INTRODUCTION

This document has been elaborated to provide guidance to Notified Bodies, manufacturers and interested parties on the assessment of medical devices covered by Active Implantable Medical Device directive and Medical Device directive incorporating materials of animal origin. This principally relates to class III devices and associated conformity assessment procedures shall apply. The use of this document shall also be considered where materials of animal origin are used in manufacturing processes but where the materials are not included in the final device.

NOTE: The manufacture of some devices may use industrial raw materials, which contain small amounts of substances derived from animal tissues (e.g. tallow) through a chemical/physical process, which is likely to destroy the structure of the original molecules. Where such chemicals (e.g. stearates in plastics) are not intended to have any direct effect in relation to the medical function of the device and to be released into the body (see risk analysis), then the application of some of the following guidance may not be relevant. This is justified by the fact that the intensive industrial processing of the substance has removed the original characteristics, which are specific to the animal tissue as well as the risk of transmission of many pathogens.

1. MEETING THE ESSENTIAL REQUIREMENTS – RELEVANT STANDARDS AND OTHER DOCUMENTS.

1.1. Essential Requirements:

Essential requirements 1 - 6 of Directive 93/42/EEC of 14 June 1993 stipulate the requirements for the safety of the device, more specific requirements regarding 'Infection and microbial contamination' are detailed in Essential Requirements 8.1 and 8.2 (see Appendix 1).

The primary principle is to "eliminate or reduce risk as far as possible" and "provide optimal security"; these concepts are paramount during assessment. The application of these primary principles shall also take into account the benefit of the device as well as the generally acknowledged state of the art. It shall be understood that the risk considered in the benefit/risk analysis includes the current epidemiological risk. Furthermore it shall be considered to what extent alternative materials to those of animal origin are available and can be used. Bearing in mind the special risk of TSE (Transmissible Spongiform Encephalopathies), a rationale shall be provided for the use of ruminant origin material.

Where relevant and taking into account the risk analysis and risk management, identified residual risks shall be mentioned (including, where appropriate, the presence of a specific substance of animal origin) in the information provided with the device as required in essential requirements 2 and 13 (see Appendix 1).

1.2. Risk Analysis and Management:

In order to provide optimal security, minimisation of risks shall address all relevant aspects including those in relation to:

- Animals (species – see 2.2 and appendices 2 and 4).
- Sourcing (including geographical origin – see 2.2, 2.3 and appendix 4).
- Nature of starting material used.
- Methods used to remove and/or inactivate viruses or transmissible agents.
- Quantities of animal starting material required to produce one unit of the medical device.
- Quantities of material of animal origin coming into contact with the patients and users
- Route of administration.

These aspects are interrelated and all of them shall be considered during risk analysis. The risk management strategy will be a combination of measures related to some or all of these aspects (see 1.3).

The chosen approach shall be justified in the documentation submitted to a Notified Body and be explicitly addressed in the overall risk analysis and management.

1.3. Harmonised Standards:

Drafts of harmonised standards addressing the use of animal materials (see definition of "animal" in Appendix 2) in medical devices are available:

pr EN 12442 Animal tissues and their derivatives utilised in the manufacture of medical devices -

Part 1: Analysis and management of risk

Part 2: Controls on sourcing, collection and handling

Part 3: Validation of the elimination and/or inactivation of viruses and transmissible agents (see definition of "transmissible agents" in appendix 2).

These documents shall be utilised when performing an assessment of medical devices containing materials of animal origin. Notified Bodies shall apply the principles described in these documents as the basis for their assessment methodology. If a manufacturer chooses to follow a different approach, its relevance and adequacy in achieving an ***adequate*** level of safety has to be demonstrated.

Other guidance documents and standards are available from national, European and international sources, which may provide useful background information. Currently available documents are detailed in the bibliography.

The following standards address the essential requirements 8.1 and 8.2:

1.3.1 pr EN 12442-1: Animal tissues and their derivatives utilised in the manufacture of medical devices - Part 1: Analysis and management of risk (see appendix 2)

This standard provides requirements and guidance on:

- Definitions: ***Transmissible agents has been defined in prEN 12442-1. This term is equivalent to "Transferable agents" used in section 8.2 of Annex 1 of Directive 93/42/EEC.***
  Several definitions including "animal", "tissue", "cell", "derivative", "transmissible agents" are provided in prEN 12442-1. The definitions provided complement those in Directive 93/42/EEC.
- Risk analysis: by providing additional requirements and guidance to EN 1441,
- Risk management: Risk management shall be implemented by taking into account separately the risks related to viruses and transmissible agents. After having defined the characteristics of the product, the medical device manufacturer shall comply with the relevant requirements of Part 2 and Part 3 of prEN 12442 cumulatively. The manufacturer shall document his rationale and justification for any requirements considered not to be relevant (see 2.2).

NOTE 1: For medical devices which cannot withstand an inactivation process, without undergoing unacceptable degradation, medical device manufacturers may rely principally on Part 2 of prEN 12442 in order to meet the requirements of this Part.

NOTE 2: When the animal species is such that manufacturers cannot fully meet the requirements of Part 2 of prEN 12442, they should demonstrate a level of inactivation of viruses and transmissible agents in a validated manufacturing process, as required in Part 3 of prEN 12442, in order to meet the requirements of this Part of prEN 12442

This part of the standard also provides a specific guidance on risk analysis and risk management for transmissible agents.

1.3.2 pr EN 12442-2: Animal tissues and their derivatives utilised in the manufacture of medical devices - Part 2: Controls on sourcing, collection and handling (see appendices 2 and 4)

This standard provides requirements and guidance on:

- Quality system for the collection (including traceability),
- Requirements or guidance on the veterinarian surveillance of the animals and the slaughter,
- Requirements or guidance to avoid further cross-contamination during dissection, storage and transport.

This part of the standard also provides a specific Annex for additional requirements relating to bovine sourced materials.

1.3.3 pr EN 12442-3: Animal tissues and their derivatives utilised in the manufacture of medical devices - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible agents (see appendix 3).

This standard provides requirements and guidance on:

- Quality system for the inactivation/elimination studies,
- Requirements or guidance to assess that inactivation/elimination studies' parameters are equivalent to those of the manufacturing process,
- Requirements or guidance to design and perform inactivation/elimination studies,
- Requirements or guidance on the role of literature search.

1.4. Additional relevant Decisions and Opinions:

Particular attention is drawn to the Decisions taken at Community level in relation to the restriction of use of defined material from animal origin for the manufacture of medical devices.

The concept of level of infectivity in relation to the nature of tissues, and the concept of incidence are currently in evolution. In bibliography, the latest available versions of such concepts at the moment of issuance of the present document are referenced.

The manufacturer of medical devices shall not involve the use of "high infectivity" tissues[1] taking also into account the origin of the animal and other relevant parameters (see bibliography), unless the use of such tissues may under exceptional circumstances be justified, taking into account the benefit for the patient and the absence of adequate therapeutic alternative.

The Scientific Steering Committee[2] has adopted an opinion on the safety of gelatine dated 26-27 March 1998 (see bibliography).

The Scientific Steering Committee has also adopted an opinion on the safety of tallow derived from ruminant tissues, dated 26-27 March 1998 (see bibliography).

The Scientific Steering Committee has also adopted an opinion on BSE risk, dated 26-27 March 1998 (see bibliography).

The Scientific Steering Committee has also adopted an opinion on the definition of BSE risk for specified geographical areas, dated 23 January 1998 (see bibliography).

The Scientific Committee on Medicinal Products and Medical Devices has also adopted an opinion on the equivalency of alternative products to intestines of

[1] The definition of such tissues is provided in World Health Organization report as Category I.

[2] The web site of the Scientific Committees can be consulted: http://europa.eu.int/comm/dg24 (choose icons "Consumer health protection" "Scientific Committees").

animal origin for use as surgical sutures, dated 16 September 1998 (see bibliography).

The manufacturer shall duly take into account the aforementioned opinions of the Scientific Committee and follow further developments in this area.

2. DOCUMENTATION REQUIREMENTS

2.1 Manufacturers' documentation

Examples of documentation are laid down in prEN 12442-1, prEN 12442-2 and prEN 12442-3.

2.2 Documentation provided to the Notified Body by manufacturers

Documentation provided to the Notified Body by manufacturers shall enable the Notified Body to assess conformance with the requirements of the directives in relation to the utilization of animal material.

The result of the risk analysis report[3], including a rationale on the use of animal origin material, shall be submitted to the Notified Body (e.g. see directive 93/42/EEC, annex II point 3.2.c and 4.2 or annex III point 3 as appropriate).

The following documentation shall also be provided, depending on the nature of the material used:

- Information from the risk analysis report on the origin of animal material used (animal species, animal age, animal feeding, nature of tissue, quantity...)
- Statement on the presence of animal materials in the finished device and/or utilised during manufacture.
- Certificates or other documents establishing the origin of the animals,
- Certificates or documents to demonstrate conformance with veterinary inspection criteria and the nature of this inspection.
- Documentation related to the slaughtering of animals, and contractual arrangements with the abattoir.
- Documentation and work instructions relating to the collection, transport and storage of the material.
- Documentation relating to controls performed on raw materials and/or final product.
- Detailed documentation describing the inactivation/elimination process and validation of this inactivation/elimination process.
- Manufacturers audit and review of sub-contractors.

Where it is not possible to provide a part of this documentation, a justification shall be given with reference to the risk analysis.

[3] The risk analysis report is described in prEN 12442-1, clause 4.9.

2.3 Specific guidance for Notified Bodies

All information contained in section 1 of the present document is relevant for Notified Bodies activities.

Essential Requirements 8.2 requires Notified Bodies to retain information on the geographical origin of the animals. The concept of geographical origin includes place of birth, rearing and slaughtering. Special consideration shall be given to the feeding practices for transmissible agent's susceptible species. The depth of information required shall be commensurate with the risk of the material and the reliance on sourcing as a means of risk management.

Notified Bodies are not required to hold all batch specific information, which shall be available from the manufacturer on request. Nevertheless, the Notified Body shall be aware of how this information is kept by the manufacturer.

The manufacturer shall inform the Notified Body of changes in the geographical origin of animals, the incidence of BSE in a source country, sourcing, processing and use of animal materials.

3. CONDUCT OF CONFORMITY ASSESSMENT

The Notified Body shall review the documentation (see 2.2) as part of the assessment process (e.g. see directive 93/42/EEC).

The processes involved in sourcing control and handling and inactivation of relevant animal materials are to be considered as "special processes". Any substantial change of the quality assurance system in relation to special processes shall be notified to the Notified Body for the purpose of an additional approval prior to its implementation.

Notified Bodies shall pay particular attention to verification of manufacturer's control of raw materials, finished products and subcontractors. Notified Bodies shall consider and document the need to audit matters relating to sourcing including subcontractors.

4. NOTIFIED BODY'S SPECIFIC PROCEDURES AND EXPERTISE

4.1 Notified Bodies internal procedures

Notified Body shall establish and implement internal policy and procedures for assessing medical devices manufactured from materials of animal origin.

4.2 Expertise

The Notified Body shall possess relevant knowledge in order to:

- Identify the potential hazards and estimate the associated risks arising from the use of animal materials for the manufacture of medical devices,
- Evaluate the manufacturer's risk analysis and risk management strategy,

- Evaluate information provided by the manufacturer including information referred to in section 2.2,
- Interpret the results of any elimination and/or inactivation study and/or literature search.

This knowledge shall reside within the Notified Body, which may be supplemented by external experts. Such external experts shall have a sufficient in depth and up to date knowledge in the field concerned.

The Notified Body shall maintain awareness of legislation relevant to a particular application and of the incidence of animal disease in sourced countries.

5. BIBLIOGRAPHY

- Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (Official Journal of European Communities No. L 169/L)
- Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (Official Journal of European Communities No. L 189/17)
- pr EN 12442-1 : Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 1 : Analysis and management of risk.
- pr EN 12442-2 : Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 2 : Controls on sourcing, collection and handling.
- pr EN 12442-3 : Animal tissues and their derivatives utilized in the manufacture of medical devices - Part 3 : Validating of the elimination and/or inactivation of viruses and transmissible agents.
- European guideline CPMP/BWP/268/95, FINAL version 2 «Note for guidance on virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses.
- Notification on the marketing authorization and registration of drugs, Measures to avert risks associated with drugs, stage II, of March 28, 1996 of the Bundesinstitut für Arzneimittel, Germany (BfArM).
- Guidelines for minimizing the risk of transmission of agents causing spongiform encephalopathies via medicinal products - III/3298/91 - EN FINAL.
- Note for Guidance for minimising the risk of transmitting animal Spongiform Encephalopathy Agents via medicinal products - EMEA - CPMP/BWP/877/96 - draft of October 1997
- Commission decision 98/256/EC, Official Journal no. L113, 15.4.1998, p. 32
- Opinion of the Scientific Steering Committee on the safety of meat and bone meal from mammalian animals naturally or experimentally susceptible to transmissible spongiform encephalopathies (March 1998).
- Listing of Specified Risk Materials: a scheme for assessing relative risks to man.
- Opinion on BSE risk adopted by the Scientific Steering Committee at its plenary meeting of 26-27 March 1998, following a public consultation on the preliminary opinion adopted on 19-20 February 1998.
- Opinion on the Safety of Gelatine adopted at the Scientific Steering Committee at its plenary meeting of 26-27 March 1998 following a public consultation on the preliminary opinion adopted on 19-20 February 1998 (Version updated on 3.04.1998) – Background
- Opinion on the Safety of tallow derived from ruminant tissues – Background

- Opinion & report on the equivalency of alternative products to intestines of animal origin for use as surgical sutures adopted by the Scientific Committee on Medicinal Products and Medical Devices on 16 September 1998.
- Opinion of the Scientific Steering Committee on defining the BSE risk for specified geographical areas – 23 January 1998

APPENDIX 1

Essential Requirements Of Directive 93/42/Eec Relating To Infection And Microbial Contamination

8.1. The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.

8.2. Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues.

Notified Bodies shall retain information on the geographical origin of the animals.

Processing, preservation, testing and handling of tissues, cells and substances of animal origin must be carried out so as to provide optimal security. In particular safety with regard to viruses and other transferable agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process.

Essential requirements of Directive 93/42/EEC relating to labelling:

2. ... - inform users of the residual risks due to any shortcomings of the protection measures adopted.

13.3.k any warnings and/or precautions to take

13.6.e where appropriate, information to avoid certain risks in connection with implantation of the device

APPENDIX 2

Definitions and requirements for sourcing from Pren 12442-1 + pren 12442-2 (extracts)

Definition of "animal" from pr EN 12442-1:
All vertebrates including fish, amphibians, reptiles, birds and mammals, excluding humans (Homo sapiens).

Definition of "Transmissible agents" from pr EN 12442-1:
Unclassified pathogenic entities, prions and similar entities.
Note: e.g. BSE agent, scrapie agent.

Requirements on sourcing from pr EN 12442-2:

6 Sourcing of animal materials: Inspection, certification and traceability

6.1 Sourcing of animal material shall where technically practicable 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). If individual animals cannot be inspected, the justification for this shall be documented and a relevant sampling plan provided. To minimize the potential risk of the causative agents of spongiform encephalopathies in medical devices the requirements of normative Annex A shall be applied to relevant animal species.

6.2 Material of animal origin intended for utilization in medical devices shall have originated from animals confirmed by a veterinarian as being fit for human consumption. For species not usually consumed by humans a status equivalent to "fit for human consumption" is required. Records to demonstrate conformance with veterinary inspection criteria at the abattoir, certificate details and source shall be available.

NOTE: Animals should be subject to ante-mortem veterinary inspection. Prior to certification, a post-mortem inspection should be performed immediately after slaughter and should include:

a) visual inspection;
b) palpation of specified organs;
c) incision of organs and lymph nodes;
d) investigation of anomalies, for example inconsistency, colour, and smell;
e) if necessary laboratory tests.

6.4 Depending on the source species of the tissues used, the perceived risk from pathogens, and the ability to obtain appropriate assurances, it may be necessary to specify the origin of the animals (such as place of birth; country, region or farm of rearing; and place of slaughter) and to obtain additional assurances on their state of health and system of management (see Part 1 of EN 12442). (For bovine species, see Annex A).

NOTE: When official information systems are in place, animals should be individually traceable, where the results of the risk analysis indicate that this is necessary.

APPENDIX 3

Requirements On Literature Search From Pr En 12442-3

5 Literature search

5.1 Conduct of the literature search
A literature search shall be performed as specified in Annex A, to identify and analyse data on the elimination and/or inactivation of viruses and transmissible agents (see C.2).

5.2 Application of literature search output
Technical information from the literature search shall be used in optimising the design of an inactivation and/or elimination study.

Any extrapolation based on the inactivation of viruses and transmissible agents shall be justified and documented.

Intrinsic variability of materials of animal origin utilised in medical devices and of manufacturing processes can lead to misinterpretation of the validity of published data and shall be taken into account.

5.3 Viruses
The manufacturer shall demonstrate whether the literature search provides an indication of which inactivation and/or elimination steps are likely to be effective and is a prerequisite to performing a viral inactivation study. In exceptional cases, if a manufacturer chooses not to perform a study this shall be justified and documented.

5.4 Transmissible agents
The manufacturer shall demonstrate whether the literature search provides an indication of which methods are likely to be effective in the elimination and/or inactivation of transmissible agents. In particular it shall be demonstrated that the specific materials of animal origin and the specific processes referred to in the literature are comparable to those used for the medical devices concerned. Where the materials or processes are not comparable, an inactivation study shall be performed.
If the available information does not support the elimination and/or inactivation of transmissible agents, then an alternative risk management strategy shall be implemented (see EN 12442-1).

APPENDIX 4

Requirements And Guidance On Bse/Tse Risks In Pr En 12442-2

Annex A of prEN 12442-2 stipulates

Additional requirements relating to the application of Part 2 of EN 12442 for bovine sourced materials

NOTE 1: Taking into account the current state of science and technology, similar principles to those discussed in this annex should also be applicable to other transmissible spongiform encephalopathies in animals.

NOTE 2: The agent that causes BSE presents a hazard to humans. Experimentally it has been shown that sheep and goats are susceptible to the BSE agent via the oral route The risk from the hazard of BSE will vary with the incidence of BSE in cattle, which will depend on the measures taken by government competent authorities to prevent, control or eradicate the disease. Determination of incidence of disease depends on the extent and quality of surveillance measures. The best guarantees can be given when the results of effective surveillance show that neither BSE nor scrapie exists in a country, region, herd or flock.

A.1 General aspects

Assurance on BSE incidence shall be verified using the latest information from OIE (Office International des Epizooties, Paris) and FAO (Food and Agricultural Organization, Rome), taking into account the most recent information from relevant government competent authorities. The manufacturer shall assess the incidence and trend using at least the last 3 years' data and preferably the last 5 years' data.

NOTE: The aim is to source all tissues from countries which present little or no risk. It is acknowledged that this may not always be achievable. The highest risk will be represented by high risk tissues (e.g. brain, spinal cord and eye) derived from countries of high incidence. Whether or not a risk is unacceptably high will depend on the use to which the tissue is put. Risk analysis and risk management are addressed in Part 1 of EN 12442.

The use of tissues of bovine origin shall take into account the following factors:

a) the BSE status of the country, the herd(s) or origin of the animals and the breeding history (maternal line) (see also Annex A.2);

NOTE:Factors involved in the BSE status of a country include:
i) the incidence of disease in the country,
ii) whether or not there is compulsory notification of disease (official veterinary surveillance),
iii) whether there is compulsory clinical and laboratory verification of suspected cases.

b) the age of the donor animals; and the nature of tissues used (see Annex E of Part 1 of EN 12442);

NOTE: As clinical BSE has not been diagnosed in young animals (less than 20 months), sourcing from animals particularly under 6 months of age gives an additional level of safety.

c) whether or not the tissues will be pooled or derived from single animals, and
d) feeding history (A.3).

A higher level of risk shall be assumed if a collected tissue cannot comply with the above criteria.

pr EN 12 442-2 is defining a "low risk herd"
Low risk herd ("closed herd"): a herd in which for at least the previous six 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) each animal is traceable, and
f) genetic material has been introduced only from herds with the same BSE-free status.

NOTE: Attention is drawn to possible future regulatory definition of this term

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欧州委員会

DG ENTERPRISE

Directorate G

ユニット 4 － 圧力設備、医療用具、方法

医療用具：ガイダンス文書

MEDDEV 2.5-8 rev 2

1999 年 2 月

動物由来材料を組み込んだ医療用具のウイルスおよび伝染性病原体についての評価に関するガイドライン

本ガイドラインは、様々な利害関係者との協議プロセスを通して慎重に原案が作成され、この間に中間案の回覧と本文書へのコメント募集が行われた。したがって、本文書は特に、加盟国の監督官庁（Competent Authorities）と委員会業務（Commission Services）、届出がなされた機関（Notified Bodies）、業界、および医療用具分野の他の利害関係者の代表の立場を反映している。

本ガイドラインは合法的であるが、拘束力はない。特定の状況では、例えば、科学が発達した結果として、法的要件を満たすために代替アプローチが可能または適切となる場合もある。本ガイドライン文書では、「しなければならない（shall）」という語を用いている；本ガイドラインへの適合を求めるには、これらの要素について必ず対処せねばならない。

目次

ページ

緒言

本文書は、届出機関、製造業者、利害関係者に対して、Active Implantable Medical Device directive（人体内に埋め込み留置する動力を備えた医療用具に関する指令）およびMedical Device directive（医療用具に関する指令）の対象となる、動物由来材料の組み込まれた医療用具の評価に関するガイダンスを提供するために作成された。これは原則的にクラス III 医療用具に関するものであり、関連する適合性評価手順を適用しなければならない。動物由来の材料が製造工程は用いられるが最終医療用具に含まれない場合にも、本文書の使用を考慮しなければならない。

注：一部の医療用具の製造において、少量の動物組織由来物質（獣脂など）を含む工業用原料が用いられることがある。これらは、化学的／物理的プロセスにより元の分子の構造が破壊される可能性が高い。このような化学物質（例、プラスチックにおけるステアリン酸塩）が医療用具の機能面に直接的影響を及ぼすこと、および体内に放出されることが意図されていない場合（リスク分析参照）、以下のガイダンスの全面的な適用は不適切となることもある。このことは、物質が強力な工業的プロセッシングを受けることで元の動物組織に特異的な特性ならびに多くの病原体伝染のリスクが取り除かれるという事実から正当化される。

1. 基本要件への適合－関連する基準およびその他の文書

1.1. 基本要件：

Directive 93/42/EEC（1993 年 6 月 14 日付け）の基本要件 1～6 は、医療用具の安全性に関する要件を規定している。「感染および微生物汚染」に関する、より具体的な要件は基本要件 8.1 および 8.2 に詳述されている（付録 1 参照）。

第一原則は、「可能な限りのリスク除去または削減」および「最大の安全の確保」である；これらの概念は、評価における最優先事項である。これらの第一原則の適用にあたっては、医療用具のベネフィットならびに一般に認められている最先端技術も考慮しなければならない。また、ベネフィット／リスク分析で検討されるリスクには、最新の疫学的リスクを含めることを認識しなければならない。さらに、動物由来材料の代替となる材料がどの程度入手でき、どの程度使用できるかも考慮しなければならない。反芻

動物由来材料を使用する場合、TSE（感染性海綿状脳症）の特別なリスクを念頭において、それを使用する理論的根拠を示さなければならない。

リスク分析およびリスクマネジメントが適切であり、これらを考慮する場合、基本要件2および13（付録1参照）において求められているように、特定された残留リスクについて医療用具に関する提供情報上で言及しなければならない（適切な場合には、動物由来の特定物質の存在を含める）。

1.2. リスク分析とリスクマネジメント

最大の安全を期するため、以下の関連項目を含めて、すべての関連項目についてリスク最小化の取り組みをしなければならない：

- 動物（動物種－2.2および付録2、4参照）
- 調達（地勢学的な起源を含む－2.2、2.3および付録4参照）
- 使用する出発原料の性質
- ウイルスまたは伝染性病原体を除去および／または失活するために用いる方法
- 1単位の医療用具の製造に必要とされる動物性出発原料の量
- 患者およびユーザーと接触する動物由来材料の量
- 投与経路

リスク分析では、これらの項目を相互に関連付け、そのすべてを考慮しなければならない。リスクマネジメントストラテジーは、これらの項目の一部または全部に関連した手段の組み合わせである（1.3参照）。

選択したアプローチについては、届出機関に提出する文書にその根拠を示し、全体的なリスク分析とリスクマネジメントにおいて明確に言及しなければならない。

1.3. ハーモナイズされた基準：

以下の医療用具における動物由来材料の使用について言及している、ハーモナイズされた基準案（付録2の「動物」の定義を参照）が利用できる：

pr EN 12442　医療用具の製造に用いられる動物組織およびその派生物－

パート１：　リスクの分析とマネジメント

パート２：　調達、収集、取扱いの管理

パート３：　ウイルスおよび伝染性病原体の除去および／または失活の妥当性確認（付録２の「伝染性病原体」の定義を参照）

これらの文書を利用しなければならないのは、動物由来材料を含む医療用具の評価を行なう場合である。届出機関は、評価方法の基礎としてこれらの文書に説明された原則を適用しなければならない。製造業者が別のアプローチに従うことを選択した場合、適切な安全性レベルを達成する上でのその関連性と適切性を実証する必要がある。

他のガイダンス文書および基準は、＄国内、欧州の情報源、および国際的な情報源から入手することができ、これらから有用な背景情報が得られることがある。現在利用可能な文書は、参考文献の項に示している。

以下の基準は、基本要件 8.1 および 8.2 について言及したものである：

1.3.1　pr EN 12442-1：医療用具の製造に用いられる動物組織およびその派生物－パート1：リスクの分析とマネジメント（付録２参照）

本基準は、以下に関する要件およびガイダンスとなる：

- **定義：伝染性病原体（Transmissible agents）は prEN 12442-1 に定義されている。この用語は、Directive 93/42/EEC の付属文書 1 のセクション 8.2 で使用されている「伝達性病原体（Transferable agents）」と同義である。**
  「動物」、「組織」、「細胞」、「派生物」、「伝染性病原体」等のいくつかの定義が、prEN 12442-1 に記載されている。これらの定義は、Directive 93/42/EEC の定義を補足するものである。

- リスク分析：EN 1441 の追加要件およびガイダンスの提示による

・ リスクマネジメント：リスクマネジメントは、ウイルスおよび伝染性病原体に関するリスクを個別に考慮して実施されなければならない。医療用具の製造業者は、製品の特性を定義した後、prEN 12442 の Part 2 および Part 3 の関係のある要件のいずれにも従わなければならない。製造業者は、関係ないと判断したあらゆる要件についてその理論的根拠と正当化する理由を文書化しなければならない（2.2 参照）。

注 1： 失活プロセスに耐性がない医療用具については、医療用具の製造業者は、許容できない劣化が起きなければ、このパートの要件を満たすため、主に prEN 12442 の Part 2 に依存できる。

注 2： 動物種が、製造業者にとって prEN 12442 の Part 2 の要件を完全に満たすことができないものである場合、prEN 12442 の Part 3 に要求されているように、prEN 12442 のこのパートの要件を満たすため、製造業者は妥当性が確認された製造工程におけるウイルスおよび伝染性病原体の失活の程度を実証しなければならない。

本基準の本パートは、伝染性病原体のリスク分析およびリスクマネジメントの特異的ガイダンスにもなる。

1.3.2 pr EN 12442-2：医療用具の製造に用いられる動物組織およびその派生物－パート 2：調達、収集、取扱いの管理（付録 2 および 4 参照）

本基準は、以下に関する要件およびガイダンスとなる：

・ 収集のための品質システム（トレーサビリティを含む）
・ 動物および屠殺の獣医学的監視に関する要件またはガイダンス
・ 解体、保管、輸送中のさらなる交差汚染を避けるための要件またはガイダンス

本基準の本パートは、ウシ由来材料に関する追加要件についての特異的な付属文書にもなる。