

Biological evaluation of medical devices

**Part 17: Establishment of allowable
limits for leachable substances (ISO
10993-17:2002)**

ICS 11.100.20

National foreword

This British Standard is the UK implementation of EN ISO 10993-17:2009. It is identical to ISO 10993-17:2002. It supersedes BS EN ISO 10993-17:2002 which is withdrawn.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.

Compliance with a British Standard cannot confer immunity from legal obligations.

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**Biological evaluation of medical devices - Part 17: Establishment
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17:2002)**

Évaluation biologique des dispositifs médicaux - Partie 17:
Établissement des limites admissibles des substances
relargables (ISO 10993-17:2002)

Biologische Beurteilung von Medizinprodukten - Teil 17:
Nachweis zulässiger Grenzwerte für herauslösbare
Bestandteile (ISO 10993-17:2002)

This European Standard was approved by CEN on 12 April 2009.

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 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 Management Centre has the same status as the official versions.

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



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COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Foreword

The text of ISO 10993-17:2002 has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" of the International Organization for Standardization (ISO) and has been taken over as EN ISO 10993-17:2009 by 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 October 2009, and conflicting national standards shall be withdrawn at the latest by March 2010.

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 10993-17:2002.

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 93/42/EEC on Medical Devices and 90/385/EEC on Active Implantable Medical Devices.

For relationship with the EU Directives, see informative Annexes ZA and ZB, which is an integral part 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, Cyprus, Czech Republic, Denmark, Estonia, Finland, 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 10993-17:2002 has been approved by CEN as a EN ISO 10993-17:2009 without any modification.

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 Communities 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 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 — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	Annex I: 7.1, 7.2, 7.5	

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

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 Communities 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 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 — Correspondence between this European Standard and Directive 90/385/EEC on active implantable medical devices

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	Annex I : 9	

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 3.

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 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.

ISO 10993-17 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*

— *Part 18: Chemical characterization of materials*

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

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

Introduction

The determination of the suitability of a medical device for a particular use involves balancing any identified risks with the clinical benefit to the patient associated with its use. Among the risks to be considered are those arising from exposure to leachable substances arising from medical devices.

Risks associated with exposure to hazardous leachable substances are managed by identifying the leachable substances, quantifying the associated risks and limiting exposure within tolerable levels. This part of ISO 10993 provides a method by which maximum tolerable levels can be calculated from available data on health risks. Allowable limits may be based upon health risks that can be systemic or local, immediate or delayed, and range in severity from minor localized adverse effects to life-threatening risks. These allowable limits are intended to be derived, using this part of ISO 10993, by toxicologists or other knowledgeable and experienced individuals, capable of making informed decisions based upon scientific data and a knowledge of medical devices.

The allowable limits derived may be used by anyone. In addition to use by ISO, other standards-developing organizations, government agencies, regulatory bodies, and other users for setting allowable limits as standards or regulations, manufacturers and processors may use the allowable limits derived to optimize processes and aid in the choice of materials in order to protect patient health. Where risks associated with exposure to particular leachable substances are unacceptable, this part of ISO 10993 can be used to qualify alternative materials or processes.

Biological evaluation of medical devices —

Part 17:

Establishment of allowable limits for leachable substances

1 Scope

This part of ISO 10993 specifies a method for the determination of allowable limits for substances leachable from medical devices. It is intended for use in deriving standards and estimating appropriate limits where standards do not exist. It describes a systematic process through which identified risks arising from toxicologically hazardous substances present in medical devices can be quantified.

This part of ISO 10993 is not applicable to devices that have no patient contact (e.g. *in vitro* diagnostic devices).

Exposure to a particular chemical substance may arise from sources other than the device, such as food, water or air. This part of ISO 10993 does not address the potential for exposure from such sources.

2 Normative reference

The following normative document contains 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 edition of the normative document 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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

3 Terms and definitions

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

3.1

allowable limit

AL

largest amount of a leachable substance that is deemed acceptable on a daily basis, when taken into the body through exposure to a medical device

NOTE Allowable limits are expressed in dose to the patient for each applicable exposure period. The units used are mass per unit time, e.g. milligrams per day. These doses represent tolerable risks for medical devices under the circumstances of intended use.

3.2

benefit factor

BF

numerical factor that takes into account the health benefit from use of the medical device(s) containing the leachable substance in question