American National Standard

ANSI/AAMI/ISO 10993-15:2019

Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys

AAMI
Advancing Safety in Health Technology

Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys

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Abstract: Specifies general requirements for the design of tests for identifying and quantifying degradation products from final metallic medical devices or corresponding material samples finished as ready for clinical use.

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

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Committee representation

Association for the Advancement of Medical Instrumentation

BE/WG2, Degradation aspects related to biological testing working group

The adoption of ISO 10993-15 as an American National Standard was initiated by the AAMI/BE/WG2 Material characterization working group. AAMI/BE/WG2 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/WG2 and the TAG played an active part in developing the ISO document.

At the time this document was published, **AAMI/BE/WG2** had the following members:

Cochair: Scott G. McNamee, PhD

Members:
James M. Anderson, MD PhD, Case Western Reserve University
Carolyn Braithwaite-Nelson, Philips
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Keith Milner, PhD, Cook Research Incorporated
Rodney D. Parker, QA/RA/CS, Stryker Instruments Division
Deanna Porter, Abbott Laboratories
Beau Rollins, ConvaTec Inc QARAC Global Headquarters
Anita Y. Sawyer, Anita Sawyer Consulting
Stacie Schulze BS, DABT, Avanos Medical
Raymond Simas, Boston Scientific Corporation
Chris Steele, Alcon Research Ltd
Brian Wallace, Intuitive Surgical Inc

Alternates:
Jeanine L. Bussiere, Amgen Inc
Timothy Fulghum, Baxter Healthcare Corporation
Paul Johnson, Cardinal Health
Hooman T Kashani, Intuitive Surgical Inc
Joyce V. Lee, PhD, CQA, Owens & Minor
Jianwei Li, PhD, Medtronic Rice Creek Campus
Yijun Lu, PhD, Ethicon USA
Taryn K. Meade, Fresenius Kidney Care
Anurag Mishra, Avanos Medical
Thor Rollins, BS, Nelson Laboratories LLC
Sandi Schaible, WuXi AppTec Inc
Brian Sidow, Stryker Instruments Division
Shelby Skoog, PhD, FDA - CDRH

Carl Swanson, NAMSA
Janel K. Warmka, PhD, Boston Scientific
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 10993-15:2019

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 10993-15, the AAMI Biological Evaluation Committee and the AAMI/BE/WG decided to adopt it verbatim, as ANSI/AAMI/ISO 10993-15.

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 10993-15:2019.

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 of 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 www.iso.org/iso/foreword.html.

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

This second edition cancels and replaces the first edition (ISO 10993 15:2000), which has been technically revised.

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

a) the document now considers materials designed to degrade in the body as well as materials that are not intended to degrade;

b) the information on test methods has been amended to consider nanomaterials and relevant material specific standards;

c) the test solution (electrolyte) has been specified more;

d) the sample shape has been specified more;

e) the immersion test procedure has been expanded;

f) the status of Annex C in the previous edition has been changed and now included as Annex A.

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

Any feedback or questions on this document should be directed to the user’s national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

One of the potential health hazards resulting from medical devices can be due to the interactions of their electrochemically induced degradation products with the biological system. Therefore, the evaluation of potential degradation products from metallic materials by methods suitable for testing the electrochemical behaviour of these materials is a necessary step in the biological performance testing of materials.

The body environment typically contains cations of sodium, potassium, calcium, and magnesium, and anions of chloride, bicarbonate, phosphate, and organic acids generally in concentrations between 2×10^{-3} mol/l and 150×10^{-3} mol/l. A range of organic molecules such as proteins, enzymes, and lipoproteins are also present, but their concentrations can vary to a great extent. Earlier studies assumed that organic molecules did not exert a significant influence on the degradation of metallic implants, but newer investigations indicate that implant–tissue interactions should be taken into account. Depending on a particular product or application, altering the pH of the testing environment may also need to be considered.

In such biological environments, metallic materials may undergo a certain degradation, and the different degradation products can interact with the biological system in different ways. Therefore, the identification and quantification of these degradation products is an important step in evaluating the biological performance of medical devices.

Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys

1 Scope

This document specifies general requirements for the design of tests for identifying and quantifying degradation products from final metallic medical devices or corresponding material samples finished as ready for clinical use.

This document is applicable only to those degradation products generated by chemical alteration of the final metallic device in an *in vitro* degradation test. Because of the nature of *in vitro* tests, the test results approximate the *in vivo* behaviour of the implant or material. The described chemical methodologies are a means to generate degradation products for further assessments.

This document is applicable to both materials designed to degrade in the body as well as materials that are not intended to degrade.

This document is not applicable to evaluation of degradation which occurs by purely mechanical processes; methodologies for the production of this type of degradation product are described in specific product standards, where available.

NOTE Purely mechanical degradation causes mostly particulate matter. Although this is excluded from the scope of this document, such degradation products can evoke a biological response and can undergo biological evaluation as described in other parts of ISO 10993.

Because of the wide range of metallic materials used in medical devices, no specific analytical techniques are identified for quantifying the degradation products. The identification of trace elements ($<10^{-6}$ w/w) contained in the specific metal or alloy is not addressed in this document, nor are specific requirements for acceptable levels of degradation products provided in this document.

This document excludes the biological activity of the degradation products. (See instead the applicable clauses of ISO 10993-1 and ISO 10993-17).

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 3585, *Borosilicate glass 3.3 — Properties*

ISO 3696, *Water for analytical laboratory use — Specification and test methods*

ISO 8044, *Corrosion of metals and alloys — Basic terms and definitions*

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