List of Titles

American National Standard

ANSI/AAMI/ISO 10993-14:2001

Biological evaluation of medical devices— Part 14: Identification and quantification of degradation products from ceramics

AAMI Association for the Advancement of Medical Instrumentation

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, referee 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 decisionmaking.

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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Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the Manager for Technical Development. An official interpretation must be approved by letter ballot of the originating committee and subsequently reviewed and approved by the AAMI Standards Board. The interpretation will become official and representation of the Association only upon exhaustion of any appeals and upon publication of notice of interpretation in the "Standards Monitor" section of the *AAMI News*. The Association for the Advancement of Medical Instrumentation disclaims responsibility for any characterization or explanation of a standard or recommended practice which has not been developed and communicated in accordance with this procedure and which is not published, by appropriate notice, as an *official interpretation* in the *AAMI News*.

American National Standard ANSI/AAMI/ISO 10993-14:2001

Biological evaluation of medical devices—Part 14: Identification and quantification of degradation products from ceramics

Approved 24 September 2001 by
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Approved 11 October 2001 by
American National Standards Institute, Inc.

Abstract: Specifies two methods for obtaining solutions of degradation products from ceramics (including glasses) for the purposes of quantification.

Keywords: biological evaluation, degradation, ceramics

List of Titles

AAMI Standard

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List of Titles

Contents

Page

Glossary of equivalent standards v

Committee representation vii

Background of AAMI adoption of ISO 10993-14:2001 viii

Foreword ix

Introduction x

1 Scope 1

2 Normative references 1

3 Terms and definitions 1

4 Test procedures 2

4.1 Principle 2
4.2 Testing of dental devices 2
4.2.1 General 2
4.2.2 Test methods for dental devices exposed to the oral cavity 3
4.2.3 Specimen characterization 3
4.2.4 Analysis 3
4.3 General testing techniques 3
4.3.1 Mass determination 3
4.3.2 Drying techniques 3
4.4 Extreme solution test 3
4.4.1 Principle 3
4.4.2 Application range 3
4.4.3 Extreme test sample preparation 3
4.4.3.1 Specimen configuration 3
4.4.3.2 Granulation 3
4.4.3.3 Sizing 3
4.4.3.4 Specimen preparation 4
4.4.4 Extreme test sample characterization 4
4.4.4.1 Surface area characterization 4
4.4.4.2 Density 4
4.4.4.3 Solubility characterization 4
4.4.4.4 Microstructural and X-ray characterization 4
4.4.5 Test equipment 4
4.4.5.1 Test container 4
4.4.5.2 Büchner funnel 4
4.4.6 Citric acid buffer solution 4
4.4.7 Test procedure 4
4.5 Simulation solution test 5
4.5.1 Principle 5
4.5.2 Application range 5
4.5.3 Simulation test specimen configuration 5
4.5.3.1 Coated ceramics 5
4.5.3.2 All other ceramics 5
4.5.4 Simulation test sample characterization 5
4.5.4.1 General 5
4.5.4.2 Density 6
4.5.4.3 Microstructural and X-ray characterization 6
4.5.4.4 Surface area characterization 6
4.5.5 Test equipment 6
4.5.5.1 Test container 6
4.5.5.2 Büchner funnel 6
4.5.6 Buffer solution 6

4.5.7 Coated disk test procedure....6
4.5.7.1 General....6
4.5.7.2 Blank disk test....6
4.5.7.3 Coated disk test....6
4.5.8 Test procedure (all other ceramics)....7

5 Analysis of filtrate....7

5.1 General....7
5.2 Choice of chemicals or elements to be analyzed....7
5.3 Sensitivity of the analysis method....7

6 Test report....8

Annex

Bibliography....9

Figure

1 Flowchart of the decision making process for the extreme solution test and the simulation solution tests (see text for details)....2

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 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 & Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:1998	Major technical variations
ISO 5840:1996	ANSI/AAMI/ISO 5840:1996	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996	Identical
ISO 10993-1:1997	ANSI/AAMI/ISO 10993-1:1997	Identical
ISO 10993-2:1992	ANSI/AAMI/ISO 10993-2:1993	Identical
ISO 10993-3:1992	ANSI/AAMI/ISO 10993-3:1993	Identical
ISO 10993-4:1992	ANSI/AAMI/ISO 10993-4:1993	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:1994	ANSI/AAMI/ISO 10993-6:1995	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995	Identical
ISO 10993-8:2000	ANSI/AAMI/ISO 10993-8:2000	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999	Identical
ISO 10993-10:1995	ANSI/AAMI/ISO 10993-10:1995	Identical
ISO 10993-11:1993	ANSI/AAMI 10993-11:1993	Minor technical variations
ISO 10993-12:1996	ANSI/AAMI/ISO/CEN 10993-12:1996	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999	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	Identical
ISO 11134:1994	ANSI/AAMI/ISO 11134:1993	Identical
ISO 11135:1994	ANSI/AAMI/ISO 11135:1994	Identical
ISO 11137:1995	ANSI/AAMI/ISO 11137:1994	Identical
ISO 11138-1:1994	ANSI/AAMI ST59:1999	Major technical variations
ISO 11138-2:1994	ANSI/AAMI ST21:1999	Major technical variations
ISO 11138-3:1995	ANSI/AAMI ST19:1999	Major technical variations
ISO 11140-1:1995 and Technical Corrigendum 1:1998	ANSI/AAMI ST60:1996	Major technical variations
ISO 11607:200x[1]	ANSI/AAMI/ISO 11607:2000	Identical

International designation	U.S. designation	Equivalency
ISO 11737-1:1995	ANSI/AAMI/ISO 11737-1:1995	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO TR 13409:1996	AAMI/ISO TIR 13409:1996	Identical
ISO 13485:1996	ANSI/AAMI/ISO 13485:1996	Identical
ISO 13488:1996	ANSI/AAMI/ISO 13488:1996	Identical
ISO 14155:1996	ANSI/AAMI/ISO 14155:1996	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 14969:1999	ANSI/AAMI/ISO 14969:1999	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO 14971:2000	ANSI/AAMI/ISO 14971:2000	Identical
ISO 15223:2000	ANSI/AAMI/ISO 15223:2000	Identical
ISO 15225:2000	ANSI/AAMI/ISO 15225:2000	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 TR 15844:1998	AAMI/ISO TIR15844:1998	Identical
ISO TR 16142:1999	ANSI/AAMI/ISO TIR16142:2000	Identical

[1] FDIS approved; being prepared for publication.

Committee representation

Association for the Advancement of Medical Instrumentation

Biological Evaluation Committee

The adoption of ISO 10993-14:2001 as an American National Standard was initiated by 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). U.S. representatives from the AAMI Degradation Aspects Related to Biological Testing Working Group (U.S. Sub-TAG for ISO/TC 194/WG 2), cochaired by Edward Mueller, formerly of FDA and now a consultant in Annapolis, MD, played an active part in developing the ISO standard. Mr. Mueller also serves as the convener of the responsible ISO working group.

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

Cochairs:	Donald F. Gibbons, PhD
	Donald E. Marlowe
Members:	James M. Anderson, MD, PhD, Case Western Reserve University
	Eric R. Claussen, PhD, Becton Dickinson
	Roger Dabbah, PhD, U.S. Pharmacopeial Convention, Inc.
	Donald F. Gibbons, PhD, 3M
	Jean A. Goggins, PhD, Consultant, San Diego, CA
	Donald E. Marlowe, FDA Center for Devices and Radiological Health
	Edward Mueller, Consultant, Annapolis, MD
	Barry F. Page, Consultant, Garner, NC
	Harold Stanley, DDS, American Dental Association
	Paul Upman, NAmSA
Alternates:	Sumner A. Barenberg, PhD, Bernard Technologies
	Sharon Northup, PhD, U.S. Pharmacopeial Convention, Inc.
	Mel Stratmeyer, PhD, FDA Center for Devices and Radiological Health

At the time this document was published, the **AAMI Degradation Aspects Related to Biological Testing Working Group** had the following members:

Chair:	Edward Mueller
Members:	David Albert, DPM, North American Science Associates, Inc.
	Brad Anderson, Sims Deltec, Inc.
	James M. Anderson, MD, PhD, Case Western Reserve University
	Robert R. Baier, PhD, PE, Society for Biomaterials
	William C. Bradbury, PhD, Viromed Biosafety Labs
	Jon Cammack, PhD, DABT, Baxter Healthcare
	Eric R. Claussen, PhD, Becton Dickinson
	Charles A. Daniels, MS, PhD, Polymer Diagnostic, Inc.
	Lee Ellis, Boston Scientific Corp.
	Gary Fischman, University of Illinois
	Gloria Frost, PhD, Allegiance Healthcare Corp.
	Donald F. Gibbons, PhD, 3M
	John Grillo, PhD, Abbott Laboratories
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	Scott McNamee, PhD, FDA Center for Devices and Radiological Health

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 10993-14:2001

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

International standard ISO 10993-14 was developed by Technical Committee ISO/TC 194, Biological evaluation of medical devices, to provide guidance on general requirements for the design of tests for identifying and quantifying degradation products from ceramics (including glasses) for the purposes of quantification.

U.S. participation in this ISO TC is organized through the U.S. Technical Advisory Group for ISO/TC 194, administered by the Association for the Advancement of Medical Instrumentation on behalf of the American National Standards Institute. The U.S. made a considerable contribution to this International Standard.

AAMI encourages its committees to harmonize their work with International Standards in the area of biological evaluation of medical devices as much as possible in order to help reduce unnecessary repetition of testing. Upon review of ISO 10993-14, the AAMI Biological Evaluation Committee and the AAMI Degradation Working Group decided to adopt ISO 10993-14 verbatim as a new American National Standard.

AAMI (and ANSI) have adopted other ISO standards. 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 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, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

NOTE—Beginning with the foreword on page ix, this American National Standard is identical to ISO 10993-14:2001.

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 3.

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 part of ISO 10993 may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 10993-14 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 8: Selection and qualification of reference materials for biological tests*

— *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 substance using health-based risk assessment*

— *Part 18: Chemical characterization of materials*

Introduction

This part of ISO 10993 consists of two tests for the biological evaluation of medical devices: an extreme solution test and a simulation solution test. The extreme solution test is developed as a worst case environment and the simulation test is developed as a very common environment.

Degradation products covered by this part of ISO 10993 are formed primarily by dissolution in an aqueous environment. It is recognized that additional biological factors such as enzymes and proteins can alter the rate of degradation. Degradation by such outside factors is not addressed in this part of ISO 10993.

It should be kept in mind that a ceramic device might have extraneous chemical phases and/or elements in extremely minor amounts. While these components might not be named in the original specification, they can often be suspected by the relationship that the material in question has to other materials and the expected history of the material's processing.

Once identified and quantified, the chemical composition of the degradation products form the basis for risk assessment and, if appropriate, biological safety studies according to the principles of ISO 10993-1.

American National Standard ANSI/AAMI/ISO 10993-14:2001

Biological evaluation of medical devices—Part 14: Identification and quantification of degradation products from ceramics

1 Scope

This part of ISO 10993 specifies two methods of obtaining solutions of degradation products from ceramics (including glasses) for the purposes of quantification. It also gives guidance on the analysis of these solutions in order to identify the degradation products. Because of the generalized nature of this part of ISO 10993, product specific standards, when available, that address the degradation product formation under more relevant conditions of use, should be considered first.

This part of ISO 10993 considers only those degradation products generated by a chemical dissociation of ceramics during *in vitro* testing. No degradation induced by mechanical stress or external energy is covered. It is noted that while ISO 6872 and ISO 9693 are chemical degradation tests, they do not address the analysis of degradation products.

Because of the range of ceramics used in medical devices and the different requirements for accuracy and precision of the results, no specific analytical techniques are identified. Further, this part of ISO 10993 provides no specific requirements for acceptable levels of degradation products.

Although these materials are intended for biomedical applications, the biological activity of these degradation products is not addressed in this part of ISO 10993.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 10993. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 10993 are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 3310-1, *Test sieves—Technical requirements and testing—Part 1: Test sieves of metal wire cloth*

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

ISO 5017, *Dense shaped refractory products—Determination of bulk density, apparent porosity, and true porosity*

ISO 6474, *Implants for surgery—Ceramic materials based on high purity alumina*

ISO 6872:1995, *Dental ceramic*

ISO 10993-1, *Biological evaluation of medical devices—Part 1: Evaluation and testing*

ISO 10993-9, *Biological evaluation of medical devices—Part 9: Framework for identification and quantification of potential degradation products*

3 Terms and definitions

For the purposes of this part of ISO 10993, the terms and definitions given in ISO 10993-1 and ISO 10993-9 as well as the following apply.

3.1 ceramics: Typically crystallized materials that are physically nonmetallic and chemically inorganic.

3.2 blank disk: Noncoated circular plate made of the substrate material to be used in the finished device.

3.3 retentate: Undissolved solids remaining in the filter paper after filtration.

3.4 filtrate: Solution which passes through the filter paper.

4 Test procedures

4.1 Principle

This part of ISO 10993 consists of two tests. The first test, an extreme solution test conducted at low pH, serves as a screen for most ceramics for the observation of possible degradation products. The second test simulates a more frequently encountered *in vivo* pH. A flowchart of the decision process for using these test methods is given in Figure 1.

The test methods in this part of ISO 10993 shall be used for ceramics in bulk and granular form as well as ceramic coatings.

When deviations from the recommended test specimen or solution volumes are used, full justification shall be provided.

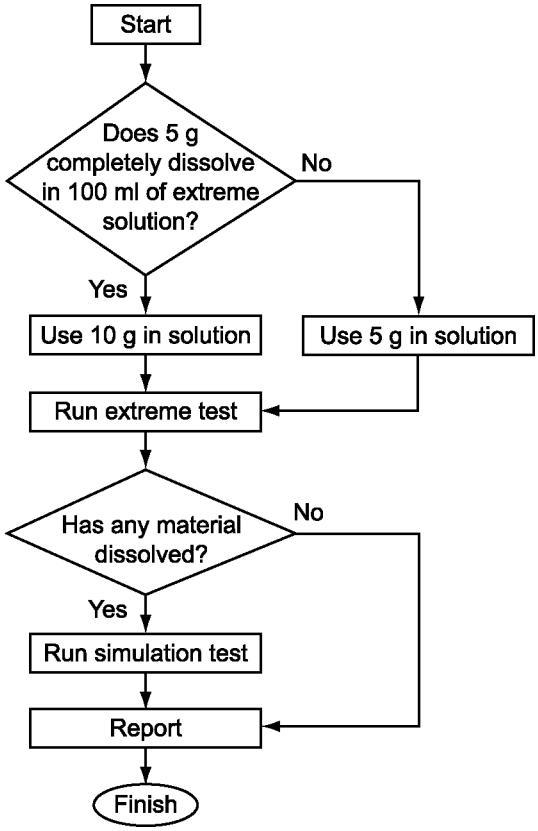

Figure 1—Flowchart of the decision making process for the extreme solution test and the simulation solution tests (see text for details)

4.2 Testing of dental devices

4.2.1 General

This part of ISO 10993 is intended to simulate worst-case exposure to tissue environments. For dental ceramics exposed to the oral cavity (e.g., ceramic veneering material), a more appropriate test environment is given in ISO 6872. However, for dental devices not exposed to the oral cavity, such as dental implant stems, the specifications given in 4.4 of this standard shall apply.

4.2.2 Test methods for dental devices exposed to the oral cavity

For dental devices exposed to the oral cavity, the method given in 8.4 of ISO 6872:1995, 8.4 shall be used as the extreme solution test.

4.2.3 Specimen characterization

The specimen shall be characterized as described in 4.4.4. If the specimen density is greater than 99 % of the theoretical maximum density, and the specimen has an average surface roughness (*Ra*) of less than 5 µm, the surface may be calculated by direct geometrical measurement.

Low surface roughness is required for geometrical measurement in order to avoid grossly underestimating surface area.

4.2.4 Analysis

The filtrate for analysis shall be separated from the retentate as described in 4.4.7.6 to 4.4.7.11.

4.3 General testing techniques

4.3.1 Mass determination

Mass shall be determined using a balance with an accuracy of no less than 0.0005 g. All mass determinations shall have 6 replicates.

4.3.2 Drying techniques

Drying in an oven at a temperature of (100 ± 2) °C shall continue until a mass change of <0.1 % occurs between mass determinations. This is normally accomplished by drying overnight and weighing at 2 h intervals the next day.

4.4 Extreme solution test

4.4.1 Principle

The extreme solution test is a test based on a low pH citric acid buffer solution. The pH value of 3 is defined here as a worst case low-end service environment. For devices exposed to an environment where the pH is lower than 3, an alternative lower pH solution shall be used and justification shall be provided. In the event of a chemical reaction between the extreme solution and the test specimen, an alternative extreme test at similar pH shall be justified and performed.

4.4.2 Application range

This test is applicable to all ceramics. It should be noted that the mechanisms of degradation may not be the same for all materials at low pH as they are at blood pH (approximately pH 7.35 to pH 7.45). Nonetheless, as an extreme condition for the production of possible degradation products, this severe test can serve as a screen for most materials.

It is expected that materials will dissolve up to their solubility limit in the solution. To accelerate the test to the solubility limit endpoint, the test is carried out on a granulated specimen (see 4.4.3.3).

4.4.3 Extreme test sample preparation

4.4.3.1 Specimen configuration

Specimens shall be granulated from a specimen manufactured according to the method intended for material use. If the specimen is a ceramic coating, it shall be removed from the substrate material and granulated to an appropriate size. Under some circumstances (e.g., thin coatings), insufficient ceramic material is available to perform the extreme test. In these cases, a scaled down test may be used in which a sample may be prepared using the ratio of 1 g per 20 mL of test solution. When this is done, the precision and accuracy of the mass determination shall be appropriately scaled and justified in order to accommodate the alternate sample size.

4.4.3.2 Granulation

Granulation shall be accomplished by grinding with a tungsten carbide mortar and pestle.

4.4.3.3 Sizing

The granulated specimen shall pass through a 400 µm screen but be retained on a 315 µm screen using a dry screen method such as that described in ISO 3310-1.

If it is not possible to produce granules of this size (e.g., due to the grinding of a coating), granules of a size smaller than that defined in this part of ISO 10993 shall be used, and the size shall be reported.

NOTE—The use of a particle size smaller than that specified in this clause is likely to lead to increased dissolution and therefore is not expected to reduce the yield of dissolution products and not expected to compromise risk analysis for biological safety.

4.4.3.4 Specimen preparation

The mass of starting material is dependent upon the solubility of the material as determined by the solubility characterization in 4.4.4.3:

— For low solubility granulated material, (5.00 ± 0.05) g shall be used.

— For high solubility granulated material, (10.00 ± 0.05) g shall be used.

4.4.4 Extreme test sample characterization

4.4.4.1 Surface area characterization

The specimen shall be characterized by gas adsorption in accordance with an appropriate method, e.g., such as those given in ASTM D4780.

4.4.4.2 Density

The specimen shall be characterized for density in accordance with ISO 5017.

4.4.4.3 Solubility characterization

From information about the material available from the producer or other sources, the materials shall be characterized as “high” or “low” solubility materials in the following manner.

— Consult Figure 1 for a flowchart of the decision making process.

— If (5.00 ± 0.05) g of the material are expected to totally dissolve in 100 mL during testing as described in 4.4.8, steps 1 through 5, the material shall be considered high solubility.

— If (5.00 ± 0.05) g of the material are not expected to totally dissolve in 100 mL, the material shall be considered low solubility.

— If the information is unavailable, the material shall be considered as high solubility material.

4.4.4.4 Microstructural and X-ray characterization

X-ray diffraction shall be performed with an X-ray diffractometer. The 2Θ resolution and reproducibility shall be better than 0.02°. Microstructure analysis shall conform with that specified in ISO 6474.

4.4.5 Test equipment

4.4.5.1 Test container

A 250 mL polypropylene or high density polyethylene container shall be used. A fresh specimen container shall be used for each test. Glass containers shall not be used since they may contaminate test solutions.

4.4.5.2 Büchner funnel

A Büchner or similar type funnel fitted appropriately to retain undissolved particles shall be used.

4.4.6 Citric acid buffer solution

The buffered citric acid solution shall be freshly prepared and have a pH of 3.0 ± 0.2 at a temperature of (37 ± 1) °C. The solution shall be prepared as follows:

Dissolve 21 g of citric acid monohydrate in 500 mL water (ISO 3696, grade 2) in a 1000 mL volumetric flask. Add 200 mL of 1 mol/L sodium hydroxide solution and dilute to the mark with water (ISO 3696, grade 2). Mix 40.4 mL of this solution with 59.6 mL of 0.1 mol/L hydrochloric acid yielding the buffered citric acid solution.

4.4.7 Test procedure

4.4.7.1 Weigh the container without the top.

4.4.7.2 Weigh the container and specimen. Report the difference in mass between the container with specimen and the container without specimen as the mass of the specimen.

4.4.7.3 Add (100 ± 1) mL of buffered citric acid. Care should be taken to ensure that all of the specimen is in contact with the solution.

4.4.7.4 Place container with specimen in a controlled temperature environment at (37 ± 1) °C for (120 ± 1) h. The container shall be agitated at 2 Hz using a longitudinal or circular movement. If the test specimen is totally dissolved before 120 h, terminate the test and note the time in the test report.

4.4.7.5 Remove the container and specimen and allow them to cool to room temperature.

4.4.7.6 Weigh the filtering medium (e.g., filter paper) to determine its mass without retentate.

4.4.7.7 Remove the specimen via filtration and retain filtrate for analysis. Filtrate should not be stored in glass containers.

4.4.7.8 Rinse the filtering medium and retentate three times with small amounts of water (ISO 3696, grade 2) to remove the citric acid buffer.

4.4.7.9 Dry the specimen and filtering medium with retentate to a constant mass (see 4.3.2).

4.4.7.10 Weigh the filtering medium with retentate. The difference in mass between the filtering medium with and without retentate is the mass of the retentate.

4.4.7.11 The difference between the mass of the specimen and the mass of retentate is the mass of the dissolved material.

4.5 Simulation solution test

4.5.1 Principle

The simulation test is based on a buffer solution of pH 7.4 ± 0.1, as defined in 4.5.6. This will simulate the body's normal pH level.

4.5.2 Application range

This test is applicable to all ceramics.

NOTE—The mechanism of degradation in this test may not be the same as in the extreme test.

4.5.3 Simulation test specimen configuration

4.5.3.1 Coated ceramics

4.5.3.1.1 Blank disks

Test specimens shall be prepared as coatings on blank disks.

Blank disks shall be of diameter of (36 ± 1) mm and thickness of (2 ± 0.1) mm using the same substrate material and preparation techniques as in the finished device.

4.5.3.1.2 Coated disks

Blank disks shall be coated on all sides using coating techniques that are used in the production of the finished device.

NOTE—Because of the reduced surface area to volume ratio, the sensitivity of the test will be reduced using this method.

4.5.3.2 All other ceramics

Test specimens shall be granulated using the methods described in 4.4.3.2 and 4.4.3.3 from a specimen manufactured by methods used to produce the finished device.

4.5.4 Simulation test sample characterization

4.5.4.1 General

For coated samples, surface area, microstructure, and X-ray characterization shall be recorded. For all other ceramics, density, surface area, microstructure, and X-ray characterization shall be recorded.

4.5.4.2 Density

The specimen shall be characterized for density in accordance with ISO 5017.

4.5.4.3 Microstructural and X-ray characterization

X-ray diffraction shall be performed with an X-ray diffractometer. The resolution and reproducibility shall be better than 0.02°. Microstructure analysis shall conform with that specified in ISO 6474.

4.5.4.4 Surface area characterization

The specimen shall be characterized by gas adsorption in accordance with an appropriate method, e.g., such as those given in ASTM D4780.

4.5.5 Test equipment

4.5.5.1 Test container

A 250 mL polypropylene or high density polyethylene container shall be used. A fresh specimen container shall be used for each test. Glass containers shall not be used since they may contaminate test solutions.

4.5.5.2 Büchner funnel

A Büchner or similar type funnel fitted appropriately to retain undissolved particles shall be used.

4.5.6 Buffer solution

The solution shall be freshly prepared TRIS-HCI buffer. It shall be prepared by dissolving 13.25 g of tris(hydroxymethyl)aminomethane in 500 mL of water (ISO 3696, grade 2). Adjust the pH with an appropriate amount of 1 mol/L hydrochloric acid to pH 7.4 ± 0.1 at temperature of (37 ± 1) °C. Make up to 1000 mL with water (ISO 3696, grade 2).

4.5.7 Coated disk test procedure

4.5.7.1 General

Both the coated and uncoated disks are exposed to the simulation test solution to determine whether degradation products are generated under simulated test conditions.

4.5.7.2 Blank disk test

4.5.7.2.1 Place blank disk in test container for the exposure test.

4.5.7.2.2 Add (100 ± 1) mL of buffer solution to the container with the blank disk. Care should be taken to ensure that the entire blank disk is in contact with the solution.

4.5.7.2.3 Maintain the container with blank disk at (37 ± 1) °C in a controlled temperature chamber for (120 ± 1) h. The container shall be agitated at 2 Hz using longitudinal or circular movement.

4.5.7.2.4 Remove the container with specimen and allow them to reach room temperature.

4.5.7.2.5 Filter the solution and retain the filtrate for analysis (see clause 5).

4.5.7.3 Coated disk test

4.5.7.3.1 Determine the mass of the ceramic coating by subtracting the mass of the coated disk from the mass of the blank disk for each test specimen.

Each disk shall be weighed before and after coating to determine the mass of the coating.

4.5.7.3.2 Place coated disk in a test container for the exposure test.

4.5.7.3.3 Add (100 ± 1) mL of buffer solution to the container with the coated disk. Care should be taken to ensure that the entire coated disk is in contact with the solution.

4.5.7.3.4 Maintain the container with coated disk at (37 ± 1) °C in a controlled temperature chamber for (120 ± 1) h. The container shall be agitated at 2 Hz using longitudinal or circular movement.

4.5.7.3.5 Remove the container with specimen and allow them to cool to room temperature.

4.5.7.3.6 Weigh the filtering medium (e.g., filter paper).

4.5.7.3.7 Filter the solution and retain filtrate for analysis (see clause 5).

4.5.7.3.8 Rinse the filtering medium and retentate three times with small amounts of water (ISO 3696, grade 2).

4.5.7.3.9 Dry the coated disk and filtering medium with retentate to a constant mass.

4.5.7.3.10 Weigh filtering medium with retentate. The difference in mass between the filtering medium with and without retentate is the mass of the retentate.

4.5.7.3.11 The difference between the original mass of the coating and the mass of the retentate is the mass of the materials dissolved.

4.5.8 Test procedure (all other ceramics)

4.5.8.1 Weigh the container without the top.

4.5.8.2 Weigh the container and specimen. Report the difference in mass between the container with specimen and the container without specimen as the mass of the specimen.

4.5.8.3 Add (100 ± 1) mL of buffer solution. Care should be taken to ensure that the entire specimen is in contact with the solution.

4.5.8.4 Place the container with the specimen in a controlled temperature environment at (37 ± 1) °C for (120 ± 1) h. The container shall be agitated at 2 Hz using a longitudinal or circular movement. If the test specimen is totally dissolved before 120 h, terminate the test and note the time in the test report.

4.5.8.5 Remove the container and specimen and allow them to cool to room temperature.

4.5.8.6 Weigh the filtering medium (e.g., filter paper) to determine its mass without retentate.

4.5.8.7 Remove the specimen via filtration and retain the filtrate for analysis. Filtrate should not be stored in glass containers.

4.5.8.8 Rinse the filtering medium and retentate three times with small amounts of water (ISO 3696, grade 2).

4.5.8.9 Dry the specimen and filtering medium with retentate to a constant mass (see 4.3.2).

4.5.8.10 Weigh the filtering medium with retentate. The difference in mass between the filtering medium with and without retentate is the mass of the retentate.

4.5.8.11 The difference between the mass of the specimen and the mass of retentate is the mass of the material dissolved.

5 Analysis of filtrate

5.1 General

After each experiment a qualitative and quantitative analysis of the solution shall be performed in triplicate.

The number of test methods, practices, accuracy, and precision on analytic techniques is large and changeable. Samples should be analyzed using Inductively Coupled Plasma Spectroscopy (ICP), if possible. Other tests, such as Atomic Absorption Spectroscopy (AAS), while less useful, may provide information at the desired concentration levels.

5.2 Choice of chemicals or elements to be analyzed

The chemicals or elements to be analyzed in the filtrate solutions should include both chemical constituents known to exist in the material and possible impurities such as small amounts of elements that are due to commonly known substitutions in the raw material and possible addition to the material during processing. The volume of filtrate should be made up to a fixed volume of 125 mL or 250 mL, depending on the starting volume. Larger volumes should be justified.

5.3 Sensitivity of the analysis method

Analysis methods applied shall be of adequate sensitivity (e.g., at least 10^{-6} by atomic absorption or mass spectroscopy). Record only compositional constituents that have been detected above the limits of quantification. Hazardous materials shall be recorded in accordance with the appropriate International Standards, if available.

6 Test report

The test report shall include all data identified in accordance with this part of ISO 10993 during characterization, testing, and analysis:

a) Test institution;

b) Date of measurement;

c) A statement that this test was conducted in accordance with ISO 10993-14 and describing any deviations from the standard protocols, with justifications;

d) Description of test material including batch or lot number;

e) Type of test:

   1) High solubility,

   2) Low solubility,

   3) Extreme (intra-oral),

   4) Extreme (10993-14),

   5) Simulated;

f) Surface area and method;

g) Sample density, microstructure, and X-ray diffraction pattern;

h) Duration of test;

i) Test results:

   1) Specimen mass,

   2) Volume of solution added,

   3) Drying time,

   4) Mass of retentate,

   5) Mass of material dissolved,

   6) Volume of filtrate,

   7) Chemical analysis and method (for coated specimens, the degradation products from the ceramic are differentiated from the substrate by comparing the analysis of filtrate of the blank disk with that from the coated disk),

   8) For each element identified in filtrate, calculate mass dissolved per total surface area.

Bibliography

[1] ISO 9693, *Metal-ceramic dental restorative systems.*

[2] ISO 10993-12, *Biological evaluation of medical devices—Part 12: Sample preparation and reference materials*.

[3] ISO 10993-16, *Biological evaluation of medical devices—Part 16: Toxicokinetic study design for degradation products and leachables*.

[4] ISO/DIS 10993-17, *Biological evaluation of medical devices—Part 17: Establishment of allowable limits for leachable substances using health-based risk assessment.*

[5] ASTM C92, *Standard Test Methods for Sieve Analysis and Water Content of Refractory Materials*.

[6] ASTM D4780, *Standard Test Method for Determination of Low Surface Area of Catalysts by Multipoint Krypton Adsorption*.