Singapore Standards Council

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SINGAPORE STANDARD

Biological evaluation of medical devices

– Part 11 : Tests for systemic toxicity

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The National Mirror Working Group for ISO/TC 150 and 194, appointed by the Biomedical and Health Standards Committee to assist in the preparation of this standard, comprises the following experts who contribute in their *individual capacity*:

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Biomedical Engineering Society (Singapore)
Cordlife Group Limited
Denova Sciences Pte Ltd
Edwards Lifesciences (Singapore) Pte Ltd
Emcero Pte Ltd
Health Sciences Authority
Institute of Material Research & Engineering
Nanyang Technological University
National Universtiy of Singapore
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National Foreword

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

This Singapore Standard is an identical adoption of International Standard ISO 10993-11:2017 "Biological evaluation of medical devices — Part 11: Tests for systemic toxicity" published by the International Organization for Standardization.

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 10993-6	SS ISO 10993-6
ISO 10993-10	SS ISO 10993-10
ISO 10993-12	SS ISO 10993-12

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.

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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.*

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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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 194 *Biological and clinical evaluation of medical devices*.

This third edition cancels and replaces the second edition (ISO 10993-11:2006), which has been technically revised with the following changes:

a) reduction in group size for chronic toxicity testing in Table 1;

b) a new Annex F was added;

c) the original Annex F was moved to Annex G;

d) a new Annex H was added;

e) the Bibliography was updated.

A list of all parts in the ISO 10993 series can be found on the ISO website.

Introduction

Systemic toxicity is a potential adverse effect of the use of medical devices. Generalized effects, as well as organ and organ system effects can result from absorption, distribution and metabolism of leachates from the device or its materials to parts of the body with which they are not in direct contact. This document addresses the evaluation of generalized systemic toxicity, not specific target organ or organ system toxicity, even though these effects may result from the systemic absorption and distribution of toxicants.

Because of the broad range of medical devices, and their materials and intended uses, this document is not overly prescriptive. While it addresses specific methodological aspects to be considered in the design of systemic toxicity tests, proper study design has to be uniquely tailored to the nature of the device's materials and its intended clinical application.

Other elements of this document are prescriptive in nature, including those aspects that address compliance with good laboratory practices and elements for inclusion in reporting.

While some systemic toxicity tests (e.g. long term implantation or dermal toxicity studies) can be designed to study systemic effects as well as local, carcinogenic or reproductive effects, this document focuses only on those aspects of such studies, which are intended to address systemic effects. Studies which are intended to address other toxicological end points are addressed in ISO 10993-3, ISO 10993-6, ISO 10993-10 and ISO/TS 10993-20.

Prior to conducting a systemic toxicity study, all reasonably available data and scientifically sound methods in the planning and refinement of the systemic toxicity study design should be reviewed. This includes the suitability of use of input data such as existing toxicological data, data from chemical characterization studies and/or other biological tests (including *in vitro* tests and less invasive *in vivo* tests) for the refinement of study design, dose selection, and/or selection of pathological end points to cover in the evaluation of a study. For the repeated exposure systemic toxicity study in particular, the use of scientifically sound study design, the use of pilot studies and statistical study design and the use of unbiased, quantitative end points/methods in the pathological (including histopathological) and clinical chemistry methods are important so as to obtain data which have sufficient scientific validity.

Finally, toxicology is an imperfect science. The outcome of any single test should not be the sole basis for making a determination of whether a device is safe for its intended use.

Biological evaluation of medical devices –

Part 11:
Tests for systemic toxicity

1 Scope

This document specifies requirements and gives guidance on procedures to be followed in the evaluation of the potential for medical device materials to cause adverse systemic reactions.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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, *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*