American National Standard

ANSI/AAMI/ISO 10993-4:2017

Biological evaluation of medical devices—Part 4: Selection of tests for interactions with blood

AAMI
Advancing Safety in Health Technology

Biological evaluation of medical devices—Part 4: Selection of tests for interactions with blood

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

Keywords: biological evaluation, medical device, blood

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Committee representation

Association for the Advancement of Medical Instrumentation

BE/WG09, Effects on blood

The adoption of ISO 10993-4 as an American National Standard was initiated by the AAMI/BE/WG09, Effects on blood working group. AAMI/BE/WG09 provides input to the AAMI Biological Evaluation committee (AAMI/BE), which is the responsible group for providing the U.S. input to the relevant group in ISO/TC 194. U.S. representatives from AAMI/BE/WG09 and the TAG played an active part in developing the ISO document.

At the time this document was published, **AAMI/BE/WG09** has the following members:

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NOTE—Participation by federal agency representatives in the development of this standard does not constitute endorsement by the federal government or any of its agencies.

Background of ANSI/AAMI adoption of ISO 10993-4:2017

As indicated in the foreword to the main body of this document (page vii), the International Organization for Standardization (ISO), is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard, which was developed by ISO/TC 194 to specify the general requirements for evaluating the interactions of medical devices with blood.

U.S. participation in ISO/TC 194 is organized through the U.S. Technical Advisory Group, AAMI Biological Evaluation Committee, administered by the Association for the Advancement of Medical Instrumentation. Experts from the United States made a considerable contribution to this standard.

AAMI encourages its committees to harmonize their work with International Standards in the area of biological and evaluation of medical devices. Upon review of ISO 10993-4, the AAMI Biological Evaluation Committee and the AAMI/BE/WG09 decided to adopt it verbatim, as ANSI/AAMI/ISO 10993-4.

AAMI and ANSI procedures require that standards be reviewed and, if necessary, revised every five years to reflect technological advances that may have occurred since publication.

As used within the context of this document, “shall” indicates requirements strictly to be followed to conform to the recommended practice. “Should” indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action should be avoided but is not prohibited.

“May” is used to indicate that a course of action is permissible within the limits of the standard. “Can” is used as a statement of possibility and capability. Finally, “must” is used only to describe “unavoidable” situations, including those mandated by government regulation.

NOTE Users of this standard are advised that this document is an AAMI identical adoption of an ISO document and that the following international conventions have been carried over to the AAMI publication:

- British English spelling (e.g. colour instead of color)
- Use of SI units (e.g. metres instead of feet, Celsius instead of Fahrenheit, etc.)
- Decimal comma instead of a decimal point (e.g. 1 000,15 instead of 1,000.15)

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data comes to light.

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 901 N. Glebe Road, Suite 300, Arlington, VA 22203.

NOTE—Beginning with the ISO foreword on page vii, this American National Standard is identical to ISO 10993-4:2017.

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*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 10993-1, ISO 10993-12 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

3.1
anticoagulant
agent which prevents or delays blood coagulation