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**Biological evaluation of medical devices —  
Part 17:  
Establishment of allowable limits for  
leachable substances**

*Évaluation biologique des dispositifs médicaux —*

*Partie 17: Établissement des limites admissibles des substances  
relargables*



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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.

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## 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