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Australian Standard™

Biological evaluation of medical devices

Part 15: Identification and quantification of degradation products from metals and alloys

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 10993-15:2000, *Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys.*

The objective of this Standard is to provide guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding material samples finished as ready for clinical use. This Standard is only applicable to those degradation products generated by chemical alteration of the finished metallic device in an in vitro accelerated degradation test.

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
10993-16	Part 16: Toxicokinetic study design for degradation products and leachables	10993.16	Part 16: Toxicokinetic study design for degradation products and leachables

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
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 (this Standard)
Part 16: Toxicokinetic study design for degradation products and leachables

CONTENTS

INTRODUCTION

One of the potential health hazards resulting from medical devices may be due to the interactions of their electrochemically-induced degradation products with the biological system. Therefore, the evaluation of potential degradation products from metallic materials by methods suitable for testing the electrochemical behavior of these materials is a necessary step in the biological performance testing of materials.

The body environment typically contains cations of sodium, potassium, calcium and magnesium and anions of chloride, bicarbonate, phosphate and organic acids generally in concentrations between 2×10^{-3} mol and 150×10^{-3} mol. A range of organic molecules such as proteins, enzymes and lipoproteins is also present but their concentrations may vary to a great extent. Earlier studies assumed that organic molecules did not exert a significant influence on the degradation of metallic implants, but newer investigations indicate that implant — protein interactions should be taken into account. Depending on a particular product or application, altering the pH of the testing environment may also need to be considered.

In such biological environments, metallic materials may undergo a certain degradation and the different degradation products may interact with the biological system in different ways. Therefore, the identification and quantification of these degradation products is an important step in evaluating the biological performance of medical devices.

NOTES

AUSTRALIAN STANDARD

Biological evaluation of medical devices

Part 15: Identification and quantification of degradation products from metals and alloys

1 Scope

This part of ISO 10993 provides guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding material samples finished as ready for clinical use. It is applicable only to those degradation products generated by chemical alteration of the finished metallic device in an *in vitro* accelerated degradation test. Because of the accelerated nature of these tests, the test results may not reflect the implant or material behavior in the body. The described chemical methodologies are a means to generate degradation products for further assessments.

This part of ISO 10993 is not applicable to degradation products induced by applied mechanical stress.

NOTE Mechanically induced degradation, such as wear, may be covered in the appropriate product-specific standard. Where product-group standards provide applicable product-specific methodologies for the identification and quantification of degradation products, those standards should be considered.

Because of the wide range of metallic materials used in medical devices, no specific analytical techniques are identified for quantifying the degradation products. The identification of trace elements ($< 10^{-6}$) contained in the specific metal or alloy is not addressed in this part of ISO 10993, nor are specific requirements for acceptable levels of degradation products provided in this part of ISO 10993.

This part of ISO 10993 does not address the biological activity of the degradation products; see instead the applicable clauses of ISO 10993-1 and ISO 10993-17.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard 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 3585, *Borosilicate glass 3.3 — Properties*.

ISO 3696, *Water for analytical laboratory use — Specification and test methods*.

ISO 8044, *Corrosion of metals and alloys — Basic terms and definitions*.

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

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