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Biological evaluation of medical devices —

Part 14: Identification and quantification of degradation products from ceramics

Évaluation biologique des dispositifs médicaux —
Partie 14: Identification et quantification des produits de dégradation des céramiques

Reference number
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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 substances 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. Whilst 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.

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 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 cover 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 disc
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 described 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.

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 part of ISO 10993 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 shall be used as the extreme solution test.

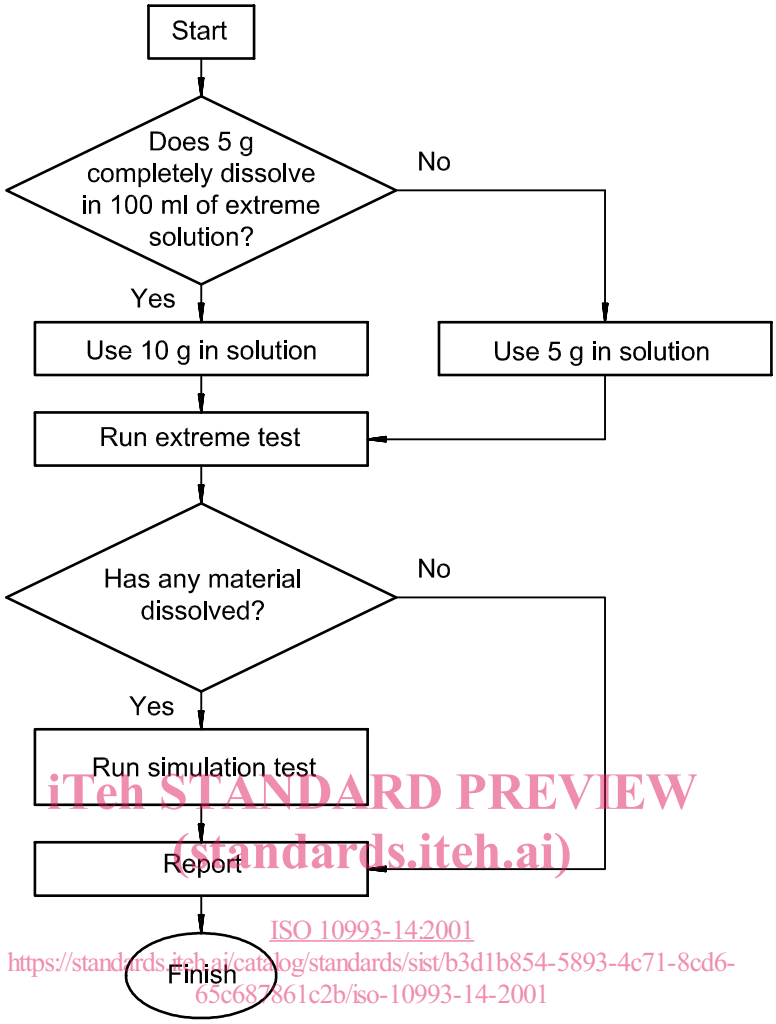

Figure 1 — Flowchart of the decision-making process for the extreme solution test and the simulation solution tests (see text for details)

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 area may be calculated by direct geometrical measurement.

Low surface roughness is required for geometrical measurement in order to avoid grossly underestimating the 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 0,000 5 g. All mass determinations shall have 6 replicates.