First edition
2006-08-01

# Biological evaluation of medical devices —

## Part 20: Principles and methods for immunotoxicology testing of medical devices

*Évaluation biologique des dispositifs médicaux —*

*Partie 20: Principes et méthodes relatifs aux essais d'immunotoxicologie des dispositifs médicaux*

Reference number
ISO/TS 10993-20:2006(E)

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

# Contents

Page

## 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.

In other circumstances, particularly when there is an urgent market requirement for such documents, a technical committee may decide to publish other types of normative document:

— an ISO Publicly Available Specification (ISO/PAS) represents an agreement between technical experts in an ISO working group and is accepted for publication if it is approved by more than 50 % of the members of the parent committee casting a vote;

— an ISO Technical Specification (ISO/TS) represents an agreement between the members of a technical committee and is accepted for publication if it is approved by 2/3 of the members of the committee casting a vote.

An ISO/PAS or ISO/TS is reviewed after three years in order to decide whether it will be confirmed for a further three years, revised to become an International Standard, or withdrawn. If the ISO/PAS or ISO/TS is confirmed, it is reviewed again after a further three years, at which time it must either be transformed into an International Standard or be withdrawn.

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/TS 10993-20 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*.

ISO/TS 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 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*

— *Part 19: Physico-chemical, morphological and topographical characterization of materials*

— *Part 20: Principles and methods for immunotoxicology testing of medical devices*

# Introduction

International and European Standards are the main focus for demonstration of the safety and compliance of medical devices. There has been increasing attention over the past few years on the potential for medical devices to cause changes in the immune system. It was felt necessary to provide guidance on how to address adverse effects of medical devices on the immune system. As there are no standardized tests available, this document provides a framework on how to approach the evaluation of immunotoxicity.

The intention of this document is:

— to summarize the current state of knowledge in the area of immunotoxicology, including information on methods of assessment of immunotoxicity and their predictive value;

— to identify what the problems are and how they have been dealt with in the past.

For clinical indications of immune alterations due to medical devices, an extensive literature review has been performed, primarily through Medline. The key areas which have been researched are:

— immunosuppression;

— immunostimulation;

— hypersensitivity;

— chronic inflammation;

— autoimmunity.

These key words are linked with the following materials:

— plastics and other polymers;

— metals;

— ceramics, glasses and composites;

— biological materials.

NOTE See also Table 1 for possibilities of interaction of materials with the immune system.