SLOVENSKI STANDARD

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Ţivalska tkiva in njihovi derivati, uporabljeni v proizvodnji medicinskih pripomoļkov ï 1. del: Analize in obvladovanje tveganja

Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 1: Analysis and management of risk

Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden - Teil 1: Analyse und Handhabung von Risiken

Tissus animaux et leurs dérivés utilisés dans la fabrication des dispositifs médicaux - Partie 1: Analyse et gestion des risques

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Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 1: Analysis and management of risk

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Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden - Teil 1: Analyse und Handhabung von Risiken

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Foreword

This European Standard has been prepared by Technical Committee CEN/TC 316 "Medical devices utilizing tissues", the secretariat of which is held by IBN.

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of an identical text or by endorsement, at the latest by March 2000, and conflicting national standards shall be withdrawn at the latest by March 2000.

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZA, which is an integral part of this standard.

This part of EN 12442 has been considered by CEN/TC 316 as one of a series of European Standards concerned with the development of European Standards for medical devices manufactured utilizing tissues or derivatives of animal origin, non-viable or rendered non-viable. These standards are:

EN 12442-2	Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 2: Controls on sourcing, collection and handling
EN 12442-3	Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible agents

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Introduction

Certain medical devices may contain materials of animal origin.

The use of animal tissues and derivatives will give performance characteristics expected to be superior to non-animal based materials such as metal, plastics or textiles. The range and quantities of materials of animal origin in medical devices vary. These materials may comprise a major part of the device (e.g. bovine/porcine heart valves, catgut sutures, haemostatic devices), a product coating or impregnation (e.g. heparin, gelatin, collagen), or an aid to the manufacturing stages of production (e.g. tallow).

EN 1441 is a general standard which specifies a procedure for the manufacturer to investigate, using available information, the safety of a medical device, including in vitro diagnostic devices or accessories, by identifying hazards and estimating the risk associated with the device. EN 12442-1 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 Part of EN 12442 can only be used in combination with EN 1441 and is not a “stand-alone” standard.

NOTE: To show compliance with this standard, its specified requirements should be fulfilled. The guidance given in the NOTES and informative Annexes is not obligatory and is not provided as a checklist for auditors.

1 Scope

1.1 This Part of EN 12442 applies to medical devices (excluding in-vitro diagnostic medical devices) manufactured utilizing animal tissue or products derived from animal tissue, which are non-viable or have been rendered non-viable. It specifies, in conjunction with EN 1441, a procedure to investigate, using available information, the safety of such devices by identifying hazards and estimating the risks associated with the device (risk analysis).

1.2 This Part of EN 12442 is intended to provide requirements and guidance on risk analysis related to the typical hazards of medical devices manufactured utilizing animal tissues or derivatives such as

a) contamination by bacteria, moulds or yeasts;
b) contamination by viruses or transmissible agents such as pathogenic entities, or agents causing spongiform encephalopathies, prions and similar entities (e.g. BSE, scrapie);
c) undesired pyrogenic, immunological or toxicological reactions.

1.3 This Part of EN 12442 does not stipulate levels of acceptability which, because they are determined by a multiplicity of factors, cannot be set down in such a standard.

1.4 In addition, this Part of EN 12442 is intended to provide requirements and guidance on risk management.

1.5 This Part of EN 12442 does not cover the utilization of human tissues in medical devices.

NOTE: There are materials which do not fall under the scope of this standard because these are not derived from animals. In this standard a specific definition of animal has been given.

1.6 This Part of EN 12442 does not describe a quality assurance system for the control of all stages of manufacture.

NOTE: Attention is drawn to the standards for quality systems (see EN ISO 9001 and EN 46001 or EN ISO 9002 and EN 46002) which relate to all stages of manufacture. It is not a requirement of this standard to have a complete quality system during manufacture but certain elements of such a system are required.

1.7 The principles of this Part of EN 12442 may also be applied by analogy to medical devices manufactured utilizing material derived from a non-vertebrate organism, in cases where the risks addressed in this standard are relevant.

2 Normative references

This European standard incorporates, by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references, the latest edition of the publication referred to applies (including amendments).

EN 1441:1997	Medical Devices - Risk Analysis
EN 12442-2:2000	Animal tissues and their derivatives utilized in the manufacture of medical devices – Part 2: Control on sourcing, collection and handling.
EN 12442-3:2000	Animal tissues and their derivatives utilized in the manufacture of medical devices – Part 3: Validation of the elimination and/or inactivation of viruses and transmissible agents.

3 Terms and definitions

For the purposes of this Part of EN 12442 the following terms and definitions apply in addition to the terms and definitions contained in EN 1441.

3.1
animal
all vertebrates including fish, amphibians, reptiles, birds and mammals, excluding humans (*Homo sapiens*) [EN 12442-2 and EN 12442-3].

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
material obtained from an animal tissue by a manufacturing process [EN 12442-2].

NOTE 1: Examples of derivatives are: hyaluronic acid, collagen, gelatin, monoclonal antibodies.

NOTE 2: Natural substances such as milk, hair, and wool are excluded by this definition.

3.4
elimination/removal
process by which the number of viruses and transmissible agents is reduced [EN 12442-3].

NOTE 1: The effectiveness of the process should be expressed mathematically in terms of a reduction factor (See Annex D of EN 12442-3:2000).

NOTE 2: Elimination/removal aims to prevent infection or pathogenic reaction caused by viruses and/or transmissible agents.

3.5
inactivation
process by which the ability to cause infection or pathogenic reaction by a virus and/or transmissible agent is reduced [EN 12442-2 and EN 12442-3].

NOTE 1: The effectiveness of the process should be expressed mathematically in terms of a reduction factor (See Annex D of EN 12442-3:2000).

NOTE 2: Inactivation aims to prevent infection by and replication of viruses or transmissible agents.

3.6
medical device
any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:
- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

NOTE: This definition is identical with that given in Council Directive 93/42/EEC.

3.7
non-viable
having no potential for metabolism or multiplication.

3.8
tissue
organization of cells and/or extra-cellular constituents [EN 12442-2 and EN 12442-3].

3.9
transmissible agents
unclassified pathogenic entities, prions and similar entities [EN 12442-3].

NOTE: e.g. BSE agent, scrapie agent.

4 Procedure

The risk analysis procedure is described in 4.1 to 4.9. The same headings as in EN 1441 have been used.

4.1 General (step 1 of Figure 1 of EN 1441:1997)

3.1 of EN 1441:1997 is applicable.

The manufacturer shall justify the use of animal material (including animal species and tissues) taking into account the expected clinical benefit and residual risk.

4.2 Identification of qualitative and quantitative characteristics related to medical devices (step 2 of Figure 1 of EN 1441:1997)

3.2 of EN 1441:1997 is applicable.

The risk analysis shall take into account:

a) the point at which viable animal tissues or derivatives are utilized in the manufacture of the medical device, and

b) the medical device manufacturer's demonstration that the medical device, at the time it is placed on the market, contains no viable animal tissues.

Note 1 of 3.2 of EN 1441:1997 is not applicable.

4.2.1 What is the intended use and how is the device to be used?

a) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.2 Is the device intended to contact the patient or other persons?

b) of Note 3 of 3.2 of EN 1441:1997 is applicable.

Additional guidance:

The quantity of material, the contact surface area and the type of the tissue coming into contact with body tissues and fluids are additional factors to consider.

NOTE: The quantity of material coming into contact may be a factor in producing systemic effects. Additionally, the structure of animal tissues being processed may affect the inactivation and/or elimination of viruses and transmissible agents, and the potential for retaining viable cells may be affected by the structure of the animal tissues and derivatives being processed. The inactivation of bacteria, moulds and yeasts may be similarly affected.

4.2.3 What materials and/or components are incorporated in the device or are used?

c) of Note 3 of 3.2 of EN 1441:1997 is applicable.

Additional guidance:

Factors that should be considered include:

a) the intended use of any animal tissue or derivative;
b) origin, species, age and feeding (including use of animal-derived protein) of animals;
c) veterinary control, possible pathogen contaminants;
d) the source location within the animal; and
e) the implementation of a production process which uses materials pooled from more than one animal.

Special attention should be paid to the nature of material utilized, from an intact tissue down to a highly purified derivative, and the method of its incorporation into the medical device.

NOTE 1: Guidance on risk analysis and risk management for transmissible agents is contained in Annex D.

NOTE 2: In the case of medical devices utilizing several relevant constituents (e.g. from various species, origin or tissues) or several similar types of constituents produced using different methods, each individual constituent should be analysed separately.

4.2.4 Is energy delivered to and/or extracted from the patient?

d) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.5 Are substances delivered to and/or extracted from the patient?

e) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.6 Are biological materials processed by the device for subsequent re-use?

f) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.7 Is the device supplied sterile or intended to be sterilized by the user or are other microbiological controls applicable?

g) of Note 3 of 3.2 of EN 1441:1997 is applicable.

Additional guidance:

Given the biological nature of animal tissues or derivatives, variations in the initial bioburden should be considered. (See for example EN 1174-1 and EN ISO 14160).

4.2.8 Is the device intended to modify the patient environment?

h) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.9 Are measurements made?

i) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.10 Is the device interpretative?

j) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.11 Is the device intended to control or to interact with other devices or drugs?

k) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.12 Are there unwanted outputs of energy or substances?

l) of Note 3 of 3.2 of EN 1441:1997 is applicable.

Additional guidance:

The possible presence of toxic residue related to the manufacturing process utilized should be considered due to the physical characteristics (e.g. porosity, heterogeneity) and chemical composition of animal tissues or derivatives.

4.2.13 Is the device susceptible to environmental influences?

m) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.14 Are there essential consumables or accessories associated with the device?

n) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.15 Is maintenance and/or calibration necessary?

o) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.16 Does the device contain software?

p) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.17 Does the device have a restricted "shelf-life"?

q) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.18 Possible delayed and/or long term use effects?

r) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.19 To what mechanical forces will the device be subjected?

s) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.20 What determines the lifetime of the device?

t) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.2.21 Is the device intended for single use or re-use?

u) of Note 3 of 3.2 of EN 1441:1997 is applicable.

4.3 Identification of possible hazards (step 3 of Figure 1 of EN 1441:1997)

3.3 of EN 1441:1997 is applicable with the following addition:

The possible hazards associated with animal tissues or derivatives shall be identified and documented. Particular attention shall be applied to possible hazards posed by animal tissues or derivatives with regard to:

- Potential contamination by bacteria, moulds, yeasts, parasites, viruses and transmissible agents and their susceptibility to elimination and/or inactivation during processing.
- Potential for contaminants on the finished material which may cause an undesired