List of Titles

American National Standard

ANSI/AAMI/ISO 10993-15:2000

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

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 10993-15:2000

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

Approved 16 October 2000 by
Association for the Advancement of Medical Instrumentation

Approved 1 November 2000 by
American National Standards Institute, Inc.

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

Keywords: metals, alloys, degradation, medical devices, biological evaluation

List of Titles

AAMI Standard

This Association for the Advancement of Medical Instrumentation (AAMI) standard implies a consensus of those substantially concerned with its scope and provisions. The existence of an AAMI standard does not in any respect preclude anyone, whether they have approved the standard or not, from manufacturing, marketing, purchasing, or using products, processes, or procedures not conforming to the standard. AAMI standards are subject to periodic review, and users are cautioned to obtain the latest editions.

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All AAMI standards, recommended practices, technical information reports, and other types of technical documents developed by AAMI are *voluntary*, and their application is solely within the discretion and professional judgment of the user of the document. Occasionally, voluntary technical documents are adopted by government regulatory agencies or procurement authorities, in which case the adopting agency is responsible for enforcement of its rules and regulations.

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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 60601-2-21:1994 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 VP20:1994	Major technical variations
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 10993-15:2000	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
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

[1)] FDIS approved; being prepared for publication.

International designation	U.S. designation	Equivalency
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

Committee representation

Association for the Advancement of Medical Instrumentation

Biological Evaluation Committee

The adoption of ISO 10993-15:2000 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 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, ISO/TC 194/WG 2, *Degradation aspects related to biological testing*.

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, Cobe Laboratories, Inc.
	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
	Daniel E. McLain, PhD, Becton Dickinson
	Edward Mueller, Consultant. Annapolis, MD
	Barry F. Page, Consultant, Garner, NC
	Harold Stanley, DDS, American Dental Association
	Paul J. Upman, North American Science Associates, Inc.
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 Working Group** had the following members:

Chair:	Edward Mueller
Members:	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
	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
	Emanuel Horowitz, PhD, Johns Hopkins University
	Daniel E. McLain, PhD, Becton Dickinson
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	Sumner A. Barenberg, PhD, Bernard Technologies
	John Becker, Allegiance Healthcare Corp.

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 10993-15:2000

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 10993-15 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 finished metallic medical devices ready for clinical use.

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 10993-15, the AAMI Biological Evaluation Committee and the AAMI Degradation Working Group decided to adopt ISO 10993-15 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. For the standard 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 10993-15:2000.

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 10993-15 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 substances using health-based risk assessment*

— *Part 18: Chemical characterization of materials*

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

Annex C forms a normative part of this part of ISO 10993. Annexes A and B are for information only.

Introduction

One of the potential health hazards resulting from medical devices may 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 behavior 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 and 150×10^{-3} mol. A range of organic molecules such as proteins, enzymes, and lipoproteins is also present, but their concentrations may 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–protein 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 may 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.

American National Standard ANSI/AAMI/ISO 10993-15:2000

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

1 Scope

This part of ISO 10993 provides guidance on general requirements for the design of tests for identifying and quantifying degradation products from finished metallic medical devices or corresponding material samples finished as ready for clinical use. It is applicable only to those degradation products generated by chemical alteration of the finished metallic device in an *in vitro* accelerated degradation test. Because of the accelerated nature of these tests, the test results may not reflect the implant or material behavior in the body. The described chemical methodologies are a means to generate degradation products for further assessments.

This part of ISO 10993 is not applicable to degradation products induced by applied mechanical stress.

NOTE—Mechanically induced degradation, such as wear, may be covered in the appropriate product-specific standard. Where product-group standards provide applicable product-specific methodologies for the identification and quantification of degradation products, those standards should be considered.

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 ($< 10^{-6}$) contained in the specific metal or alloy is not addressed in this part of ISO 10993, nor are specific requirements for acceptable levels of degradation products provided in this part of ISO 10993.

This part of ISO 10993 does not address 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 normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard 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 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*.

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

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

ISO 10993-13, *Biological evaluation of medical devices—Part 13: Identification and quantification of degradation products from polymeric medical devices*.

ISO 10993-14, *Biological evaluation of medical devices—Part 14: Identification and quantification of degradation products from ceramics*.

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

3 Terms and definitions

For the purposes of this part of ISO 10993, the terms and definitions given in ISO 8044, ISO 10993-1, ISO 10993-9, ISO 10993-12, and the following apply.

3.1 alloy: Material composed of a metallic element with one or more addition(s) of other metallic and/or non-metallic elements.

3.2 electrolyte: Solution containing ions with the capacity to conduct electric current.

3.3 open-circuit potential: Potential of an electrode measured with respect to a reference electrode or another electrode when no current flows to or from it.

3.4 passive limit potential E_a: Electrode potential of the positive limit of the passive range (see Figure 1).

3.5 breakdown potential E_p: Critical electrode potential above which localized or transpassive corrosion is found to occur (see Figure 1).

4 Degradation test methods

4.1 General

To identify and quantify degradation products from metals and alloys in medical devices, a combination of two procedures is described. The choice of test procedure shall be justified according to the function of the medical device.

The first procedure described is a combination of a potentiodynamic test and a potentiostatic test. The second procedure described is an immersion test.

The potentiodynamic test is used to determine the general electrochemical behavior of the material under consideration and to determine certain specific points (E_a and E_p) on the potential/current density curve.

The immersion test is used to chemically degrade the test material to generate degradation products to be analyzed.

If there is the possibility of the loss of a coating from a metallic substrate due to degradation, the potential degradation products from the substrate material shall be considered, as well as the coating itself. In addition, if a metallic substrate coated with a non-metallic material is to be tested, the requirements of ISO 10993-13 and/or ISO 10993-14 shall be considered in order to determine the potential degradation products of the coating.

The identified and quantified degradation products form the basis for evaluation of biological response and, if appropriate, toxicokinetic studies in accordance with ISO 10993-16.

4.2 Prerequisites

The rates of electrochemical degradation reactions are sensitive to small variations in test conditions, instrumentation, sample conditions, and preparation. Therefore, electrochemical degradation testing shall be carried out in an appropriately equipped laboratory by experienced and qualified personnel. This includes proper maintenance and calibration of the test equipment. The methods and operating conditions of the equipment shall also be validated.

NOTE—Fulfillment of electrochemical test conditions for stability, warm-up time, etc., can be demonstrated by conformance to [1].

5 Reagent and sample preparation

5.1 Sample documentation

The general composition of the material(s) under test shall be documented.

5.2 Test solution (electrolyte)

The test solution (electrolyte) to be used shall be appropriate for the intended use of the medical device. All chemicals shall be of analytical grade and dissolved in water of grade 2 in accordance with ISO 3696.

The first choice for the electrolyte shall be an aqueous solution of 0.9 % sodium chloride.

NOTE—Other electrolytes may be used, such as artificial saliva or artificial plasma. Examples of composition are given in annex C.

In the test report, the choice of electrolyte shall be justified. If other than an aqueous solution of 0.9 % sodium chloride is used, the pH of the electrolyte shall be specified.

5.3 Preparation of test samples

5.3.1 Test samples

The sensitivity of chemical degradation testing is related to variation in material composition, to material processing, and to surface-finishing procedures. The sampling procedure, sample shape, and surface preparation are critical. The samples shall be representative of the finished devices.

5.3.2 Sampling

For each chemical test, at least two test samples shall be prepared as specified in ISO 10993-12. If substantial deviations in the test results are found, the reasons for the deviation shall be determined, and more samples shall be tested.

If the metallic sample has anisotropic properties due to manufacturing conditions, tests involving single-surface exposure should include samples cut parallel to both the transverse and longitudinal manufacturing directions.

5.3.3 Sample shape

Standard samples, either circular- or rectangular-section bars or flat coupons, or one single free surface, may be used for degradation testing if they are prepared in a manner comparable to the representative medical device. Samples of actual device components may be of any shape and condition; however, the testing shall be carried out under well-controlled conditions which shall be reported.

The surface area of the sample exposed to the electrolyte shall be determined to an accuracy of better than 10 % of the total geometrical area to assure an accurate and repeatable determination of the degradation rates.

5.3.4 Sample surface condition

Since the surface condition of a material may affect its electrochemical behavior, the surface condition of the test sample shall be identical to the finished medical device and shall be described in the test report. For comparing test results of different materials, the surface condition of the test samples shall be the same.

6 Electrochemical tests

6.1 Apparatus

6.1.1 Test cells of borosilicate glass, in appropriate sizes, in accordance with ISO 3585, with a means of controlling the bath temperature within ± 1 °C.

6.1.2 Scanning potentiostat with a potential range ± 2 V and a current output range from 10^{-9} A to 10^{-1} A.

6.1.3 Potential-measuring instrument with a high input impedance (>10^{11} Ω) and a sensitivity and accuracy to detect a change of 1 mV over a potential range between ± 2 V.

6.1.4 Current-measuring instrument capable of measuring a current to ± 1 % of the absolute value over a current range between 10^{-9} A to 10^{-1} A.

6.1.5 Working electrode (test sample).

6.1.6 Counter-electrode(s) such as platinum (grid, plate, or wire) or vitreous carbon with an area at least 10 times that of the working electrode.

6.1.7 Reference electrode.

6.1.8 pH-meter with a sensitivity of ± 0.1.

A schematic diagram of the electrochemical measurement circuit which may be used as a system with variable potential is given in annex A.

A schematic drawing of an electrolytic cell is given in annex B.

6.2 Sample preparation

Mount the test sample in a watertight electrode holder so that only the test surface is in contact with the electrolyte. Take care to avoid the creation of conditions where crevice corrosion can occur due the formation of a crevice between the mounting and the sample. Before testing, clean the specimen ultrasonically for 10 min to 15 min in ethanol, carefully rinse with water of grade 2 in accordance with ISO 3696, and immediately transfer into the test cell.

6.3 Test conditions

Fill the test cell with the test solution (electrolyte). If the electrochemical behavior is temperature sensitive in the range of 10 °C to 50 °C, maintain the electrolyte cell at (37 ± 1) °C. Reduce the oxygen level in the electrolyte by bubbling oxygen-free nitrogen or argon at a rate of approximately 100 $cm^3 \cdot min^{-1}$ for not less than 30 min prior to the start of the test. The electrolyte shall be agitated either by the bubbling gas or mechanical means to avoid concentration gradients. If gas agitation is used, take care not to have any gas bubbles adhering to the active test surface.

Magnetic stirrers often interfere with electrochemical test cells. If they are used, their effect on the test cell shall be determined as part of the validation of test equipment (see 4.2).

6.4 Potentiodynamic measurements

Measure the open-circuit potential not less than 2 h after the immersion of the working electrode. This potential shall be the starting potential for potentiodynamic measurements. The sweep rate shall be 1.0 $mV \cdot s^{-1}$, except in tests where the sweep rate has little effect, where the test may be accelerated by increasing the sweep rate to 10 $mV \cdot s^{-1}$. Record the potential/current density curve up to a maximum of 2000 mV or a maximum current density of 1.0 $mA \cdot cm^{-2}$, whichever comes first, to evaluate the transpassive range of the sample (see Figure 1). To ensure consistency, reverse the scan and continue back at least to the open-circuit potential. Then repeat the test back to 2000 mV or 1.0 $mA \cdot cm^{-2}$. If the curves are not reproducible, then continue cycling 5 to 10 times. If consistent potential/current density curves are not achieved after 5 to 10 cycles, investigate possible causes such as test set-up, electrode function, innate material properties, etc. The log current density/potential curves should also be recorded (see Figure 2). Record the breakdown potential (E_p) from the last cycle taken (see Figure 1).

Noble metals may behave differently from passivating metals during an electrochemical test. Therefore, take care in determining the breakdown potential (E_p) for different metal systems.

6.5 Potentiostatic measurements

This method permits qualitative and quantitative determination of degradation products which might be dissolved in the electrolyte.

Hold a new test sample at a constant electrode potential during the test time, and record the current density/time curve. The potential used to determine the degradation products shall be the breakdown potential (E_p) + 50 mV. Depending upon the material studied, the polarization duration shall be either 1 h or 5 h and shall be reported. Measure and record the volume of the electrolyte for use in future calculations.

7 Immersion test

7.1 Apparatus

7.1.1 Test cells of borosilicate glass, of appropriate sizes, in accordance with ISO 3585, with a means of controlling the bath temperature within ± 1 °C.

7.1.2 pH-meter with a sensitivity of ± 0.1.

7.2 Sample preparation

The test sample shall be placed in a separate glass container. The size of the glass container should be selected so that an electrolyte volume of less than 1 ml/cm^2 of sample surface shall completely cover the sample(s).

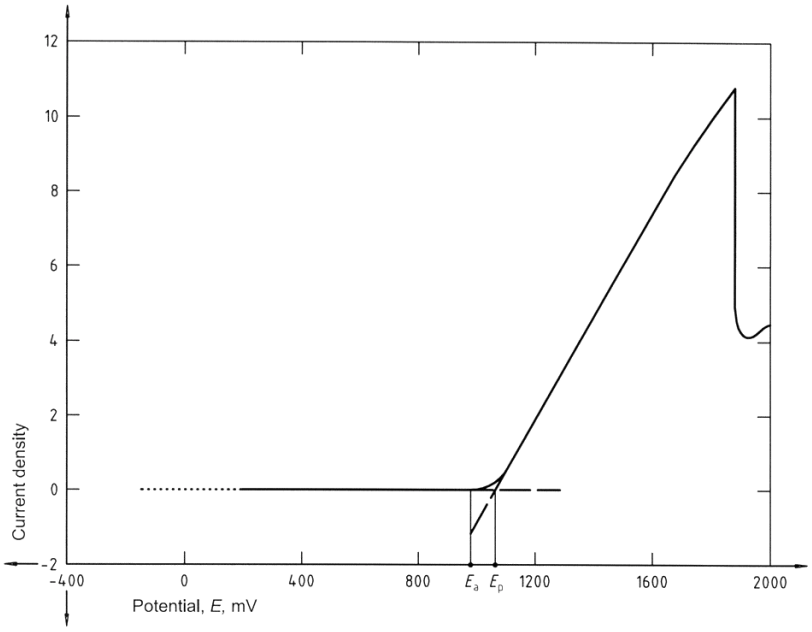
Do not compromise the data through biological contamination. For example, the electrolyte may need to be prepared under aseptic conditions.

NOTE—The surface area and volume of electrolyte should be sufficient for the intended method of analysis (see 8).

Care should be taken such that the samples do not touch the glass surface except in a minimum support line or point. If the test sample is small, the proper surface area/volume ratio may not be attainable with a single test sample. Therefore, if the test sample must be made up of two or more pieces, the pieces shall not touch each other.

7.3 Immersion test procedure

Measure the pH of the electrolyte containing the test sample at the start of the test. Then tightly close the test cell to prevent evaporation and maintain at (37 ± 1) °C for (7 ± 0.1) days. Then remove the sample and measure the pH of the residual electrolyte.



NOTE—E_p is determined by extrapolation of the linear part of the oxidation curve to zero current density.

Figure 1—Plot of current density versus potential, showing the start of corrosion current at E_a and breakdown potential, E_p

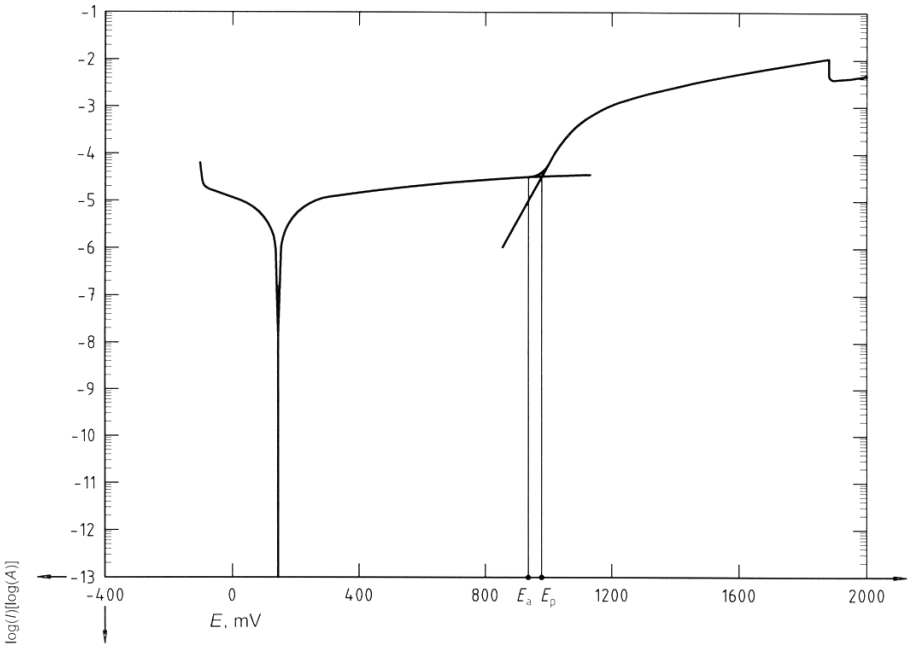


Figure 2—Log current density versus potential plot showing the breakdown potential, E_p, at the inflection point of the curve

8 Analysis

Observe and record the condition of the test sample under low-power microscopy (> 50 ×) and report any significant changes to the surface. More detailed analysis of the surface may be undertaken if appropriate.

After each experiment, perform a qualitative and quantitative analysis of the electrolyte using a method of adequate sensitivity (at least 1.0×10^{6} by atomic absorption, ICP, or mass spectroscopy, for example). Report compositional constituents detected above the limits of quantification. If potentially biologically hazardous constituents are identified but not quantified, other analytical analyses may be necessary. In addition, any deposits on the counter-electrode shall be accounted for in the analysis.

9 Test report

The test report shall contain at least the following details:

a) complete identification of the test sample, including the chemical composition;

b) ratio of the exposed surface area of the sample to the volume of the electrolyte;

c) composition and pH (with an uncertainty of ± 0.1) of the electrolyte and a description of the natural or reference electrode for the electrochemical test;

d) composition and initial and final pH of the electrolyte for the immersion test;

e) temperature of the electrolyte;

f) current density vs. potential curve(s), optionally the log (current density) vs. potential curve for comparison;

g) open-circuit potential;

h) breakdown potential E_p and the current density at the breakdown potential;

i) sweep rate;

j) current density vs. time curve(s) and total test time;

k) brief comments on the curves (e.g., hysteresis, peaks);

l) description of any significant changes of the sample surface and/or of the electrolyte;

m) results of analysis of degradation elements in the electrolyte, including degradation rate, reported in micrograms per square centimeter per hour (μg/cm^2/h) for the electrostatic test or per 7 days (μg/cm^2/7 days) for the immersion test;

n) method of chemical analysis of electrolyte;

o) type of reference electrode [all potentials should be referenced to the normal hydrogen electrode (NHE)];

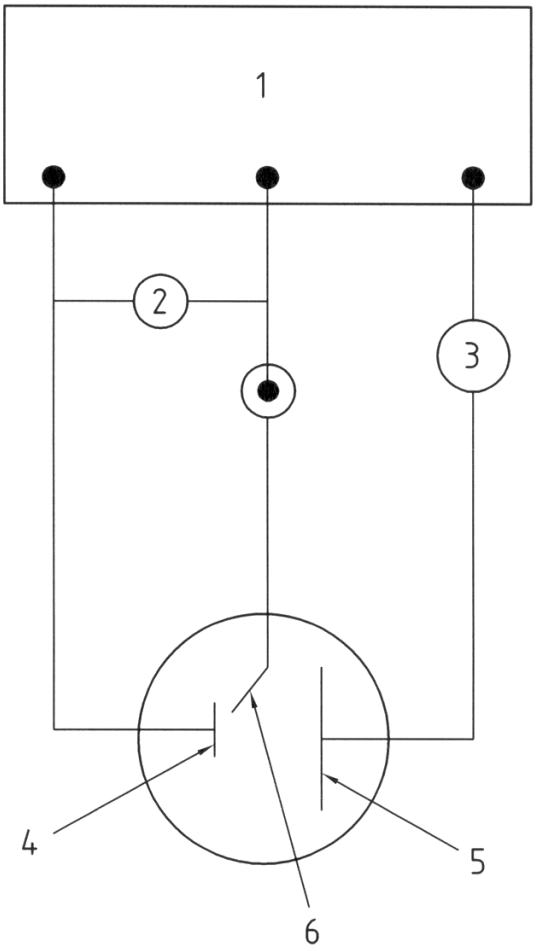
p) name of investigator;

q) date(s) of investigation;

r) signature of the investigator.

Annex A
(informative)

Schematic diagram of the electrochemical measuring circuit

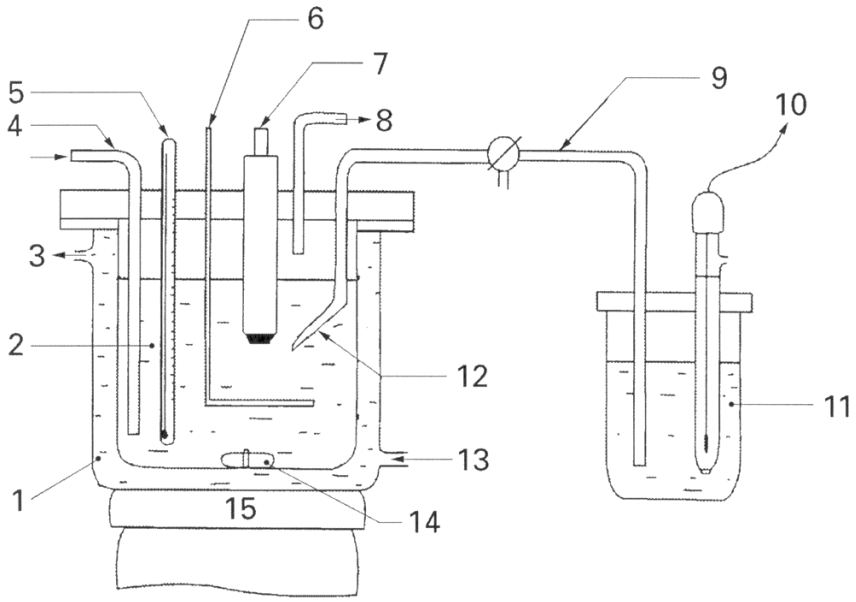


Key
1 Potentiostat
2 Potential measurement
3 Current measurement
4 Working electrode
5 Counter-electrode
6 Reference electrode

Figure A.1—Schematic diagram of the electrochemical measuring circuit

Annex B
(informative)

Schematic drawing of an electrolytic cell



Key

1	Constant-temperature cell	9	Electrolytic bridge
2	Electrolyte	10	Reference electrode
3	Water outlet	11	Saturated KCl solution
4	Gas inlet	12	Luggin capillary
5	Thermometer	13	Constant-temperature water inlet
6	Counter-electrode	14	Magnetic stirring bar
7	Working electrode	15	Magnetic stirrer
8	Gas outlet		

Figure B.1—Schematic drawing of an electrolytic cell

Annex C
(normative)

Electrolytes for the electrochemical tests

C.1 General

All chemicals shall be of analytical grade and dissolved in high purity water, grade 2 in accordance with ISO 3696. Care shall be taken to avoid precipitation when preparing these solutions.

C.2 Isotonic aqueous solution of 0.9 % sodium chloride

C.3 Artificial saliva (see [2])

Na_2HPO_4	0.260 g/L
NaCl	0.700 g/L
KSCN	0.330 g/L
KH_2PO_4	0.200 g/L
$NaHCO_3$	1.500 g/L
KCl	1.200 g/L

C.4 Artificial plasma (see [2])

NaCl	6.800 g/L
$CaCl_2$	0.200 g/L
KCl	0.400 g/L
$MgSO_4$	0.100 g/L
$NaHCO_3$	2.200 g/L
Na_2HPO_4	0.126 g/L
NaH_2PO_4	0.026 g/L

Bibliography

[1] ASTM G 5-94, Reference Test Method for Making Potentiostatic and Potentiodynamic Anodic Polarization Measurements.

[2] AFNOR NF 91-141G 5-94, Biodegradability of dental metal alloys—Standardization of electrochemical test.

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

[4] ISO 10271, Dental metallic materials—Corrosion test methods.