Singapore Standards Council

SS ISO 10993-4 : 2017
ISO 10993-4:2017, IDT
(ICS 11.100.20)

SINGAPORE STANDARD

Biological evaluation of medical devices

– Part 4 : Selection of tests for interactions with blood

Published by
Enterprise Singapore

SS ISO 10993-4 : 2017
ISO 10993-4:2017, IDT
(ICS 11.100.20)

SINGAPORE STANDARD

Biological evaluation of medical devices

– Part 4 : Selection of tests for interactions with blood

ISBN 978-981-47-8481-8

This Singapore Standard was approved by the Biomedical and Health Standards Committee on behalf of the Singapore Standards Council on 8 December 2017.

First published, 2018

The Biomedical and Health Standards Committee, appointed by the Standards Council, consists of the following members:

		Name	Capacity
Chairman	:	Dr Yong Chern Chet	*Individual Capacity*
Deputy Chairman 1	:	Ms Wong Woei Jiuang	*Health Sciences Authority*
Deputy Chairman 2	:	Mr Vincent Cheung	*Individual Capacity*
Deputy Chairman 3	:	Ms Selina Seah	*Changi General Hospital*
Advisor	:	Ms Jacqueline Monteiro	*Individual Capacity*
Secretary	:	Mr Choi Kwok Keong	*Singapore Manufacturing Federation – Standards Development Organisation*
Members	:	Prof Kishore Bhakoo	*Singapore Bioimaging Consortium*
		Mr Chung Kwong Yuew	*Temasek Polytechnic (BioMedical Engineering Faculty)*
		Ms Heidi Goh	*Singapore Manufacturing Federation (Medical Technology Industry Group)*
		Prof James Goh	*Biomedical Engineering Society (Singapore)*
		Dr Christopher Lam	*Health Sciences Authority*
		Ms Audrey Lee	*Medtronic International Ltd*
		Assoc Prof Leo Hwa Liang	*National University of Singapore*
		Dr Lin Jianhua	*TUV SUD PSB Pte Ltd*
		Dr Leonard Loh	*Nanyang Polytechnic*
		Assoc Prof Eddie Ng Yin Kwee	*Nanyang Technological University*
		Dr Ong Siew Hwa	*Acumen Research Laboratories Pte Ltd*
		Mr Peh Ruey Fung	*Advent Access Pte Ltd*
		Mr Justine Phoon	*Biomedical Research Council*
		Dr Padmanabhan Saravanan	*Temasek Polytechnic (Centre of Innovation for Complementary Health Products)*
		Ms Celine Tan	*SPRING Singapore*
		Prof Tan Puay Hoon	*Singapore Health Services Pte Ltd*
		Ms Wang Dan	*Biosensors International Group*
		Ms Wong Shi Xuan	*Eu Yan Sang International Ltd*
		Dr Sidney Yee	*DxD Hub*

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*:

		Name
Convenor	:	Prof James Goh
Secretary	:	Mr Edwin Tan
Members	:	Assoc Prof Chew Sing Yan
		Mr Fan Mingwei
		Ms Heidi Goh
		Ms Ho Yuan Lu
		Prof James Hui Hoi Po
		Dr Lim Jing
		Dr Margam Chandrasekaran
		Dr Ong Lee Lee
		Assoc Prof Phan Toan-Thang
		Prof Seeram Ramakrishna
		Mr Tan Ming Jie
		Dr Tang Kin Fai

The organisations in which the experts of the Working Group are involved are:

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
Osteopore International Pte Ltd
Wise Consultancy and Services Pte Ltd

(blank page)

Contents

Page

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 10993-4:2017 "Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood" 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 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 10993-6	SS ISO 10993-6
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.

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.

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).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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 10993-4:2002), which has been technically revised.

It also incorporates the Amendment ISO 10993-4:2002/Amd 1:2006.

The following changes were made:

a) some definitions have been revised and new definitions have been added;

b) Tables 1 and 2 have been consolidated into a single new Table 1 with test categories and headers reorganized to emphasize and include material and mechanical-induced haemolysis testing and *in vitro* and *in vivo* testing for assessment of risk for thrombosis;

c) Tables 3 and 4 have been consolidated into a single new Table 2 with a simplified list of suggested and most common tests;

d) Annex B has been updated to cover only the most common practiced tests for assessing blood interactions;

e) Annex C has been added to cover the topic of *in vivo* thrombosis and methods for testing;

f) Annex D, which was Annex C in the previous edition, has been updated and now includes added information on mechanically-induced haemolysis;

g) Annex E has been added to cover the topic of complement testing and best test method practices;

h) Annexes F and G have been added to present the less common tests used to assess interactions with blood and the tests that are not recommended for preclinical assessment of medical device blood interaction, respectively. Many of these methods were previously included in Annex B;

i) subtle language refinements can be found throughout the revised document;

j) the Bibliography has been reorganized by common subjects of interest and updated with additional and more current references.

Introduction

The selection and design of test methods for the interactions of medical devices with blood should take into consideration device design, materials, clinical utility, usage environment and risk benefit. This level of specificity can only be covered in vertical standards.

The initial source for developing this document was the publication, *Guidelines for blood/material interactions*, Report of the National Heart, Lung, and Blood Institute[14] chapters 9 and 10. This publication was subsequently revised[15].

Biological evaluation of medical devices –

Part 4:
Selection of tests for interactions with blood

1 Scope

This document specifies general requirements for evaluating the interactions of medical devices with blood.

It describes

a) a classification of medical devices that are intended for use in contact with blood, based on the intended use and duration of contact as defined in ISO 10993-1,

b) the fundamental principles governing the evaluation of the interaction of devices with blood,

c) the rationale for structured selection of tests according to specific categories, together with the principles and scientific basis of these tests.

Detailed requirements for testing cannot be specified because of limitations in the knowledge and precision of tests for evaluating interactions of devices with blood. This document describes biological evaluation in general terms and may not necessarily provide sufficient guidance for test methods for a specific device.

The changes in this document do not indicate that testing conducted according to prior versions of this document is invalid. For marketed devices with a history of safe clinical use, additional testing according to this revision is not recommended.

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 10993-12, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials*