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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.

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 22442-2 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 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.

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 2:
Controls on sourcing, collection and handling

1 Scope

This part of ISO 22442 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 1 Selective sourcing is considered to be especially important for transmissible spongiform encephalopathy (TSE) risk management.

NOTE 2 Manufacturers should refer to ISO 22442-3 for information on the validation of the elimination and/or inactivation of viruses and TSE agents.

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 a part of a quality management system conforming to ISO 13485.

NOTE 4 A general principle for the application of ISO 22442 is that it is advisable to give due consideration to the requirements and recommendations contained in all three parts of the standard.

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*

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
collection
removal of tissues from animals

3.2
low risk herd
closed herd
herd of bovine animals in which for at least the previous eight years:

a) there has been documented veterinary monitoring;

b) there has been no case of BSE;

c) there has been no feeding of mammalian-derived protein;

d) there is a fully documented breeding history;

e) there is a fully documented use of veterinary medicines and vaccines;

f) each animal is traceable;

g) genetic material has been introduced only from herds with the same BSE-free status

NOTE By analogy, low risk herd is applicable to other species naturally affected by TSE. Additional precautionary measures may be required.

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 Under certain jurisdictions it is a requirement that the veterinarian be a professionally qualified person in veterinary medicine.

NOTE 2 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 part of ISO 22442 as determined by the 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.

This system shall address the animal source and the following factors:

a) specification 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;

NOTE 1 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.

NOTE 2 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 3 The use of risk analysis/risk management tools (such as HACCP, FMEA, see Annex G of ISO 14971:2007) are useful in determining residual risk.

4.3 Procedures

The documented procedures and instructions required by this part of ISO 22422 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 part of ISO 22442. 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 [4].

5 Sourcing

5.1 General

Subclauses 5.2, 5.3, 5.4, 5.5, 5.6, and Clauses 6, 7 and 8, shall be applied by 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).

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

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.

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). If individual animals cannot be inspected, the justification for this shall be documented and a relevant sampling plan provided.

Bovine, caprine, cervid, equine, ovine, and porcine species shall be subject to ante-mortem veterinary inspection. Animals showing locomotive system abnormalities or neurological disorders shall not be used for the production of medical devices except for tallow derivatives, animal charcoal, and amino acids that are acceptable as discussed in 4.4.2 and 4.4.3 of ISO 22442-1:2007 due to their processing and not their sourcing.

Prior to certification, a post-mortem inspection of bovine, caprine, cervid, equine, ovine, and porcine species shall be performed by a veterinarian immediately after slaughter according to local custom and practice. The inspection shall include at least:

a) visual inspection;

b) palpation of specified organs;

c) incision of organs and lymph nodes;

d) investigation of anomalies, e.g. inconsistency, colour and smell;

e) if necessary, laboratory tests.

Where indicated by risk assessment, for materials (including pooled blood supplies) for direct use in medical devices and that are not subject to a validated process to reduce TSE risk in line with ISO 22442-3, consideration shall be given to the application of a test for the presence of TSE in the source animal.

NOTE Animal tissues derived from certain species (e.g. fish, crustaceans) require a modified approach since veterinary surveillance is not practicable in the same way as for other animal tissues. Manufacturers should apply relevant sections of this International Standard to such materials but may need to rely on other procedures which have been shown to be effective for risk reduction (see ISO 22442-1).

5.5 Certification

Material of animal origin intended for utilization in medical devices shall originate from animals confirmed by a veterinarian as being fit for human consumption. Records to demonstrate conformance with veterinary inspection criteria at the abattoir, certificate details and source shall be available (see for example Annex B). For species where such certification by a veterinarian cannot be obtained, a status equivalent to “fit for human consumption” is required, such as a confirmation of apparent good health.

5.6 Traceability

Where the risk management undertaken according to ISO 22442-1 indicates that it is both necessary and feasible, a traceability system shall be established. The extent of traceability shall be defined by the outcome of the risk assessment taking into account those official information systems that exist.

NOTE Traceability may not be practicable if materials of animal origin are collected, pooled and manufactured by processed animal material suppliers.

6 Collection

6.1 Between the manufacturer of the medical device and the supplier of material of animal origin there shall be a technical agreement defining:

— the limits of responsibilities;

— specifications of the material;

— documentation;

— inspection criteria;

— procedures (including specific measures to prevent cross-contamination);

— audits;

— procedures for ensuring that all deliveries have traceability of relevant certificates.