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# Biological evaluation of medical devices —

## Part 15: Identification and quantification of degradation products from metals and alloys

*Évaluation biologique des dispositifs médicaux —*

*Partie 15: Identification et quantification des produits de dégradation issus des métaux et alliages*

Reference number
ISO 10993-15:2000(E)

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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 10993-15 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 hypersensitiviy*

— *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 $2 \times 10^{-3}$ mol and $150 \times 10^{-3}$ 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.