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Australian Standard™

Biological evaluation of medical devices

Part 10: Tests for irritation and delayed-type hypersensitivity

Standards Australia

This Australian Standard was prepared by Committee HE-012, Surgical Implants and Committee HE-009, Hypodermic Equipment—General Medical. It was approved on behalf of the Council of Standards Australia on 29 May 2003 and published on 30 June 2003.

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PREFACE

This Standard was prepared by the Australian members of the Joint Standards Australia/ Standards New Zealand Committees HE-012, Surgical Implants and HE-009, Hypodermic Equipment—General Medical. 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.

This Standard is identical with and has been reproduced from ISO 10993-10:2002, *Biological evaluation of medical devices—Part 10: Tests for irritation and delayed-type hypersensitivity*. This second edition cancels and replaces AS ISO 10993.10—2002, which has been technically revised.

The objective of this Standard is to specify the procedure for the assessment of medical devices and their constituent materials with regard to their potential to produce irritation and delayed-type hypersensitivity, including pretest considerations, details of the test procedures, and key factors for the interpretation of the results.

The terms 'normative' and 'informative' are used to define the application of the annex to which they apply. A normative annex is an integral part of a standard, whereas an informative annex is only for information and guidance.

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.

References to International Standards should be replaced by references to Australian or Australian/New Zealand Standards as follows:

Reference to International Standard		*Australian Standard*	
ISO		AS ISO	
10993	Biological evaluation of medical devices	10993	Biological evaluation of medical devices
10993-1	Part 1: Evaluation and testing	10993.1	Part 1: Evaluation and testing
10993-9	Part 9: Framework for identification and quantification of potential degradation products	10993.9	Part 9: Framework for identification and quantification of potential degradation products
10993-12	Part 12: Sample preparation and reference materials	10993.12	Part 12: Sample preparation and reference materials
10993-13	Part 13: Identification and quantification of degradation products from polymeric medical devices	10993.13	Part 13: Identification and quantification of degradation products from polymeric medical devices
10993-14	Part 14: Identification and quantification of degradation products from ceramics	10993.14	Part 14: Identification and quantification of degradation products from ceramics
10993-15	Part 15: Identification and quantification of degradation products from metals and alloys	10993.15	Part 15: Identification and quantification of degradation products from metals and alloys
14155	Clinical investigation of medical devices	14155	Clinical investigation of medical devices

AS ISO 10993, Biological evaluation of medical devices, consists of the following parts:

Part 1: Evaluation and testing
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 8: Selection and qualification of reference materials for biological tests
Part 9: Framework for identification and quantification of potential degradation products
Part 10: Tests for irritation and delayed-type hypersensitivity (this Standard)
Part 11: Tests for systematic 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

CONTENTS

INTRODUCTION

This part of ISO 10993 assesses possible contact hazards from chemicals released from medical devices that may produce skin and mucosal irritation, eye irritation and delayed contact hypersensitivity

Some materials that are included in medical devices have been tested, and their skin or mucosal irritation or sensitization potential has been documented. Other materials and their chemical components have not been tested and may induce adverse effects when in contact with biological tissues. The manufacturer is thus obliged to evaluate each device for potential adverse effects prior to marketing.

Traditionally, small animal tests are performed prior to testing on humans to help predict human response. More recently, *in vitro* tests as well as human tests have been added as alternatives. Despite progress and considerable effort in this direction, a review of findings suggests that currently no satisfactory *in vitro* tests have been devised to eliminate the requirement for *in vivo* testing. Where appropriate, the preliminary use of *in vitro* methods is encouraged for screening purposes prior to animal testing. In order to reduce the number of animals used, this part of ISO 10993 presents a step-wise approach, with review and analysis of test results at each stage. An animal test is usually required prior to human testing.

It is intended that these studies be conducted using Good Laboratory Practice and comply with regulations related to animal welfare. Statistical analysis of data is recommended and should be used whenever appropriate.

The tests included in this part of ISO 10993 are important tools for the development of safe products, provided that these are executed and interpreted by trained personnel.

NOTES

AUSTRALIAN STANDARD

Biological evaluation of medical devices

Part 10: Tests for irritation and delayed-type hypersensitivity

1 Scope

This part of ISO 10993 describes the procedure for the assessment of medical devices and their constituent materials with regard to their potential to produce irritation and delayed-type hypersensitivity.

This part of ISO 10993 includes

a) pretest considerations,

b) details of the test procedures, and

c) key factors for the interpretation of the results.

Instructions are given in annex A for the preparation of materials specifically in relation to the above tests.

Supplementary tests which are required specifically for devices used intradermally in the ocular, oral, rectal, penile and vaginal areas are given in annex B.

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

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

ISO 10993-9, *Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products*

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

ISO 10993-13, *Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices*

ISO 10993-14 *Biological evaluation of medical devices — Part 14: Identification and quantification of degradation products from ceramics*

ISO 10993-15, *Biological evaluation of medical devices — Part 15: Identification and quantification of degradation products from metals and alloys*

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