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Biologisk värdering av medicintekniska produkter – Del 1: Utvärdering och provning inom en riskhanteringsprocess (ISO 10993-1:2009)

Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2009)

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Denna standard ersätter SS-EN ISO 10993-1:2009, utgåva 3.

The European Standard EN ISO 10993-1:2009 has the status of a Swedish Standard. This document contains the official English version of EN ISO 10993-1:2009.

This standard supersedes the Swedish Standard SS-EN ISO 10993-1:2009, edition 3.

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Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2009)

Évaluation biologique des dispositifs médicaux - Partie 1: Évaluation et essais au sein d'un processus de gestion du risque (ISO 10993-1:2009)

Biologische Beurteilung von Medizinprodukten - Teil 1: Beurteilung und Prüfungen im Rahmen eines Risikomanagementsystems (ISO 10993-1:2009)

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Foreword

This document (EN ISO 10993-1:2009) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 206 “Biological evaluation of medical devices” the secretariat of which is held by NEN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by April 2010, and conflicting national standards shall be withdrawn at the latest by April 2010.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN ISO 10993-1:2009, June.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directives.

For relationship with EU Directives, see informative Annex ZA and ZB, which are integral parts of this document.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

Endorsement notice

The text of ISO 10993-1:2009 has been approved by CEN as a EN ISO 10993-1:2009 without any modification.

Introduction

The primary aim of this part of ISO 10993 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 be a guidance document for the biological evaluation of medical devices within a risk management process, as part of the overall evaluation and development of each 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. It must be appreciated that the term “medical device” is wide-ranging and, at one extreme, consists of a single material, which may exist in more than one physical form, and at the other extreme, of a complex instrument or piece of apparatus, consisting of numerous components made of more than one material.

ISO 10993 addresses the determination of the effects of medical devices on tissues, mostly in a general way, rather than in a specific device-type situation. Thus, for a complete biological safety evaluation, it classifies medical devices according to the nature and duration of their anticipated contact with human tissues when in use and indicates, in matrices, the biological data sets that are thought to be relevant in the consideration of each device category.

The range of biological hazards is wide and complex. The tissue interaction with a constituent material alone cannot be considered in isolation from the overall device design. Thus, in designing a device, the choice of the best material with respect to its tissue interaction might result in a less functional device, tissue interaction 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.

Tissue interactions 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 device is used in humans can be adjudged only with caution, as it cannot be unequivocally concluded that the same tissue reactions 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 role of this part of ISO 10993 is to serve as a framework in which to plan a biological evaluation which, as scientific knowledge advances our understanding of the basic mechanisms of tissue responses, minimizes the number and exposure of test animals by giving preference to chemical constituent testing and *in vitro* models, in situations where these methods yield equally relevant information to that obtained from *in vivo* models.

It is not intended that ISO 10993 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.

This part of ISO 10993 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 device, its intended use and the current knowledge of the medical device provided by review of the scientific literature and previous clinical experience.

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

Biological evaluation of medical devices —

Part 1:
Evaluation and testing within a risk management process

1 Scope

This part of ISO 10993 describes:

— the general principles governing the biological evaluation of medical devices within a risk management process;

— the general categorization of devices based on the nature and duration of their contact with the body;

— the evaluation of existing relevant data from all sources;

— the identification of gaps in the available data set on the basis of a risk analysis;

— the identification of additional data sets necessary to analyse the biological safety of the medical device;

— the assessment of the biological safety of the medical device.

This part of ISO 10993 does not cover testing of materials and devices that do not come into direct or indirect contact with the patient's body, nor does it cover biological hazards arising from any mechanical failure. Other parts of ISO 10993 cover specific tests, as indicated in the Foreword.

2 Normative references

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

ISO 10993-3, *Biological evaluation of medical devices — Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity*

ISO 10993-4, *Biological evaluation of medical devices — Part 4: Selection of tests for interaction with blood*

ISO 10993-5, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 10993-6, *Biological evaluation of medical devices — Part 6: Tests for local effects after implantation*

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO 10993-9, *Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products*

ISO 10993-10, *Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization*

ISO 10993-11, *Biological evaluation of medical devices — Part 11: Tests for systemic toxicity*

ISO 10993-12, *Biological evaluation of medical devices — Part 12: Sample preparation and reference materials*

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*

ISO 10993-16, *Biological evaluation of medical devices — Part 16: Toxicokinetic study design for degradation products and leachables*

ISO 10993-17, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

ISO 10993-18:2005, *Biological evaluation of medical devices — Part 18: Chemical characterization of materials*

ISO/TS 10993-19, *Biological evaluation of medical devices — Part 19: Physico-chemical, morphological and topographical characterization of materials*

ISO/TS 10993-20, *Biological evaluation of medical devices — Part 20: Principles and methods for immunotoxicology testing of medical devices*

ISO 14971, *Medical Devices — Application of risk management to medical devices*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
medical device
any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury,

— investigation, replacement, modification, or support of the anatomy or of a physiological process,

— supporting or sustaining life,

— control of conception,

— disinfection of medical devices,

— providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body,

and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means

NOTE 1 This definition has been developed by the Global Harmonization Task Force (GHTF).

[ISO 13485:2003, definition 3.7]

NOTE 2 Products which might be considered to be medical devices in some jurisdictions but for which there is not yet a harmonized approach, are:

1) aids for disabled/handicapped people;

2) devices for the treatment/diagnosis of diseases and injuries in animals;

3) accessories for medical devices (see Note 4);

4) disinfection substances;

5) devices incorporating animal and human tissues, which might meet the requirements of the above definition but are subject to different controls.

NOTE 3 Accessories intended specifically by manufacturers to be used together with a “parent” medical device to enable that medical device to achieve its intended purpose, should be subject to ISO 10993.

NOTE 4 Medical devices are different from drugs/biologics, and their biological evaluation requires a different approach.

NOTE 5 Medical devices can include dental devices.

3.2
material
any synthetic or natural polymer, metal, alloy, ceramic or other non-viable substance, including tissue rendered non-viable, used as a medical device or any part thereof

3.3
final product
medical device in its “as-used” state, as defined by the manufacturer's specification or labelling

3.4
chemical constituent
any synthetic or natural substance that is used in a process for manufacturing materials and/or medical devices, such as additives (antioxidants, UV stabilizers, dyestuff, etc.), processing aids (solvents, lubricants, antifoaming agents, etc.)

3.5
data set
information from a variety of sources necessary to characterize the biological response of a device

4 General principles applying to biological evaluation of medical devices

4.1 The biological evaluation of any material or medical device intended for use in humans shall form part of a structured biological evaluation programme within a risk management process in accordance with ISO 14971, as set out in Figure 1. Annex B provides guidance on this process. The biological evaluation shall be planned, carried out, and documented by knowledgeable and experienced professionals. See Annex C for how to perform a literature review of existing data.

The risk management plan should identify aspects of the biological evaluation requiring specific technical competencies and shall identify the person(s) responsible for the biological safety evaluation.

The evaluation programme shall include documented, informed decisions that assess the advantages/disadvantages and relevance of:

a) the physical and chemical characteristics of the various candidate materials;

NOTE Where this information is already documented within the risk management for the device it can be included by reference.