INTERNATIONAL STANDARD

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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

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)

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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.

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 22442-3 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*, Subcommittee SC 1, *Tissue product safety*.

ISO 22442 consists of the following parts, under the general title *Medical devices utilizing animal tissues and their derivatives*:

— *Part 1: Application of risk management*

— *Part 2: Controls on sourcing, collection and handling*

— *Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents*

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*