Fifth edition
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Biological evaluation of medical devices —

Part 1: Evaluation and testing within a risk management process

Évaluation biologique des dispositifs médicaux —

Partie 1: Évaluation et essais au sein d'un processus de gestion du risque

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices.*

This fifth edition cancels and replaces the fourth edition (ISO 10993-1:2009), which has been technically revised. It also incorporates the Technical Corrigendum ISO 10993-1:2009/Cor.1:2010.

The main changes compared to the previous edition are as follows:

a) revised Annex A "Endpoints to be addressed in a biological risk assessment" with new columns for "physical and/or chemical information" and "material mediated pyrogenicity" as well as columns for "chronic toxicity," "carcinogenicity," "reproductive/developmental toxicity," and "degradation" which now indicates "endpoints" to be considered with "E" (instead of "tests" to be conducted with an "X");

b) replaced Annex B "Guidance on the risk management process" with "Guidance on the conduct of biological evaluation within a risk management process" (formerly ISO TR 15499);

c) additional definitions for terms used throughout the ISO 10993 series of standards;

d) additional information on the evaluation of "Non-contacting medical devices" and new information on the evaluation of "Transitory-contacting medical devices";

e) additional information on the evaluation of nanomaterials, and absorbable materials;

f) additional reference to ISO 18562 (all parts) for "Biocompatibility evaluation of breathing gas pathways in healthcare applications";

g) significant editing changes throughout the document;

A list of all parts in the ISO 10993 series can be found on the ISO website.

Introduction

The primary aim of this document is the protection of humans from potential biological risks arising from the use of medical devices. It is compiled from numerous International and national standards and guidelines concerning the biological evaluation of medical devices. It is intended to describe the biological evaluation of medical devices within a risk management process, as part of the overall evaluation and development of each medical device. This approach combines the review and evaluation of existing data from all sources with, where necessary, the selection and application of additional tests, thus enabling a full evaluation to be made of the biological responses to each medical device, relevant to its safety in use. The term “medical device” is wide-ranging and, at one extreme, consists of a single material, which can exist in more than one physical form, and at the other extreme, of a medical device consisting of numerous components made of more than one material.

This document addresses the determination of the biological response to medical devices, mostly in a general way, rather than in a specific device-type situation. Thus, for a complete biological evaluation, it classifies medical devices according to the nature and duration of their anticipated contact with human tissues when in use and indicates, in a matrix, the biological endpoints that are thought to be relevant in the consideration of each medical device category. See also 3.14, Note 1 to entry.

The range of biological hazards is wide and complex. The biological response to a constituent material alone cannot be considered in isolation from the overall medical device design. Thus, in designing a medical device, the choice of the best material with respect to its biocompatibility might result in a less functional medical device, biocompatibility being only one of a number of characteristics to be considered in making that choice. Where a material is intended to interact with tissue in order to perform its function, the biological evaluation needs to address this.

Biological responses that are regarded as adverse, caused by a material in one application, might not be regarded as such in a different situation. Biological testing is based upon, among other things, *in vitro* and *ex vivo* test methods and upon animal models, so that the anticipated behaviour when a medical device is used in humans can be judged only with caution, as it cannot be unequivocally concluded that the same biological response will also occur in this species. In addition, differences in the manner of response to the same material among individuals indicate that some patients can have adverse reactions, even to well-established materials.

The primary role of this document is to serve as a framework in which to plan a biological evaluation. A secondary role is to utilize scientific advances in our understanding of basic mechanisms, to minimize the number and exposure of test animals by giving preference to *in vitro* models and to chemical, physical, morphological, and topographical characterization testing, in situations where these methods yield equally relevant information to that obtained from *in vivo* models.

It is not intended that this document provide a rigid set of test methods, including pass/fail criteria, as this might result in either an unnecessary constraint on the development and use of novel medical devices, or a false sense of security in the general use of medical devices. Where a particular application warrants it, experts in the product or in the area of application concerned can choose to establish specific tests and criteria, described in a product-specific vertical standard.

ISO 10993 series is intended for use by professionals, appropriately qualified by training and experience, who are able to interpret its requirements and judge the outcome of the evaluation for each medical device, taking into consideration all the factors relevant to the medical device, its intended use and the current knowledge of the medical device provided by review of the scientific literature and previous clinical experience.

Informative Annex A contains a table that is generally helpful in identifying endpoints recommended in the biocompatibility evaluation of medical devices, according to their category of body contact and duration of clinical exposure. Informative Annex B contains guidance for the application of the risk management process to medical devices which encompasses biological evaluation.