

Australian Standard™

Biological evaluation of medical devices

Part 10: Tests for irritation and delayed-type hypersensitivity

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.

The following are represented on Committee HE-012:

HE-012 and (HE-009):

Australian Chamber of Commerce and Industry (HE-009)
Australian College of Operating Room Nurses (HE-009)
Australian Dental Association
Australian Industry Group
Australian Orthopaedic Association
Australian Society for Biomaterials
Commonwealth Department of Health and Ageing (HE-009)
Department of Defence (Australia)
Medical Industry Association of Australia Inc (HE-009)
Neurological Society of Australasia
Royal Australasian College of Surgeons
Royal Perth Hospital
University of New South Wales
University of Sydney

HE-009 only:

Australian Infection Control Association
Australian Medical Association
Certification Bodies (Australia)
Department of Human Services (Victoria)
Federation of Sterilizing Research and Advisory Council of Australia
Hunter Area Health Service
NSW Health Department
Queensland Health
Royal Australian College of General Practitioners
Royal College of Pathologists of Australasia
Royal Melbourne Hospital

Keeping Standards up-to-date

Standards are living documents which reflect progress in science, technology and systems. To maintain their currency, all Standards are periodically reviewed, and new editions are published. Between editions, amendments may be issued. Standards may also be withdrawn. It is important that readers assure themselves they are using a current Standard, which should include any amendments which may have been published since the Standard was purchased.

Detailed information about Standards can be found by visiting the Standards Australia web site at www.standards.com.au and looking up the relevant Standard in the on-line catalogue.

Alternatively, the printed Catalogue provides information current at 1 January each year, and the monthly magazine, *The Global Standard*, has a full listing of revisions and amendments published each month.

We also welcome suggestions for improvement in our Standards, and especially encourage readers to notify us immediately of any apparent inaccuracies or ambiguities. Contact us via email at mail@standards.com.au, or write to the Chief Executive, Standards Australia International Ltd, GPO Box 5420, Sydney, NSW 2001.

Australian Standard™

Biological evaluation of medical devices

Part 10: Tests for irritation and delayed-type hypersensitivity

Formulated as AS ISO 10993.10—2002.
Second edition 2003.

COPYRIGHT

© Standards Australia International

All rights are reserved. No part of this work may be reproduced or copied in any form or by any means, electronic or mechanical, including photocopying, without the written permission of the publisher.

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

ISBN 0 7337 5369 8

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:

<i>Reference to International Standard</i>		<i>Australian Standard</i>	
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.....	v
1 Scope.....	1
2 Normative references.....	1
3 Terms and definitions.....	2
4 General principles — Step-wise approach.....	3
5 Pretest considerations.....	4
5.1 General.....	4
5.2 Types of material.....	4
5.3 Information on chemical composition.....	4
5.4 Material characterization.....	5
6 Irritation tests.....	5
6.1 <i>In vitro</i> irritation tests.....	5
6.2 Factors to be considered in design and selection of <i>in vivo</i> tests.....	5
6.3 Animal skin irritation test.....	6
6.4 Human skin irritation test.....	10
7 Delayed hypersensitivity tests.....	14
7.1 Choice of test.....	14
7.2 Choice of test sample concentrations.....	14
7.3 Other important factors affecting the outcome of the tests.....	14
7.4 Maximization test for delayed hypersensitivity.....	15
7.5 Closed-patch test for delayed hypersensitivity.....	18
8 Key factors in interpretation of test results.....	20
Annex A (normative) Preparation of materials for irritation/sensitization testing.....	21
Annex B (informative) Additional irritation tests.....	23
Annex C (informative) Background information.....	41
Bibliography.....	45

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* test has 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.

Currently in preview, click buy full vers.

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*