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Medicintekniska produkter som innehåller vävnader från djur och derivat därav – Del 3: Validering av eliminering och/eller inaktivering av virus och överföring av spongiform encefalopati (ISO 22442-3:2007)

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 (ISO 22442-3:2007)

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Denna standard ersätter SS-EN 12442-3, utgåva 1.

The European Standard EN ISO 22442-3:2007 has the status of a Swedish Standard. This document contains the official English version of EN ISO 22442-3:2007.

This standard supersedes the Swedish Standard SS-EN 12442-3, edition 1.

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EUROPEAN STANDARD

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English Version

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 (ISO 22442-3:2007)

Dispositifs médicaux utilisant des tissus animaux et leurs dérivés - Partie 3: Validation de l'élimination et/ou de l'inactivation des virus et autres agents responsables d'encéphalopathie spongiforme transmissible (EST) (ISO 22442-3:2007)

Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden - Teil 3: Validierung der Eliminierung und/oder Inaktivierung von Viren und Erregern der übertragbaren spongiösen Enzephalopathie (TSE) (ISO 22442-3:2007)

This European Standard was approved by CEN on 14 December 2007.

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COMITÉ EUROPÉEN DE NORMALISATION
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Foreword

This document (EN ISO 22442-3:2007) has been prepared by Technical Committee ISO/TC 194 "Biological evaluation of medical devices" in collaboration with Technical Committee CEN/TC 316 “Medical devices utilizing tissues” the secretariat of which is held by NBN.

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of an identical text or by endorsement, at the latest by June 2008, and conflicting national standards shall be withdrawn at the latest by June 2008.

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 12442-3:2000.

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 EC Directive(s).

This European Standard has been developed for medical devices regulated by the Medical Device Directive 93/42/EC as amended by 2003/32/EC (see Annex ZA). By analogy, it could be applied for active implantable medical devices regulated by the Active Implantable Medical Device Directive 90/385/EC.

For relationship with EC Directive(s), see informative Annex ZA, which is an integral part 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 22442-3:2007 has been approved by CEN as a EN ISO 22442-3:2007 without any modification.

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 were 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).

It is important to be aware that the exposure to a properly validated and accurately controlled method of viral and TSE inactivation/elimination is not the only factor associated with demonstrating product safety. Attention has also to be given to a number of factors including sourcing, collecting, handling, storage, processing, testing of tissues and/or cells of animal origin, and to the control of the environment in which the product is manufactured, assembled and packaged. The manufacturer should consider the fact that each manufacturing phase can contribute to contamination as well as elimination and/or inactivation of viruses and TSE agents.

For the safety of medical devices there are two complementary approaches (see ISO 22442-1) that can be adopted to control the potential contamination of tissues. These typically are:

a) selecting source material for minimal contamination with viruses and/or TSE agents (see ISO 22442-1 and ISO 22442-2);

b) providing valid scientific evidence to demonstrate the ability of the production processes to eliminate or inactivate viruses and/or TSE agents (this part of ISO 22442).

Requirements for a quality system for medical devices for regulatory use are specified in ISO 13485. The standards for quality management systems recognize that, for certain processes used in manufacturing, the effectiveness of that process cannot be fully verified by subsequent inspection and testing of the product. The elimination and/or inactivation of viruses and TSE agents is an example of a special process because process efficacy cannot be verified by inspection and testing of the product. For this reason, the following need to be considered in particular:

— definition of the process(es) and materials to be used;

— adequate inactivation validation before routine use;

— performance monitoring of the process during manufacture;

— appropriate equipment maintenance;

— staff training, etc.

Historically there have been many instances of unknown or unsuspected viral contamination during manufacture. For this reason, evaluation of the manufacturing process can provide a measure of confidence that a wide number of viruses, including unknown pathogenic viruses are eliminated. Similar principles may apply to TSE agents.

NOTE To show compliance with this part of ISO 22442, its specified requirements should be fulfilled. The guidance given in the Notes and informative annexes is not normative and is not provided as a checklist for auditors.

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

1 Scope

This part of ISO 22442 specifies requirements for the validation of the elimination and/or inactivation of viruses and TSE agents during the manufacture of medical devices (excluding *in vitro* diagnostic medical devices) utilizing animal tissue or products derived from animal tissue, which are non-viable or have been rendered non-viable. It applies where required by the risk management process as described in ISO 22442-1. It does not cover other transmissible and non-transmissible agents.

NOTE 1 Analysis and management of risk is described in ISO 22442-1. Conventional processes used for sterilization, when used for the treatment of animal tissues for medical devices, have not been shown to be completely effective in inactivating the causative agents of transmissible spongiform encephalopathy. Selective sourcing is extremely important (see ISO 22442-1 and ISO 22442-2).

NOTE 2 ISO 11135, ISO 11137, ISO 11737-1, ISO 13408, ISO 14160, ISO 14937 and ISO 17665 may be relevant for bacteria, moulds and yeast (see Bibliography).

This part of ISO 22442 does not cover the utilization of human tissues in medical devices.

This part of ISO 22442 does not specify a quality management system for the control of all stages of production of medical devices.

NOTE 3 It is not a requirement of this part of ISO 22442 to have a full quality management system during manufacture, but it does specify requirements for some of the elements of a quality management system. Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices. The quality management system elements that are required by this part of ISO 22442 can form part of a quality management system conforming to ISO 13485.

This part of ISO 22442 does not consider the effect of any method of elimination and/or inactivation on the suitability of the medical device for its intended use.

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 22442-1:2007, *Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management*

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

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 22442-1 and the following apply.

3.1
model TSE agent
TSE agent that displays a known resistance to physical and/or chemical processing used as reference by analogy for the inactivation of relevant TSE agents, and thereby demonstrating the effectiveness of the process used for inactivation

3.2
model virus
virus that displays a known resistance to physical and/or chemical processing used as reference by analogy for the inactivation of relevant viruses, and thereby demonstrating the effectiveness of the process used for inactivation

NOTE This includes viral models (RNA, DNA, enveloped, non-enveloped) and bacteriophage models.

3.3
overall reduction factor
sum of the reduction factors of the individual process steps

3.4
permissive cell
cell that can become infected with the virus under study and in which that virus replicates

3.5
reduction factor
ratio of the virus or TSE agent load in the relevant material used or the device prior to the inactivation or elimination step and the virus or TSE agent load after the inactivation or elimination step when it is ready for the next step in the manufacturing process, expressed as the number of ten fold reduction ($\log_{10}$)

3.6
relevant TSE agent
TSE agent known to, or likely to, contaminate the source material or other materials used in the manufacturing process

3.7
relevant virus
virus known to, or likely to, contaminate the source material or other materials used in the manufacturing process

3.8
revalidation
set of documented procedures to confirm an established validation

3.9
scaled down process
scaling down
process at a specified reduced scale which simulates the performance parameters as used in the full scale production process

3.10
sterilization
validated process used to render a product free of all forms of viable microorganisms

3.11
validation
documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications

[ISO/TS 11139:2006, definition 2.55]

4 General requirements

4.1 Risk management

Analysis and management of risk shall be carried out in accordance with ISO 22442-1.

Due account shall be taken of manufacturing processes that are considered to be effective for certain animal materials as discussed in Annex C of ISO 22442-1:2007.

4.2 Sourcing and manufacturing process

A documented system shall be established and maintained to control the source of raw materials of animal origin. ISO 22442-2 shall be used to meet this requirement as far as applicable.

The manufacturing process shall be established to minimize the load of viruses and TSE agents in starting materials, intermediate products and finished products.

Appropriate documented protocols and procedures shall be established to ensure that the validated processing parameters will be applied during the routine manufacturing processes.

NOTE Employing a quality management system complying with ISO 13485 could be used to meet the requirements of this subclause.

4.3 General requirements related to validation

4.3.1 Documented procedures

The documented procedures and requirements of this part of ISO 22442 shall be implemented. Documentation and records shall be reviewed and approved by designated personnel (see 4.3.2).

Procedures for any literature review and/or any inactivation study shall be documented and records shall be retained for a period defined by the manufacturer.

4.3.2 Personnel

Responsibility for the implementation of this part of ISO 22442 shall be assigned to qualified personnel.

The requirements for the qualification, training or experience of personnel shall be documented and appropriate to the individual's work, responsibility and authority.

NOTE The level of qualification, training and experience required by personnel at various levels depends upon the activities being performed.

4.3.3 Calibration

An effective system shall be established, documented and maintained for the calibration of all controlling, indicating and recording instruments used for validation.