

Assessment of Medical Devices Incorporating Material of Animal Origin – Information Required by TÜV SÜD Product Service as the Notified Body

Conformity with Council Directive 93/42/EEC and Commission Directive 2003/32/EC

For all medical devices incorporating tissue or its derivatives obtained from TSE-relevant species, a consultation procedure has to be initiated. A detailed evaluation report has to be submitted by the Notified Body to the competent authority, seeking their opinion on the evaluation of and conclusion on the risk analysis and risk management as established by the manufacturer.

For the purpose of the consultation process, TÜV SÜD Product Service has to establish an evaluation and conclusion report. This report includes an assessment of the risk analysis and risk management strategy, as well as studies of the methods applied for TSE/BSE inactivation.

The documentation provided by the manufacturer should, with respect to material of animal origin, particularly address the following points:

- 1. Product description and composition**
- 2. Information on intended use (including a current IFU)**
- 3. Nature of the starting tissue(s), animal species, and geographical source(s)**

3.1 Geographical origin and boarding of animals

Species:
Country:
Herd:
Feeding:
Age:

3.2 Origin of material used/nature of starting tissue

(Specified risk material: organ, tissue, body fluid?)
For TSE-relevant species:
Is a certificate of suitability of starting materials with respect to TSE issued by EDQM available?

3.3 Veterinary controls

Required certificates:
Certificate demonstrating conformance with veterinary inspection criteria indicating that the raw material was fit for human consumption. Certificate documenting that the applied techniques for stunning and slaughtering were suitable to avoid cross-contamination with specified risk material. (References: EN 12442-2/SSC guidelines/EC decisions.)

4. A description of the key elements adopted to minimize the risk of infection:

4.1 Risk analysis of the manufacturer

Risk analysis performed according to EN 14971 and EN 12442-1.

Including immunological, toxicological, and liquid sterilization risks.

4.2 Documentation of significant processing steps

A flowchart including the starting material and all intermediate and relevant process parameters such as temperature, duration, and pH are required. Furthermore, a detailed description of the manufacturing process including in-process controls shall be provided.

4.3 Procedure for reduction or inactivation of potentially existing infectious agents

With respect to infectious agents (viruses, TSE) a current study on the validation of the inactivation/elimination potential of defined production steps shall be included. A current literature survey on potential relevant zoonoses is required. Furthermore, risk of contamination during processing and potential contaminants on the finished material shall be addressed, as well as measures adopted to avoid contamination and to decontaminate the facility following a contamination.

4.4 Slaughtering, transport, and handling

Include a statement and respective certificates that requirements of Regulation 1774/2002/EC are met. Traceability: Will a lot-wise documentation of individual animals be implemented? Measures adopted to avoid cross-contamination during slaughter, transport, and storage?

4.5 Combination with other medical devices

Does combination with other medical devices have an impact on the materials of animal origin used?

4.6 Score obtained according to the internal scheme (see attachment)

Risk assessment and Sum of Category Numbers (SCN) for TSE-relevant material only.

4.7 Labeling, instructions for use

Labeling (and/or) IFU clearly indicate(s) the relevant animal materials.

5. An estimate of the TSE risk arising from the use of the product, taking into account the likelihood of contamination of the product, and the nature and duration of patient exposure:

5.1 Quantity of raw material per medical product

Raw material required for one daily dose: (Certificates to be provided for all tissues and derivatives including gelatine, tallow, and collagen).

5.2 Possible number of applications of medical device

Number of daily doses

5.3 Route of application

(Product coming into contact with the central nervous system region, central circulatory system, damaged/breached skin, mucosal membrane, undamaged skin, etc.)

6. A justification for the use of animal tissues or derivatives in the medical device, including a rationale for the acceptability of the overall (TSE) risk estimate, the evaluation of alternative materials, and the expected clinical benefit

Additionally required:

6.1 Clinical benefit

- Justification for the use of material of animal origin
- Critical discussion of alternatives (synthetic, allogenic, autologous, or xenogenic material from non-TSE-relevant species)
- Unique characteristics of the product under consideration

6.2 Biological hazards

Potential for the finished material to cause harm with respect to the following reactions has to be indicated: pyrogenic, immunological, toxicological.

7. The approach to the auditing of source establishments and/or third party suppliers for the animal material used by the device manufacturer

Documentation of the contractual agreements and the procedures in place with regard to the auditing of source establishments and/or third party suppliers for the animal material used by the medical device manufacturer.

Table 1:
Assessment of the risk of a medical device containing animal material to transmit TSE agents

Parameter	Numbers of risk categories (CN)				
	I	II	III	IV	CN
Geographical origin	GBR IV Incidence < 1 : 10000	GBR III Incidence < 1 : 1 million	GBR II Others	GBR I No BSE, no risk	
Specified risk material	High risk	Medium risk	Low risk	No risk	
Inactivation	None	2–4 log	4–6 log	> 6 log	
Quantity/dose of raw material	> 100 g	1–100 g	10 mg–1 g	< 10 mg	
Route of administration	Intracerebral	Other parenteral	Mucous membrane	External skin	
Sum of Category Numbers (SCN):					

Table 2:
Risk assessment on the basis of the Sum of Category Numbers (SCN)

Sum of Category Numbers (SCN)	Significance and consequences
20	Highest possible score, virtually no risk
>12	Acceptable risk, that is lower than the risk of acquiring the sporadic form of human TSE (CJD)
10–12	Risk is acceptable only if the disease is serious and the benefit of the medical device is high and scientifically well-established
6–9	Unacceptably high risk
5	Lowest possibly score, unacceptably high risk

Applicable standards and guidelines:

- EN 12442-1, -2, -3:2000
- MEDDEV 2.8 – 5, Revision 2
- MEDDEV 2.11/1