 *Genetic Toxicology:* Saccharomyces cerevisiae, *Gene Mutation Assay.*

481 *Genetic Toxicology:* Saccharomyces cerevisiae, *Mitotic Recombination Assay.*

1) To be published.

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