

American
National
Standard



ANSI/AAMI/
ISO 10993-1:
2018

Biological evaluation of
medical devices—Part 1:
Evaluation and testing
within a risk management
process

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Biological evaluation of medical devices—Part 1: Evaluation and testing within a risk management process

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AAMI

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Abstract: This document specifies: — the general principles governing the biological evaluation of medical devices within a risk management process; — the general categorization of medical devices based on the nature and duration of their contact with the body; — the evaluation of existing relevant data from all sources; — the identification of gaps in the available data set on the basis of a risk analysis; — the identification of additional data sets necessary to analyse the biological safety of the medical device; — the assessment of the biological safety of the medical device.

Keywords: biological evaluation, medical device, risk management, biological safety

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Committee representation

Association for the Advancement of Medical Instrumentation

BE/WG01, Risk assessment, terminology and global aspects

The adoption of ISO 10993-1 as an American National Standard was initiated by the AAMI/BE/WG01, Risk assessment, terminology and global aspects working group. AAMI/BE/WG01 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/WG01 and the TAG played an active part in developing the ISO document.

At the time this document was published, **AAMI/BE/WG01** has the following members:

Cochairs: James M. Anderson, MD PhD
Anita Y. Sawyer

Members: James M. Anderson, MD PhD
Kristen Bisanz, Teleflex Medical
Carolyn Braithwaite-Nelson, Philips
David J. Brodersen, Getinge USA
Jon Cammack, PhD, Nevakar, Inc
Seraya Carr, Baxter Healthcare Corporation
Joseph Carraway, DVM, MS, NAMSA
Julia Cesur-Levinsky, Medline Industries Inc
Grantley Charles, Edwards Lifesciences
Yan Chen, American Preclinical Services LLC
Gordon M. Ely, LexaMed Ltd
Gloria H. Frost MS, PhD, DABT, Cardinal Health
Chad Geiger, DexCom Inc
Jennifer Goode, FDA/CDRH/ODE/DCD
Michael Groendyk, Arthrex Inc
Mollie J. Holter, MicroBio Consulting LLC
Frances Hsia, Boston Scientific Corporation
John Iannone, BME, John Iannone LLC
Melissa Kinne, Smiths Medical
Jack Lemons, PhD, Society for Biomaterials/Surgery
Taryn K. Meade, Fresenius Kidney Care
Jennifer Nalepka, STERIS Corporation
Laura Perkins DVM, PhD, DACVP, Abbott Vascular
Raji Pidikiti, Terumo BCT
Robert T. Przygoda, PhD, WuXi AppTec Inc
Keith Reiner, Terumo Cardiovascular Systems Corp
Sandra Savidge, Johnson & Johnson
Sharmilee Sawant, PhD, Avanos Medical
Anita Y. Sawyer, Anita Sawyer Consulting
Amy Sessions, WL Gore & Associates Inc
Brian Sidow, Stryker Instruments Division
Kenneth R. St John, PhD, University of Mississippi Medical Center
Audrey Turley, BS RM (NRM), Nelson Laboratories LLC
Lisa Walker, Alcon Laboratories Inc
Brian Wallace, Intuitive Surgical Inc
Janel K. Warmka, PhD, 3M Health Care
Michael F. Wolf, Medtronic Inc Campus
Mingyu Zhang, MicroVention

Alternates:

- Michael Bailey, FDA - CDRH
- Kevin Connor, Boston Scientific Corporation
- Francesco Famosi, Arthrex Inc
- Austin Griggs, Edwards Lifesciences
- Donna Haraden, Baxter Healthcare Corporation
- Michael Hendershot, B.S., NAMSA
- George Hickey, Cardinal Health
- Hooman T Kashani, Intuitive Surgical Inc
- Anurag Mishra, Avanos Medical
- James Moore, WL Gore & Associates Inc
- Rodney D. Parker, QA/RA/CS, Stryker Instruments Division
- Anthony M. Piotrkowski, STERIS Corporation
- Deanna Porter, Abbott Laboratories
- Edward Rankin, Medtronic Inc/Physiological Research Laboratory
- Thor Rollins, BS Nelson Laboratories LLC
- Sandi Schaible, WuXi AppTec Inc
- Roberto Zumbado, CISS-EO, Philips

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 10993-1:2018

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 principles governing the biological evaluation of medical devices within a risk management process.

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 10993-1, the AAMI Biological Evaluation Committee and the AAMI/BE/WG01 decided to adopt it verbatim, as ANSI/AAMI/ISO 10993-1.

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 10993-1:2018.

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 fifth edition cancels and replaces the fourth edition (ISO 10993-1:2009), which has been technically revised. It also incorporates the Technical Corrigendum ISO 10993-1:2009/Cor.1:2010.

The main changes compared to the previous edition are as follows:

- a) revised Annex A "Endpoints to be addressed in a biological risk assessment" with new columns for "physical and/or chemical information" and "material mediated pyrogenicity" as well as columns for "chronic toxicity," "carcinogenicity," "reproductive/developmental toxicity," and "degradation" which now indicates "endpoints" to be considered with "E" (instead of "tests" to be conducted with an "X");
- b) replaced Annex B "Guidance on the risk management process" with "Guidance on the conduct of biological evaluation within a risk management process" (formerly ISO TR 15499);
- c) additional definitions for terms used throughout the ISO 10993 series of standards;
- d) additional information on the evaluation of "Non-contacting medical devices" and new information on the evaluation of "Transitory-contacting medical devices";
- e) additional information on the evaluation of nanomaterials, and absorbable materials;
- f) additional reference to ISO 18562 (all parts) for "Biocompatibility evaluation of breathing gas pathways in healthcare applications";
- g) significant editing changes throughout the document;

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

This corrected version of ISO 10993-1:2018 incorporates the following correction.

—In Table A.1, 6th column, “Sensitization” has been added as a table heading.

Introduction

The primary aim of this document is the protection of humans from potential biological risks arising from the use of medical devices. It is compiled from numerous International and national standards and guidelines concerning the biological evaluation of medical devices. It is intended to describe the biological evaluation of medical devices within a risk management process, as part of the overall evaluation and development of each medical device. This approach combines the review and evaluation of existing data from all sources with, where necessary, the selection and application of additional tests, thus enabling a full evaluation to be made of the biological responses to each medical device, relevant to its safety in use. The term “medical device” is wide-ranging and, at one extreme, consists of a single material, which can exist in more than one physical form, and at the other extreme, of a medical device consisting of numerous components made of more than one material.

This document addresses the determination of the biological response to medical devices, mostly in a general way, rather than in a specific device-type situation. Thus, for a complete biological evaluation, it classifies medical devices according to the nature and duration of their anticipated contact with human tissues when in use and indicates, in a matrix, the biological endpoints that are thought to be relevant in the consideration of each medical device category. See also 3.14, Note 1 to entry.

The range of biological hazards is wide and complex. The biological response to a constituent material alone cannot be considered in isolation from the overall medical device design. Thus, in designing a medical device, the choice of the best material with respect to its biocompatibility might result in a less functional medical device, biocompatibility being only one of a number of characteristics to be considered in making that choice. Where a material is intended to interact with tissue in order to perform its function, the biological evaluation needs to address this.

Biological responses that are regarded as adverse, caused by a material in one application, might not be regarded as such in a different situation. Biological testing is based upon, among other things, *in vitro* and *ex vivo* test methods and upon animal models, so that the anticipated behaviour when a medical device is used in humans can be judged only with caution, as it cannot be unequivocally concluded that the same biological response will also occur in this species. In addition, differences in the manner of response to the same material among individuals indicate that some patients can have adverse reactions, even to well-established materials.

The primary role of this document is to serve as a framework in which to plan a biological evaluation. A secondary role is to utilize scientific advances in our understanding of basic mechanisms, to minimize the number and exposure of test animals by giving preference to *in vitro* models and to chemical, physical, morphological, and topographical characterization testing, in situations where these methods yield equally relevant information to that obtained from *in vivo* models.

It is not intended that this document provide a rigid set of test methods, including pass/fail criteria, as this might result in either an unnecessary constraint on the development and use of novel medical devices, or a false sense of security in the general use of medical devices. Where a particular application warrants it, experts in the product or in the area of application concerned can choose to establish specific tests and criteria, described in a product-specific vertical standard.

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

Informative Annex A contains a table that is generally helpful in identifying endpoints recommended in the biocompatibility evaluation of medical devices, according to their category of body contact and duration of clinical exposure. Informative Annex B contains guidance for the application of the risk management process to medical devices which encompasses biological evaluation.

Biological evaluation of medical devices—Part 1: Evaluation and testing within a risk management process

1 Scope

This document specifies:

- the general principles governing the biological evaluation of medical devices within a risk management process;
- the general categorization of medical devices based on the nature and duration of their contact with the body;
- the evaluation of existing relevant data from all sources;
- the identification of gaps in the available data set on the basis of a risk analysis;
- the identification of additional data sets necessary to analyse the biological safety of the medical device;
- the assessment of the biological safety of the medical device.

This document applies to evaluation of materials and medical devices that are expected to have direct or indirect contact with:

- the patient's body during intended use;
- the user's body, if the medical device is intended for protection (e.g., surgical gloves, masks and others).

This document is applicable to biological evaluation of all types of medical devices including active, non-active, implantable and non-implantable medical devices.

This document also gives guidelines for the assessment of biological hazards arising from:

- risks, such as changes to the medical device over time, as a part of the overall biological safety assessment;
- breakage of a medical device or medical device component which exposes body tissue to new or novel materials.

Other parts of ISO 10993 cover specific aspects of biological assessments and related tests. Device-specific or product standards address mechanical testing.

This document excludes hazards related to bacteria, moulds, yeasts, viruses, transmissible spongiform encephalopathy (TSE) agents and other pathogens.

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 10993-2:2006, *Biological evaluation of medical devices—Part 2: Animal welfare requirements*