AS ISO 10993.16—2002
ISO 10993-16:1997

Australian Standard™

Biological evaluation of medical devices

Part 16: Toxicokinetic study design for degradation products and leachables

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.

The following are represented on Committee HE-012:

Australian Chamber of Commerce and Industry

Australian College of Operating Room Nurses

Australian Dental Association

Australian Industry Group

Australian Orthopaedic Association

Commonwealth Department of Health and Ageing

Department of Defence (Australia)

Medical Industry Association of Australia Inc

Neurological Society of Australasia

Royal Australasian College of Surgeons

Royal Perth Hospital

The Australian Society for Biomaterials

The University of New South Wales

The University of Sydney

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 Standards may also be withdrawn.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 Australian 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.

This Standard was issued in draft form for comment as DR 02210.

Australian Standard™

Biological evaluation of medical devices

Part 16: Toxicokinetic study design for degradation products and leachables

First published as AS ISO 10993.16—2002.

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

ISBN 0 7337 4715 9

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 10993-16:1997, *Biological evaluation of medical devices — Part 16: Toxicokinetic study design for degradation products and leachables.*

The objective of this Standard is to provide principles on how toxicokinetic studies relevant to medical devices should be designed and performed.

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

This part of ISO 10993 provides guidance and requirements on the design and performance of toxicokinetic studies.

Toxicokinetics describes the absorption, distribution, metabolism and excretion of foreign compounds in the body with time. Essential to the evaluation of the safety of a medical device is consideration of the stability of the material(s) *in vivo* and the disposition of leachables and degradation products. Toxicokinetic studies may be of value in assessing the safety of materials used in the development of a medical device or in elucidating the mechanism of observed adverse reactions. The need for and extent of such studies should be carefully considered based on the nature and duration of contact of the device with the body.

The potential hazard posed by a medical device may be attributed to the interactions of its components or their metabolites with the biological system. Medical devices may release leachables (e.g. residual catalysts, processing aids, residual monomers, fillers, antioxidants, plasticizers) and/or degradation products which migrate from the material and have the potential to cause adverse effects in the body.

A considerable body of published literature exists on the use of toxicokinetic methods to study the fate of chemicals in the body (see annex B). The methodologies and techniques utilized in such studies form the basis of the guidance in this standard. A rationale for the use of this part of ISO 10993 is given in annex A.

AUSTRALIAN STANDARD

Biological evaluation of medical devices

Part 16: Toxicokinetic study design for degradation products and leachables

1 Scope

This part of ISO 10993 gives principles on how toxicokinetic studies relevant to medical devices should be designed and performed. Annex A describes the considerations for inclusion of toxicokinetic studies in the biological evaluation of medical devices.

2 Normative reference

The following standard contains provisions which, through reference in this text, constitute provisions of this part of ISO 10993. At the time of publication, the edition indicated was 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 edition of the standard indicated below. Members of IEC and ISO maintain register of currently valid International Standards.

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

3 Definitions

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

3.1 degradation product: Product of a material which is generated by the chemical breakdown or decomposition of the material.

3.2 leachable: Extractable component, such as an additive, monomeric or oligomeric constituent of polymeric material.

3.3 test substance: Degradation product or leachable used for toxicokinetic study.

3.4 absorption: Process by which a substance enters the blood and/or lymph system.

3.5 distribution: Process by which an absorbed substance and/or its metabolites circulate and partition within the body.

3.6 metabolism: Process by which an absorbed substance is structurally changed within the body by chemical and/or enzymatic reactions.

NOTE – The products of the initial reaction may subsequently be modified by either enzymatic or non-enzymatic reactions prior to excretion.

3.7 excretion: Process by which an absorbed substance and/or its metabolites are removed from the body.