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Medical devices utilizing animal tissues and their derivatives —

Part 1: Application of risk management

Dispositifs médicaux utilisant des tissus animaux et leurs dérivés — Partie 1: Application de la gestion des risques

Reference number
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Foreword

ISO (the International Organization for Standardization) and IEC (the International Electrotechnical Commission) form the specialized system for worldwide standardization. National bodies that are members of ISO or IEC participate in the development of International Standards through technical committees established by the respective organization to deal with particular fields of technical activity. ISO and IEC technical committees collaborate in fields of mutual interest. Other international organizations, governmental and non-governmental, in liaison with ISO and IEC, also take part in the work.

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 document 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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO and IEC shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents) or the IEC list of patent declarations received (see http://patents.iec.ch).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of 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 www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices*, Subcommittee SC 1, *Tissue product safety*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 206, *Biological and clinical evaluation of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 22442-1:2015), which has been technically revised.

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

— 4.4.2 has been updated;

— weblinks in C.2, bullet point 1, C.3.3 and C.4.4 have been updated;

— the weblink in D.3.3 has been updated;

— C.10 has been added;

— the bibliography has been updated.

A list of all parts in the ISO 22442 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Certain medical devices utilize materials of animal origin.

Animal tissues and their derivatives are used in the design and manufacture of medical devices to provide performance characteristics that have been chosen for advantages over non-animal based materials. The range and quantities of materials of animal origin in medical devices vary. These materials can comprise a major part of the device (e.g. bovine/porcine heart valves, bone substitutes for use in dental or orthopaedic applications, haemostatic devices), can be a product coating or impregnation (e.g. collagen, gelatine, heparin), or can be used in the device manufacturing process (e.g. tallow derivatives such as oleates and stearates, foetal calf serum, enzymes, culture media).

ISO 14971 is a general standard which specifies a process for a manufacturer by identifying hazards and hazardous situations associated with medical devices, including *in vitro* medical devices, to estimate and evaluate the risks associated with those hazards, to control these risks and to monitor the effectiveness of the control throughout the life cycle. This document provides additional requirements and guidance for the evaluation of medical devices manufactured utilizing animal tissues or derivatives which are non-viable or rendered non-viable.

This document is intended to cover medical devices including active implantable medical devices such as implantable infusion pumps.

This document does not apply to *in vitro* diagnostic devices.

This document can only be used in combination with ISO 14971 and is not a “stand-alone” standard.

NOTE Compliance to this document is shown by fulfilling its specified requirements. The guidance given in the notes and the informative annexes is not normative and is not provided as a checklist for auditors.

Medical devices utilizing animal tissues and their derivatives —

Part 1: Application of risk management

1 Scope

This document applies to medical devices other than *in vitro* diagnostic medical devices manufactured utilizing materials of animal origin, which are non-viable or have been rendered non-viable. It specifies, in conjunction with ISO 14971, a procedure to identify the hazards and hazardous situations associated with such devices, to estimate and evaluate the resulting risks, to control these risks, and to monitor the effectiveness of that control. Furthermore, it outlines the decision process for the residual risk acceptability, taking into account the balance of residual risk, as defined in ISO 14971, and expected medical benefit as compared to available alternatives. This document is intended to provide requirements and guidance on risk management related to the hazards typical of medical devices manufactured utilizing animal tissues or derivatives such as:

a) contamination by bacteria, moulds or yeasts;

b) contamination by viruses;

c) contamination by agents causing transmissible spongiform encephalopathies (TSE);

d) material responsible for undesired pyrogenic, immunological or toxicological reactions.

For parasites and other unclassified pathogenic entities, similar principles can apply.

This document does not stipulate levels of acceptability which, because they are determined by a multiplicity of factors, cannot be set down in such an international standard except for some particular derivatives mentioned in Annex C. Annex C stipulates levels of TSE risk acceptability for tallow derivatives, animal charcoal, milk and milk derivatives, wool derivatives and amino acids.

This document does not specify a quality management system for the control of all stages of production of medical devices.

This document does not cover the utilization of human tissues in medical devices.

NOTE 1 It is not a requirement of this document to have a full quality management system during manufacture. However, attention is drawn to international standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices.

NOTE 2 For guidance on the application of this document, see Annex A.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. 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 14971, *Medical devices — Application of risk management to medical devices*

ISO 22442-2, *Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling*

ISO 22442-3, *Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14971 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

3.1
animal
vertebrate or invertebrate [including amphibian, arthropod (e.g. crustacean), bird, coral, fish, reptile, mollusc and mammal] excluding humans (*Homo sapiens*)

3.2
cell
smallest organized unit of any living form which is capable of independent existence and of replacement of its own substance in a suitable environment

3.3
derivative
substance obtained from an *animal* (3.1) material which is involved directly in the manufacturing process of the medical device or is part of the final medical device

EXAMPLE Hyaluronic acid, collagen, gelatine, monoclonal antibodies, chitosan and albumin.

3.4
elimination
removal
process by which the number of transmissible agents is reduced

Note 1 to entry: The effectiveness of the process for the elimination of viruses and TSE agents should be expressed mathematically in terms of a reduction factor (see C.2 and ISO 22442-3:2007, Annex F).

Note 2 to entry: Elimination aims to prevent infection or pathogenic reaction caused by transmissible agents.

3.5
inactivation
process by which the ability to cause infection or pathogenic reaction by a transmissible agent is reduced

Note 1 to entry: The effectiveness of the process for inactivation of viruses and TSE agents should be expressed mathematically in terms of a reduction factor (see ISO 22442-3:2007, Annex F).

Note 2 to entry: Inactivation aims to prevent infection by, and replication of, transmissible agents.

3.6
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, 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 medical purpose(s) of

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

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

