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SINGAPORE STANDARD

Biological evaluation of medical devices

– Part 10 : Tests for irritation and skin sensitization

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Denova Sciences Pte Ltd
Edwards Lifesciences (Singapore) Pte Ltd
Emcero Pte Ltd
Health Sciences Authority
Institute of Material Research & Engineering
Nanyang Technological University
National University of Singapore
Osteopore International Pte Ltd
Wise Consultants and Services Pte Ltd

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Contents

National Foreword

This Singapore Standard was prepared by the National Mirror Working Group for ISO/TC 150 and 194 under the direction of the Biomedical and Health Standards Committee.

This Singapore Standard is an identical adoption of International Standard ISO 10993-10 : 2010 "Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization" published by the International Organization for Standardization.

Attention is drawn to the following:

1. Where appropriate, the words 'International Standard' shall be read as 'Singapore Standard'.

2. The comma has been used throughout as a decimal marker whereas in Singapore Standards it is a practice to use a full point on the baseline as the decimal marker.

3. The references to International Standards shall be replaced by the following Singapore Standards:

International Standard	Corresponding Singapore Standard
ISO 10993-1	SS ISO 10993-1*
ISO 10993-3	SS ISO 10993-3
ISO 10993-4	SS ISO 10993-4*
ISO 10993-5	SS ISO 10993-5
ISO 10993-6	SS ISO 10993-6*
ISO 10993-10	SS ISO 10993-10
ISO 10993-11	SS ISO 10993-11*
ISO 10993-12	SS ISO 10993-12
ISO 14155	SS ISO 14155

* Under development

Attention is drawn to the possibility that some of the elements of this Singapore Standard may be the subject of patent rights. Enterprise Singapore shall not be held responsible for identifying any or all of such patent rights.

NOTE

1. *Singapore Standards (SSs) and Technical References (TRs) are reviewed periodically to keep abreast of technical changes, technological developments and industry practices. The changes are documented through the issue of either amendments or revisions.*

2. *An SS or TR is voluntary in nature except when it is made mandatory by a regulatory authority. It can also be cited in contracts making its application a business necessity. Users are advised to assess and determine whether the SS or TR is suitable for their intended use or purpose. If required, they should refer to the relevant professionals or experts for advice on the use of the document. Enterprise Singapore shall not be liable for any damages whether directly or indirectly suffered by anyone or any organisation as a result of the use of any SS or TR.*

3. *Compliance with a SS or TR does not exempt users from any legal obligations.*

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 10993-10 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This third edition cancels and replaces the second edition (ISO 10993-10:2002), which has been technically revised.

ISO 10993 consists of the following parts, under the general title *Biological evaluation of medical devices*:

— *Part 1: Evaluation and testing within a risk management process*

— *Part 2: Animal welfare requirements*

— *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 9: Framework for identification and quantification of potential degradation products*

— *Part 10: Tests for irritation and skin sensitization*

— *Part 11: Tests for systemic 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*

— *Part 17: Establishment of allowable limits for leachable substances*

— *Part 18: Chemical characterization of materials*

— *Part 19: Physico-chemical, morphological and topographical characterization of materials* [Technical Specification]

— *Part 20: Principles and methods for immunotoxicology testing of medical devices* [Technical Specification]

Introduction

This part of ISO 10993 assesses possible contact hazards from chemicals released from medical devices, which may produce skin and mucosal irritation, eye irritation or skin sensitization.

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 human tissue. 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 adjuncts or 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.

This part of ISO 10993 is intended for use by professionals, appropriately qualified by training and experience, who are able to interpret its requirements and judge the outcomes of the evaluation for each medical device, taking into consideration all the factors relevant to the device, its intended use and the current knowledge of the medical device provided by review of the scientific literature and previous clinical experience.

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.

This part of ISO 10993 is based on numerous standards and guidelines, including OECD Guidelines, U.S. Pharmacopoeia and the European Pharmacopoeia. It is intended to be the basic document for the selection and conduct of tests enabling evaluation of irritation and dermal sensitization responses relevant to safety of medical materials and devices.

Biological evaluation of medical devices —

Part 10:
Tests for irritation and skin sensitization

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 skin sensitization.

This part of ISO 10993 includes:

a) pretest considerations for irritation, including *in silico* and *in vitro* methods for dermal exposure;

b) details of *in vivo* (irritation and sensitization) test procedures;

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. In Annex B several special irritation tests are described for application of medical devices in areas other than skin.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10993-1:2009, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

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*