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Medical devices utilizing animal tissues and their derivatives —

Part 2: Controls on sourcing, collection and handling

Dispositifs médicaux utilisant des tissus animaux et leurs dérivés —
Partie 2: Contrôles de l'origine, de la collecte et du traitement

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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.

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).

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. 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).

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 22442-2:2015).

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

— Update of the weblink on stunning technique in Annex A, A.3.2.5 Note 1;

— Clarification on scope inclusion of cervid-sourced materials, and other TSE susceptible species;

— Clarification on atypical BSE types, especially in combination with intracranial applications;

— Enhanced expectation of using validated biochemical testing to establish TSE presence.

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).

Tissues and derivatives for use in medical devices are typically obtained by the manufacturer from a range of sources such as animal herds or flocks and commercial harvesting (including fishing). Some specialized industries also process materials of animal origin to manufacture a finished product (e.g. gelatine) which is incorporated as a raw material into the finished medical device by the manufacturer.

This document is intended to be used in conjunction with the other two parts of the ISO 22442 series. Local safety regulations can apply. The manufacturers should refer to ISO 22442-3 for information on the validation of the elimination and/or inactivation of viruses and TSE agents.

It is not a requirement of this document 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 document can form a part of a quality management system conforming to ISO 13485.

Medical devices utilizing animal tissues and their derivatives —

Part 2:
Controls on sourcing, collection and handling

1 Scope

This document specifies requirements for controls on the sourcing, collection, and handling (which includes storage and transport) of animals and tissues for the manufacture of medical devices utilizing materials of animal origin other than *in vitro* diagnostic medical devices. It applies where required by the risk management process as described in ISO 22442-1.

NOTE Selective sourcing is especially important for transmissible spongiform encephalopathy (TSE) risk management, i.e. when utilising animal tissue and/or their derivative originating from bovine, ovine and caprine species, deer, elk, mink or cats.

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

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

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 22442-1:2018, *Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management*

3 Terms and definitions

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

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

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

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

3.1
collection
removal of tissues from animals

3.2
closed herd
herd governed by standard operating procedures (SOPs) that specify criteria restricting admission of new animals to ensure that all introduced animals are at the same or higher health standard, compared to the residents of the herd

Note 1 to entry: Such SOPs typically include:

Note 2 to entry: a) a documented veterinary monitoring process;

Note 3 to entry: b) a fully documented disease history, including a fully documented negligible TSE risk status of the herd including logged TSE history;

Note 4 to entry: c) a process to prevent feeding of mammalian-derived protein, including a fully documented feed history, source and traceability;

Note 5 to entry: d) a fully documented breeding history;

Note 6 to entry: e) a fully documented use of veterinary medicines and vaccines;

Note 7 to entry: f) a process of traceability towards each individual animal;

Note 8 to entry: g) a process to control introduction of genetic material from animals outside the closed herd, including from herds with the deviating TSE status;

Note 9 to entry: h) a fully documented record of animals kept with or in close proximity to the closed herd and procedures to control vermin or pest.

3.3
veterinarian
person designated by the relevant competent authority as suitably qualified for the responsibility delegated to him or her relating to ante- and post-mortem inspection of animals and/or relevant certification

Note 1 to entry: Under certain jurisdictions, it is a requirement that the veterinarian be a professionally qualified person in veterinary medicine.

Note 2 to entry: Under certain jurisdictions, the function of inspection and of certification can be carried out by different individuals. In such cases, the certificate can be signed by a person who is not designated by the competent authority. This function is covered in the quality management system of the medical device manufacturer.

4 General requirements

4.1 General

Apply the requirements of this document as determined by the benefit-risk-assessment (see ISO 22442-1).

Annex A shall be applied as appropriate.

4.2 Quality system elements

A documented system shall be established and maintained to control the quality of materials of animal origin and shall be verified by the medical device manufacturer. Specific requirements relating to collection are included in Clause 6.

Compliance is checked by inspection of the appropriate documents, including:

a) specification of the age and of the geographical origin (such as country or region) of the animal material, state of health of the animals, and acceptance criteria for animals taking into account the source-species, perceived risk from pathogens, and ability to obtain appropriate assurances, including full traceability to the slaughterhouse.

   The geographical origin can include the animal's place of birth and the countries or regions in which it has lived during its lifetime as well as its place of slaughter. It is advisable that the manufacturer document the extent to which the geographical origin of the animal can be traced taking into account the application of risk management (see ISO 22442-1);

b) hygiene and quality assurance requirements to be met by the slaughterer including the provisions in the slaughterhouse to prevent cross-contamination within and between animals;

c) procedures for the collection, preservation, handling, storage, and transport of materials of animal origin;

d) documented evidence of the effectiveness of controls defined in a), b), and c);

e) records to be maintained [including as a minimum items a), b), c), and d). See also 5.5.

For the control of processed animal material suppliers, the medical device manufacturer shall document, to the extent feasible, the practices of the specialized industries to which clauses of the various parts of ISO 22442 have been applied.

Manufacturers should apply relevant provisions of ISO 22442 to natural substances such as milk, hair, and wool, although these are not covered by the definition of derivatives.

NOTE The use of risk analysis/risk management tools (such as HACCP, FMEA [3], [4]) are useful in determining residual risk.

4.3 Procedures

The documented procedures and instructions required by this document shall be established, implemented, and maintained. These procedures and instructions shall be approved on issue and shall be controlled as follows.

The manufacturer shall establish and maintain procedures to control all documents and data that relate to the requirements of this document. These documents shall be reviewed and approved for adequacy by authorized personnel prior to issue.

This control shall ensure that:

a) the pertinent issues of appropriate documents are available at all locations where operations essential to the effective functioning of the quality system are performed, and

b) obsolete documents are promptly removed from all points of issue or use.

Changes to documents shall be reviewed and approved by the same functions/organizations that performed the original review and approval unless specifically designated otherwise. The designated organizations shall have access to pertinent background information upon which to base their review and approval.

Where practicable, the nature of each change shall be identified in the document or the appropriate attachments.

A master list or equivalent document control procedure shall be established to identify the current revision of documents in order to preclude the use of non-applicable documents.

4.4 Personnel

Responsibility for the collection, handling, and storage of materials shall be assigned to qualified personnel as follows.

The manufacturer shall establish and maintain procedures for identifying the training needs and provide for the training of all personnel performing activities affecting quality.

The manufacturer shall ensure that personnel performing specific assigned tasks are qualified on the basis of appropriate education, training, and/or experience as required. Appropriate records of training shall be maintained.

Personnel directly involved in the collection and handling of material of animal origin shall be personnel employed by the device manufacturer or designated and adequately trained abattoir employees or the equivalent. The same requirements apply to personnel of all subcontractors.

The manufacturer shall identify the in-house verification requirements and shall provide adequate resources and assign trained personnel for verification activities.

Audits shall be carried out by personnel independent of those having direct responsibility for the work being performed.

4.5 Current regulatory requirements and guidance

Due account shall be taken of relevant current regional regulatory requirements or guidance including the OIE International Animal Health Code [5], [13].

5 Sourcing

5.1 General

5.2 to 5.6 and Clauses 6 to 8 shall be applied by the suppliers of animal materials, intermediaries, and medical device manufacturers as relevant under the risk management plan in compliance with ISO 22442-1.

The animal material shall not be compromised by cross-contamination before, during, or after slaughter. Animals shall be confirmed as having been declared fit for human consumption (see 5.5).

For the animal material sourced from species that are not intended for human consumption the justification for the missing inspection and certification is to be documented. Relevant quality criteria for this type of material are to be defined by the manufacturer.

It is the responsibility of the manufacturer to ensure that the material is fit for its intended use.

In case animal by-products not intended for human consumption are sourced, these have to be 'Category 3 (i.e. safe) materials or equivalent' [16].

5.2 Species and strain

For each material or derivative, the risk of certain diseases is dependent on the animal species and possibly strain, and this shall be taken into account for the establishment of control measures.

NOTE Specific guidance as regards requirements for bovine blood can be found in the "Guideline on the use of bovine serum in the manufacture of human biological medicinal products" [14].

5.3 Geography

The risk of certain diseases is dependent on the geographical origin and this shall be taken into account for the establishment of control measures.

Geographical origin can include conception, birth, rearing, and slaughtering (for bovine species, see Annex A).

If required by the risk management process, in the case of domesticated/farmed species, the geographical region/country of birth and the summary of main locations of residence up to time of slaughter shall be recorded.

In the case of wild species, the region/location of capture and the country/region of birth shall be recorded if known. The use of wild mammalian species shall be addressed in the risk assessment (see ISO 22442-1).

5.4 Inspection

Sourcing of animal material shall be subject to control and individual inspection by a veterinarian. There will, however, be some source-species where this is not possible (e.g. fish, crustaceans, cervids,

