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BS EN ISO 10993-12:2012



BSI Standards Publication

Biological evaluation of medical devices

Part 12: Sample preparation
and reference materials

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This British Standard is the UK implementation of EN ISO 10993-12:2012. It supersedes BS EN ISO 10993-12:2009, which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/194, Biological evaluation of medical devices.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

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English Version

Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2012)

Évaluation biologique des dispositifs médicaux - Partie 12:
Préparation des échantillons et matériaux de référence
(ISO 10993-12:2012)

Biologische Beurteilung von Medizinprodukten - Teil 12:
Probenvorbereitung und Referenzmaterialien (ISO 10993-
12:2012)

This European Standard was approved by CEN on 30 June 2012.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.



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Management Centre: Avenue Marnix 17, B-1000 Brussels

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Foreword

This document (EN ISO 10993-12:2012) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 "Biological evaluation of medical devices" the secretariat of which is held by NEN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by January 2013, and conflicting national standards shall be withdrawn at the latest by January 2013.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN ISO 10993-12:2009.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directives.

For relationship with EU Directives, see informative Annex ZA and ZB, which are an integral parts of this document.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 10993-12:2012 has been approved by CEN as a EN ISO 10993-12:2012 without any modification.

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Annex ZA (informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on medical devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

Clauses of this European Standard	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10, 11	7.2 first sentence only	This standard provides a means of preparing samples to assess conformity with this part of this ER in conjunction with other relevant parts of EN ISO 10993 for the design and manufacture of medical devices. Packaging is not covered.
4, 5, 6, 7, 8, 9, 10, 11	7.5 first paragraph only	This standard provides a means of preparing samples of medical devices to assess conformity with this part of this ER in conjunction with other relevant parts of EN ISO 10993.

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

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Annex ZB (informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 90/385/EEC on active implantable medical devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 90/385/EEC on active implantable medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZB.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

**Table ZB.1 — Correspondence between this European Standard
and Directive 90/385/EEC on active implantable medical devices**

Clauses of this European Standard	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10, 11	9 (first and second indents only)	This standard provides a means of preparing samples of medical devices to assess conformity with these parts of this ER in conjunction with other relevant parts of EN ISO 10993.

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

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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 2.

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

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 10993-12 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This fourth edition cancels and replaces the third edition (ISO 10993-12:2007), which has been technically revised.

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

- *Part 1: Evaluation and testing within a risk management process*
- *Part 2: Animal welfare requirements*
- *Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*
- *Part 4: Selection of tests for interactions with blood*
- *Part 5: Tests for in vitro cytotoxicity*
- *Part 6: Tests for local effects after implantation*
- *Part 7: Ethylene oxide sterilization residuals*
- *Part 9: Framework for identification and quantification of potential degradation products*
- *Part 10: Tests for irritation and skin sensitization*
- *Part 11: Tests for systemic toxicity*
- *Part 12: Sample preparation and reference materials*
- *Part 13: Identification and quantification of degradation products from polymeric medical devices*
- *Part 14: Identification and quantification of degradation products from ceramics*
- *Part 15: Identification and quantification of degradation products from metals and alloys*
- *Part 16: Toxicokinetic study design for degradation products and leachables*
- *Part 17: Establishment of allowable limits for leachable substances*
- *Part 18: Chemical characterization of materials*
- *Part 19: Physico-chemical, morphological and topographical characterization of materials* [Technical Specification]
- *Part 20: Principles and methods for immunotoxicology testing of medical devices* [Technical Specification]

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Introduction

This part of ISO 10993 specifies methods of sample preparation and provides requirements and guidance for the selection of reference materials for the biological evaluation of medical devices.

It is important that sample preparation methods be appropriate for both the biological evaluation methods and the materials being evaluated. Each biological test method requires the selection of materials, extraction solvents and conditions.

This part of ISO 10993 is based on existing national and international specifications, regulations and standards wherever possible. It is periodically reviewed and revised.

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1 Scope

This part of ISO 10993 specifies requirements and gives guidance on the procedures to be followed in the preparation of samples and the selection of reference materials for medical device testing in biological systems in accordance with one or more parts of ISO 10993. Specifically, this part of ISO 10993 addresses the following:

- test sample selection;
- selection of representative portions from a device;
- test sample preparation;
- experimental controls;
- selection of, and requirements, for reference materials;
- preparation of extracts.

This part of ISO 10993 is not applicable to live cells, but can be relevant to the material or device components of combination products containing live cells.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10993 (all parts), *Biological evaluation of medical devices*

ISO 14971, *Medical devices — Application of risk management to medical devices*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1

accelerated extraction

extraction that provides a measure of the leachable or extractable materials of the device or material, using conditions that shorten the time for leaching of the substances into the extraction vehicle but do not result in a chemical change of the substances being extracted

EXAMPLE Elevated temperature, agitation, changing of the extraction vehicle.

3.2

blank

extraction vehicle not containing the test material, which is retained in a vessel identical to that holding the test sample and subjected to conditions identical to the ones the test sample is subjected to during its extraction

NOTE The purpose of the blank is to evaluate possible confounding effects due to the extraction vessel, extraction vehicle and extraction process.