American National Standard

ANSI/AAMI BE83:2006/(R)2011

Biological evaluation of medical devices—Part 18: Chemical characterization of materials

AAMI
Advancing Safety in Medical Technology

The Objectives and Uses of AAMI Standards and Recommended Practices

It is most important that the objectives and potential uses of an AAMI product standard or recommended practice are clearly understood. The objectives of AAMI's technical development program derive from AAMI's overall mission: the advancement of medical instrumentation. Essential to such advancement are (1) a continued increase in the safe and effective application of current technologies to patient care, and (2) the encouragement of new technologies. It is AAMI's view that standards and recommended practices can contribute significantly to the advancement of medical instrumentation, provided that they are drafted with attention to these objectives and provided that arbitrary and restrictive uses are avoided.

A voluntary *standard* for a *medical device* recommends to the manufacturer the information that should be provided with or on the product, basic safety and performance criteria that should be considered in qualifying the device for clinical use, and the measurement techniques that can be used to determine whether the device conforms with the safety and performance criteria and/or to compare the performance characteristics of different products. Some standards emphasize the information that should be provided with the device, including performance characteristics, instructions for use, warnings and precautions, and other data considered important in ensuring the safe and effective use of the device in the clinical environment. Recommending the disclosure of performance characteristics often necessitates the development of specialized test methods to facilitate uniformity in reporting; reaching consensus on these tests can represent a considerable part of committee work. When a drafting committee determines that clinical concerns warrant the establishment of *minimum* safety and performance criteria, reference tests must be provided and the reasons for establishing the criteria must be documented in the rationale.

A *recommended practice* provides guidelines for the use, care, and/or processing of a medical device or system. A recommended practice does not address device performance *per se*, but rather procedures and practices that will help ensure that a device is used safely and effectively and that its performance will be maintained.

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a fume of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards health care professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decision-making.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

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Biological evaluation of medical devices— Part 18: Chemical characterization of materials

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Association for the Advancement of Medical Instrumentation

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American National Standards Institute

Abstract: Describes a framework for the identification of a material and the identification of a material and the identification and of its chemical constituents.

Keywords: chemical constituents, chemical characterization, extraction

AAMI Standard

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Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard. NOTE: Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

International designation	U.S. designation	Equivalency
IEC 60601-1:2005	ANSI/AAMI ES60601-1:2005	Major technical variations
IEC 60601-1-2:2001 and Amendment 1:2004	ANSI/AAMI/IEC 60601-1-2:2001 and Amendment 1:2004	Identical
IEC 60601-2-04:2002	ANSI/AAMI DF80:2003	Major technical variations
IEC 60601-2-19:1990 and Amendment 1:1996	ANSI/AAMI II36:2004	Major technical variations
IEC 60601-2-20:1990 and Amendment 1:1996	ANSI/AAMI II51:2004	Major technical variations
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 and Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:2004	Major technical variations
IEC TR 60878:2003	ANSI/AAMI/IEC TIR60878:2003	Identical
IEC TR 62296:2003	ANSI/AAMI/IEC TIR62296:2003	Identical
IEC TR 62348:200x[1]	ANSI/AAMI/IEC TIR62348:2006	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2004	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996/(R)2002	Identical
ISO 10993-1:2003	ANSI/AAMI/ISO 10993-1:2003	Identical
ISO 10993-2:1992	ANSI/AAMI/ISO 10993-2:1993/(R)2001	Identical
ISO 10993-3:2003	ANSI/AAMI/ISO 10993-3:2003	Identical
ISO 10993-4:2002	ANSI/AAMI/ISO 10993-4:2002	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:1994	ANSI/AAMI/ISO 10993-6:1995/(R)2001	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999/(R)2005	Identical
ISO 10993-10:2002	ANSI/AAMI BE78:2002	Minor technical variations
ISO 10993-11:1993	ANSI/AAMI 10993-11:1993	Minor technical variations
ISO 10993-12:2002	ANSI/AAMI/ISO 10993-12:2002	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999/(R)2004	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997/(R)2003	Identical
ISO 10993-17:2002	ANSI/AAMI/ISO 10993-17:2002	Identical

International designation	U.S. designation	Equivalency
ISO 10993-18:2005	ANSI/AAMI BE83:2006	Major technical variations
ISO TS 10993-19:200x[1]	ANSI/AAMI/ISO TIR10993-19:2006	Identical
ISO TS 10993-20:200x[1]	ANSI/AAMI/ISO TIR10993-20:2006	Identical
ISO 11135:1994	ANSI/AAMI/ISO 11135:1994	Identical
ISO 11137-1:2006	ANSI/AAMI/ISO 11137-1:2006	Identical
ISO 11137-2:200x[1]	ANSI/AAMI/ISO 11137-2:2006	Identical
ISO 11137-3:2006	ANSI/AAMI/ISO 11137-3:2006	Identical
ISO 11138-1: 200x[1]	ANSI/AAMI/ISO 11138-1:2006	Identical
ISO 11138-2: 200x[1]	ANSI/AAMI/ISO 11138-2:2006	Identical
ISO 11138-3: 200x[1]	ANSI/AAMI/ISO 11138-3:2006	Identical
ISO 11138-4: 200x[1]	ANSI/AAMI/ISO 11138-4:2006	Identical
ISO 11138-5: 200x[1]	ANSI/AAMI/ISO 11138-5:2006	Identical
ISO TS 11139:2006	ANSI/AAMI/ISO 11139:2006	Identical
ISO 11140-1:2005	ANSI/AAMI/ISO 11140-1:2005	Identical
ISO 11140-5:2000	ANSI/AAMI ST66:1999	Major technical variations
ISO 11607-1:2006	ANSI/AAMI/ISO 11607-1:2006	Identical
ISO 11607-2:2006	ANSI/AAMI/ISO 11607-2:2006	Identical
ISO 11737-1: 2006	ANSI/AAMI/ISO 11737-1:2006	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO 11737-3:2004	ANSI/AAMI/ISO 11737-3:2004	Identical
ISO 13485:2003	ANSI/AAMI/ISO 13485:2003	Identical
ISO 13488:1996	ANSI/AAMI/ISO 13488:1996	Identical
ISO 14155-1:2003	ANSI/AAMI/ISO 14155-1:2003	Identical
ISO 14155-2:2003	ANSI/AAMI/ISO 14155-2:2003	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161:2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO TR 14969:2004	ANSI/AAMI/ISO TIR14969:2004	Identical
ISO 14971:2000 and A1:2003	ANSI/AAMI/ISO 14971:2000 and A1:2003	Identical
ISO 15223:2000, A1:2002, and A2:2004	ANSI/AAMI/ISO 15223:2000, A1:2001, and A2:2004	Identical
ISO 15225:2000 and A1:2004	ANSI/AAMI/ISO 15225:2000/(R)2006 and A1:2004/(R)2006	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO TS 15843:2000	ANSI/AAMI/ISO TIR15843:2000	Identical
ISO 15882:2003	ANSI/AAMI/ISO 15882:2003	Identical
ISO TR 16142:2006	ANSI/AAMI/ISO TIR16142:2006	Identical
ISO 17664:2004	ANSI/AAMI ST81:2004	Major technical variations
ISO 17665-1:200x[1]	ANSI/AAMI/ISO 17665-1:2006	Identical
ISO 18472:200x[1]	ANSI/AAMI/ISO 18472:2006	Identical
ISO TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 25539-1:2003 and A1:2005	ANSI/AAMI/ISO 25539-1:2003 and A1:2005	Identical

[1]In production

Committee representation

Association for the Advancement of Medical Instrumentation

Biological Evaluation of Medical Devices Committee

This standard was developed by the AAMI Material Characterization Working Group (U.S. Sub-TAG for ISO/TC 194/WG 14) under the auspices of the AAMI Biological Evaluation Committee, which also functions as a U.S. Technical Advisory Group to the relevant work in the International Organization for Standardization (ISO).

At the time this document was published, the **AAMI Biological Evaluation of Medical Devices Committee** had the following members:

Cochairs:
Donald E. Marlowe
Peter William Urbanski

Members:
James M. Anderson, MD, PhD, Case Western Reserve University (Independent Expert)
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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 AAMI adoption of ISO 10993-18:2005 and rationale for major technical deviations

As indicated in the foreword to the main body of this document (page xii), 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 technical specification.

International Standard ISO 10993-18 was developed by Working Group (WG) 14 *Material Characterization,* of ISO Technical Committee (TC) 194, *Biological evaluation of medical devices*, to describe a framework for the identification of a material and the identification of a material and the identification and of its chemical constituents.

U.S. participation in this ISO/TC 194/WG 14 is organized through the U.S. Technical Advisory Group for ISO/TC 194, administered by the Association for the Advancement of Medical Instrumentation (AAMI) on behalf of the American National Standards Institute (ANSI). U.S. experts made a considerable contribution to this technical specification.

AAMI encourages its committees to harmonize their work with international standards as much as possible. Upon review of ISO 10993-18, the AAMI Biological Evaluation of Medical Devices Committee and the AAMI Material Characterization Working Group decided to adopt ISO 10993-18 with major technical deviations. The primary reason for the major technical deviations was to bring Part 18 in line with ISO 10993-1:2003.

AAMI (and ANSI) have adopted other ISO documents. See the Glossary of Equivalent Standards for a list of ISO standards adopted by AAMI, which gives the corresponding U.S. designation and the level of equivalency with the ISO standard.

The concepts incorporated into this technical information report should not be considered inflexible or static. This technical information report, 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 technical information report are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

NOTE—Beginning with the ISO foreword on page xii, this American National Standard is identical to ISO 10993-18:2005, with the exception of the major national deviations listed below.

Major technical deviations from ISO 10993-18:2005

Clause 1, fourth bullet

At the end of the sentence delete, “to check the relevance of data on the latter to be used to support the assessment of the former.”

Subclause 3.6

Change to “**extraction**”

Subclause 3.6

Insert a new first sentence that reads, “the process of treating a material with a solvent to remove soluble substances.”

Subclause 3.6

Move the NOTE to the bottom of 3.6.

Add a new Subclause 3.6.1

Which reads, “**exhaustive extraction** – extraction until the amount of residues in a subsequent extraction is less than 10% of that detected in the first extraction”

Add a new Subclause 3.6.2

Which reads, “**simulated-use extraction** – extraction for evaluating potential risk to the patient or user during routine use of a device, using an extraction method with an appropriate medium that simulates product use”

Add a new Subclause 3.6.3

Which reads, “**extractable** – soluble substances removed from a material when treated with a solvent”

Subclause 3.7

Delete Subclause 3.7 “**simulated extraction**” however, use the definition for the new subclause 3.6.2 **simulated-use extraction**.

Add a new Subclause 3.7

That reads, “**leachable** – chemical removed from a medical device by the action of water or other liquids related to the use of the device”

Example—Additives, sterilant residues, process residues, degradation products, solvents, plasticizers, lubricants, catalysts, stabilizers, anti-oxidants, coloring agents, filters and monomers, among others.

[ISO 10993-7] [ISO 10993-9] [ISO 10993-11] [ISO 10993-16] [ISO 10993-17]”

Table 1

Add “CE – Capillary electrophoresis”

Add “LC – Liquid chromatography”

Change the footnote to read, “[a] Mass spectroscopy is frequently combined with chromatographic techniques such as GC-MS, LC-MS, LC-MS-MS and CE-MS.”

Clause 5

Delete the second paragraph.

Subclause 6.1

Revise the first sentence to read, “The generation of chemical characterization data is a process linked to risk assessment.”

Subclause 6.1

Revise the second sentence to read, “The chemical characterization requirements and guidance are specified in Subclauses 6.2 to 6.3.”

Subclause 6.1, third paragraph

Add a new first sentence which reads, “If the material or device contacts the body directly or indirectly then this standard is applicable (see 4.2.1 of ISO 10993-1:2003).”

Subclause 6.1, third paragraph

Change “step” to “stage”.

Subclause 6.1, NOTE 1

Revise NOTE 1 to read, “The risk assessment process referred to in Subclauses 6.2 and 6.3 is outside the scope of this part of ISO 10993 but is mentioned to indicate the important interaction between chemical characterization and risk assessment.”

Subclause 6.1, last paragraph

Delete the last paragraph entirely.

Subclause 6.2

Delete “Step 1” in title.

Subclause 6.2, third paragraph, last sentence

Change “all” to “potential”.

Subclause 6.2

Add a new last paragraph which reads, “Sufficient qualitative information shall be obtained to allow a comparison to determine whether the material is equivalent to that utilized in a device with the same clinical exposure/use and having had the same manufacturing and sterilization processes applied, e.g. established safe use of materials in a product to be used on intact skin.”

Subclause 6.3

Delete entirely.

New Subclause 6.3 (old Subclause 6.4)

Delete “Step 3” in title.

New Subclause 6.3 (old Subclause 6.4)

Add the following two sentences to the end of the first paragraph, “If the quantity of any chemical present remains of toxicological concern, in light of anticipated clinical exposure, as determined by the toxicological risk assessor, the amount of extraction of that chemical shall be measured, by performing, for example, a simulated use extraction. The extraction conditions used shall be documented and justified.”

New Subclause 6.3 (old Subclause 6.4)

Add a new last paragraph which reads, “Sufficient quantitative information shall be obtained to permit a risk assessment, when combined with existing toxicological information (see ISO 10993-17 and 4.1 of ISO 14971:2000).”

Subclause 6.5

Delete entirely.

Subclause 6.6

Delete entirely.

Subclause 7.1

First paragraph, first sentence, revise to read, “Clause 6 of this part of ISO 10993 describes the generation of qualitative and quantitative chemical characterization data for use in the toxicological risk assessment.”

Subclause 7.1

Third paragraph, first sentence revise to read, “For Subclauses 6.2 and 6.3, the material scientist and analyst in consultation with the toxicological risk assessor shall determine which parameters are relevant to the assessment of a material or medical device.”

Table 2

Add an “X” under “Quantitative” for “Residue on ignition”.

Clause 8

Delete the first sentence of the first paragraph.

Clause 8

Delete item e).

Annex A

Delete Annex A entirely.

Annex A.3.2 (old Annex B.3.2)

Revise the second and third sentences to read, “Naming and describing polymers according to these rules does present exact structural features of polymers. However, it does not give any information about additives often contained in the commercially available polymers.”

Annex C

Delete Annex C entirely.

Bibliography

Add a reference to ISO 10993-7:1995.

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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 10993-18 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

ISO 10993 consists of the following parts, under the general title *Biological evaluation of medical devices*:

— *Part 1: Evaluation and testing*

— *Part 2: Animal welfare requirements*

— *Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*

— *Part 4: Selection of tests for interactions with blood*

— *Part 5: Tests for in vitro cytotoxicity*

— *Part 6: Tests for local effects after implantation*

— *Part 7: Ethylene oxide sterilization residuals*

— *Part 9: Framework for identification and quantification of potential degradation products*

— *Part 10: Tests for irritation and delayed-type hypersensitivity*

— *Part 11: Tests for systemic toxicity*

— *Part 12: Sample preparation and reference materials*

— *Part 13: Identification and quantification of degradation products from polymeric medical devices*

— *Part 14: Identification and quantification of degradation products from ceramics*

— *Part 15: Identification and quantification of degradation products from metals and alloys*

— *Part 16: Toxicokinetic study design for degradation products and leachables*

— *Part 17: Establishment of allowable limits for leachable substances*

— *Part 18: Chemical characterization of materials*

The following parts are under preparation:

— *Part 19: Physico-chemical, mechanical and morphological characterization*

— *Part 20: Principles and methods for immunotoxicology testing of medical devices*

Future parts will deal with other relevant aspects of biological testing.

For the purposes of this part of ISO 10993, the CEN annex regarding fulfillment of European Council Directives has been removed.

Introduction

ISO 10993-1 provides a framework for a structured program of assessment for the evaluation of biological safety. Clause 3 of ISO 10993-1:2003 states that in the selection of materials to be used for device manufacture the first consideration should be fitness for purpose. This should have regard to the characteristics and properties of the material, which include chemical, toxicological, physical, electrical, morphological and mechanical properties. This information is necessary prior to any biological evaluation. Subclause 7.2 of ISO 10993-1:2003 notes that the continuing acceptability of a biological evaluation is an aspect of a quality management system.

Also ISO 14971 points out that a toxicological risk analysis should take account of the chemical nature of the materials.

The requirements specified in this document are intended to yield the following information, which will be of value in predicting the biological response of the materials:

— The chemical composition of the materials used in the manufacturing process including processing additives and residues e.g. trace chemicals, cleaning, disinfection and testing agents, acids and caustic substances.

— The characterization of materials to be used in the production of medical devices, as well as in devices in their final form.

— Identification of the materials of construction of the medical device.

— The potential of medical device materials to release substances or breakdown products due to the manufacturing process.

— Changes in the materials of construction, which result from changes in the manufacturing process or insufficient control of the manufacturing process.

The compositional characteristics of the materials of manufacture are mainly under the control of the suppliers of these materials. However other characteristics are chiefly influenced by the requirements to be met by the finished medical device as well as the processes used by the medical device manufacturer.

Biological evaluation of medical devices — Part 18: Chemical characterization of materials

1 Scope

This part of ISO 10993 describes a framework for the identification of a material and the identification and quantification of its chemical constituents. The chemical characterization information generated can be used for a range of important applications, for example:

— As part of an assessment of the overall biological safety of a medical device (ISO 10993-1 and 14971).

— Measurement of the level of a leachable substance in a medical device in order to allow the assessment of compliance with the allowable limit derived for that substance from health based risk assessment (ISO 10993-17).

— Judging equivalence of a proposed material to a clinically established material.

— Judging equivalence of a final device to a prototype device.

— Screening of potential new materials for suitability in a medical device for a proposed clinical application.

This part of ISO 10993 does not address the identification or quantification of degradation products, which is covered in ISO 10993-9, ISO 10993-13, ISO 10993-14 and ISO 10993-15.

The ISO 10993 series of standards is applicable when the material or device comes into contact with the body directly or indirectly (see 4.2.1 of ISO 10993-1:2003).

This part of ISO 10993 is intended for suppliers of materials and manufacturers of medical devices, when carrying out a biological safety assessment.