INTERNATIONAL STANDARD

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Biological evaluation of medical devices —

Part 9: Framework for identification and quantification of potential degradation products

Évaluation biologique des dispositifs médicaux —

Partie 9: Cadre pour l'identification et la quantification des produits potentiels de dégradation

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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 10993-9 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

This second edition cancels and replaces the first edition (ISO 10993-9:1999), 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]

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

Introduction

This part of ISO 10993 is intended to present the general principles on which the specific material investigations to identify and quantify degradation products described in ISO 10993-13 (polymers), ISO 10993-14 (ceramics) and ISO 10993-15 (metals and alloys) are based.

Information obtained from these studies is intended to be used in the biological evaluations described in the remaining parts of ISO 10993.

The materials used to construct medical devices can form degradation products when exposed to the biological environment, and in the body these products might behave differently to the bulk material.

Mechanical wear causes mostly particulate debris, whereas the release of substances from surfaces due to leaching, chemical breakdown of structures or corrosion can lead to free ions or to different kinds of reaction products in the form of organic or inorganic compounds.

The degradation products can be either reactive or stable and without biochemical reaction with their environment. Accumulations of substantial quantities of stable degradation products can, however, have physical effects on the surrounding tissues. Degradation products might remain at the location of their generation or might be transported within the biological environment by various mechanisms.

The level of biological tolerability of degradation products depends on their nature and concentration, and should be primarily assessed through clinical experience and focused studies. For theoretically possible, new and/or unknown degradation products, relevant testing is necessary. For well-described and clinically accepted degradation products, no further investigation may be necessary.

Note that the safety and efficacy of a medical device can be compromised as a result of degradation, and the degradation should be considered in the risk management of the device.

Biological evaluation of medical devices —

Part 9:
Framework for identification and quantification of potential degradation products

1 Scope

This part of ISO 10993 provides general principles for the systematic evaluation of the potential and observed biodegradation of medical devices and for the design and performance of biodegradation studies. Information obtained from these studies can be used in the biological evaluation described in the ISO 10993 series. This part of ISO 10993 considers both non-resorbable and resorbable materials.

This part of ISO 10993 is not applicable to:

a) evaluation of degradation which occurs by purely mechanical processes; methodologies for the production of this type of degradation product are described in specific product standards, where available;

NOTE 1 Purely mechanical degradation causes mostly particulate matter. Although this is excluded from the scope of this part of ISO 10993, such degradation products can evoke a biological response and thus need to undergo biological evaluation as described in other parts of ISO 10993.

b) leachable components which are not degradation products;

c) medical devices or components that do not contact the patient's body directly or indirectly.

NOTE 2 This part of ISO 10993 can be applied to the degradation of materials used in any kind of product that falls within the definition of “medical device” in ISO 10993-1, even if such products are subject to different regulations from those applying to medical devices, e.g. the scaffold in a tissue engineered medical product, or a carrier matrix to deliver drugs or biologics.

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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-2, *Biological evaluation of medical devices — Part 2: Animal welfare requirements*

ISO 10993-13, *Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices*

ISO 10993-14, *Biological evaluation of medical devices — Part 14: Identification and quantification of degradation products from ceramics*

ISO 10993-15, *Biological evaluation of medical devices — Part 15: Identification and quantification of degradation products from metals and alloys*

3 Terms and definitions

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

3.1
degradation
decomposition of a material

3.2
biodegradation
degradation (3.1) due to the biological environment

3.3
bioresorbable medical device
medical device intended for **degradation** (3.1) and resorption in the biological environment of the body

3.4
leachable
extractable component from a material that is not a product of degradation

3.5
corrosion
attack on metallic materials by chemical or electrochemical reactions

NOTE The term is sometimes used in a general sense for the deterioration of other materials but is in this part of ISO 10993 reserved for metallic materials.

3.6
substance
single chemical element or compound, or a complex structure of compounds

3.7
device component
one of the different parts of which a device is composed

3.8
degradation product
any particle or chemical compound that is derived from the chemical breakdown of the original material

3.9
service environment
anatomical location for the intended use of the device including surrounding fluids, tissues and biomolecules

4 Principles for design of degradation studies

4.1 General

The approach to the assessment of degradation varies with the nature of the material under investigation, the medical device and the anatomical location of the specific device. The models chosen for evaluation shall be representative of the service environment of the device. The studies to be conducted do not require a biological environment, but one that simulates the conditions of the biological environment.