AS ISO 10993.11—2002
(Incorporating Amendment No. 1)

AS ISO 10993.11—2002

Australian Standard™

Biological evaluation of medical devices

A1 | # Part 11: Tests for systemic toxicity



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Australian College of Operating Room Nurses
Australian Industry Group
Australian Orthopaedic Association
Australian Society for Biomaterials
Commonwealth Department of Health and Ageing
Medical Industry Association of Australia Inc
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PREFACE

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

This Standard incorporates Amendment No. 1 (November 2005). The changes required by the Amendment are indicated in the text by a marginal bar and amendment number against the clause, note, table, figure or part thereof affected.

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.

A1 This Standard is identical with and has been reproduced from ISO 10993-11:1993, *Biological evaluation of medical devices — Part 11: Tests for systemic toxicity.*

A1 The objective of this Standard is to specify methodologies for the evaluation of the systemic toxicity potential of medical devices which release constituents into the body.

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

When a device releases constituents into the body, the constituents may, in sufficiently large concentrations, lead to systemic toxicity. Clinical and experimental evidence of the systemic effects in this area is extremely sparse.

This part of ISO 10993 provides methodologies for the evaluation of the systemic toxicity potential of medical devices. In addition, it includes pyrogenicity testing.

Systemic toxicity is a developing experimental science and it is expected that each expert, in carrying out tests, will exercise judgement in the selection of a procedure from the lists of standards and documents quoted, thereby ensuring that the document that will best suit the needs of a particular device is chosen. It is assumed that, in selecting the most appropriate test method from the list, the individual method(s) may have to be adapted, to evaluate the device under test more appropriately.

It must be borne in mind that subchronic and/or chronic systemic toxicity testing is not always necessary for a risk assessment. Such assessment might be made on the basis of qualitative and quantitative analytical measurements to evaluate the exposure of possible leachables from the device.

This adaptation is intentional because of the developing nature of the science and because excessive rigidity or over-detailed specifications of methods could prevent application of more appropriate test methods. It is indeed intended that toxicological skill and judgement be applied during the course of study. However, it is equally necessary that, where changes from proposed methodologies are implemented, the rationale should be fully explained and supported scientifically. (See 6.4.)

It is essential, when evaluating the results of toxicological tests, to bear in mind the limitations and the potential variability of the tests. Similarly, it may not always be appropriate to extrapolate from animal studies to the human situation. While *in vivo* testing is designed to indicate possible health hazards, it does not eliminate the need for continuing monitoring and observation in humans.

AUSTRALIAN STANDARD

Biological evaluation of medical devices

A1 | Part 11: Tests for systemic toxicity

Biological evaluation of medical devices —

Part 11:
Tests for systemic toxicity

1 Scope

This part of ISO 10993 specifies methodologies for the evaluation of the systemic toxicity potential of medical devices which release constituents into the body. In addition, it includes pyrogenicity testing.

The test methods cited in this part of ISO 10993 are from International Standards, national standards, directives and regulations. This part of ISO 10993 is concerned with either the actual product or its leachables. It is intended that tests for extracts or leachables be conducted by choosing appropriate extraction vehicles to yield a maximum extraction of leachable materials, in order to conduct biological testing.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this part of ISO 10993. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this part of ISO 10993 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 10993-2:1992, *Biological evaluation of medical devices — Part 2: Animal welfare requirements.*

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

ANSI/ADA No. 41, *Biological Evaluation of Dental Materials.*

ASTM F 619:1986, *Practice for Extraction of Medical Plastics*, Vol. 13.01.

ASTM F 750:1987, *Practice for Evaluating Material Extracts by Systemic Injection in the Mouse.*

BS 5736: Part 5:1982, *Evaluation of medical devices for biological hazards — Part 5: Method of test for systemic toxicity; assessment of pyrogenicity in rabbits of extracts from medical devices.*

SN 119 800, *Biological Evaluation of Dental Materials,* Swiss Association for Standardization.

European Pharmacopoeia XXII, 1990.

OECD — *Guidelines for Testing of Chemicals.*

Official Journal of the European Communities, 79/831.

Official Journal of the European Communities, 84/449.

Official Journal of the European Communities, 87/302.

US Code of Federal Regulation 1500.40: *Method of Testing Toxic Substances.*

US/EPA PB 86/108958.

US/EPA PB 89/124077.

US/FDA *Toxicological Principles for the Safety Assessment of Direct Food Additives*, 1982.

United States Pharmacopeia XXII: *Biological Reactivity Tests, In-Vivo*; The National Formulary XVII, Rockville, MD; Pharmacopeial Convention, 1990, pp. 1497-1500.

3 Definitions

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

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