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Certification of suitability of Monographs of the European Pharmacopoeia
Content of the dossier for a substance for TSE risk assessment

有疯牛病因子传播风险物质的申请材料内容

Strasbourg施特拉斯堡

Address: 226 Avenue de Colmar (entrance rue Schertz) B.P. 907 - F 67029 Strasbourg Cedex 1
Telephone: 33 (0) 3 88 41 30 30 - E-mail: certification@pheur.org - Fax: 33 (0) 3 88 41 27 71
Internet : http://www.pheur.org

CONTENT OF THE dossier FOR A SUBSTANCE for TSE risk assessment
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Content of the dossier.
申请材料内容

1. GENERAL INFORMATION
1. 一般信息

Nomenclature
名称

The European Pharmacopoeia monograph name, the INN, or if relevant other chemical or common name(s) should be stated together with any laboratory code used in the dossier. In addition, where appropriate, any internal codes related to special grades should be indicated.

欧洲药典个论名称，国际通用名（INN）的名称，和其他化学名称，以及所有实验室代码。此外，合适时，应说明所有特殊级别物质的内部代码。

Complete name(s) and address(es) of intended holder, manufacturer(s) and manufacturing site(s)
证书持有者，生产商和生产场地的全称和地址

The certificate will be issued to the manufacturer. In special cases where the holder of the certificate will not be the manufacturer, **a formal agreement signed** by both parties shall be provided, stating that the manufacturer wishes not to be the holder and undertakes to provide the necessary information to the authorized agent. Other parties may be mentioned on the certificate where relevant.

If other parties are involved in certain stages of the process, details of their involvement and of other site addresses must be provided and information given on the contractual arrangements regarding sole or shared responsibilities. If an additional site is to provide alternative capacity, it should be established that all measures put in place in the first site are exactly transposed to the alternative site, particularly as regards supply of raw materials, production process, quality assurance system and traceability.

证书将授予生产商。若证书持有者不是生产厂，应提供一份双方**签署的正式协议**，协议应说明生产厂不希望成为持有人，并保证向指定代理人提供必要的信息。证书上也可出现有关其他各方。

若其他各方参与了某些生产过程，应申报其参与的详情、其它生产场址详情、以及独家或共同责任方面的合同条款。如果另一个生产场地生产能力不同，则必须申报杂质含量方面的批分析结果，以证明不同的生产能力所得产品与第一个场址所得产品质量等同性。

History of the product
产品历史

Length of time on the market of the substance produced by the manufacturer according to the presented dossier as an ingredient in products licensed in Europe or in any other country. In which countries it has been used, and in which medicinal products.

欧洲制剂厂或其它国家使用该生产商按申报文件生产的产品的生产销售其制剂历史；应说明国别和制剂名称。

Declaration
声明

A signed declaration that manufacture is conducted in accordance with the dossier presented and with a suitable quality assurance system such as GMP, ISO 9000 and HACCP (hazard analysis and critical control point) assuring in particular traceability and batch consistency, is required.

A signed declaration that the manufacturer is willing to be inspected, in accordance with the relevant legislation, on the request of a relevant authority before and/or after being granted a certificate of suitability is required. In cases where the applicant is not the manufacturer, this declaration should also be provided by the authorised agent.

签字声明：说明生产工艺与申报文件相符，并符合哪一个起始物料GMP规定。应符合国际或各国正式通行的GMP。也可接受其他与GMP相似的方法，但必须证明其合理性。生产商应在申报文件中说明执行的是哪一个GMP。

签字声明：说明在适用性证书授予之前或之后，应有关主管当局要求，生产厂愿意按相关规定接受现场检查。若申请人不是生产厂，指定代理人也应提供一份声明。

2. ORIGIN OF RAW MATERIAL AND TYPE OF TISSUE USED
2. 原料来源和所用动物组织类型

Detailed information on the following is required as described in the general chapter of the Ph. Eur. 5.2.8. Minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products, paragraph 3.1, 3.2 and 3.4.

Any deviation is to be discussed and justified in the dossier itself and in the expert report (see below).

必须按欧洲药典5.2.8.“最大限度减少药品传播疯牛病因子风险＂第3.1，3.2和3.4段”规定提供提供下列详细信息。

所有不符合上述药典规定的情况都应在申报文件和专家报告中进行讨论，并证明其合理性（见下文）。

- country (ies) of origin of animals
- status of the country (ies) of origin in accordance with the Office International des Epizooties (OIE)
- where appropriate, procedure in place describing the removal of skulls/vertebrae/spinal cord, during collection of the raw materials
- procedure in place for avoiding the risk of cross-contamination
- health status of animals; are the animals declared fit for human consumption?
- type of tissues used; precise description of all anatomical pieces collected
- age of animals (or range, eg more than 1 year, less than 3 years,…)

- 动物来源国
- 按《国际动物流行病办公室（OIE）》标准所判定的来源国现状
- 可行时，原料收集过程除去颅骨/脊骨/脊髓的现行操作规程描述
- 避免交叉感染的现行操作规程
- 动物健康状况：动物是否适合人类消费？
- 所用动物的组织类型；所有动物局部的解剖学详细描写
- 动物的年龄（或大致范围，如一岁多，三岁不到等……）

Relevant certificates, e.g. veterinary certificates, should be provided

应提供相关证书，例如兽医证书

3. MANUFACTURING PROCESS
3. 生产过程

- outline of the manufacturing process, accompanied by a flow chart including the starting materials and all intermediates,

- 生产工艺流程：附流程图，图中注明起始原料和所有中间体，

- detailed description of each stage of the manufacture, including information on reagents, conditions (times and temperatures) of each step, details of the final purification; a maximum batch size should be stipulated, which should correspond to batches already manufactured and referred to in the dossier,

- 生产各步详细描述：包括试剂、各步生产条件（时间和温度），最终纯化详细描述；应规定最大批量，并与现行生产和申报文件批量一致

- when necessary, information as described in the general chapter of the Ph. Eur. 5.2.8 under paragraph 3.5 Specific products; any deviation is to be discussed and justified in the dossier itself and in the expert report (see below),

- 必要时，按欧洲药典5.2.8.第3.5段“特殊产品”要求提供信息；所有不符合上述药典规定的情况都应在申报文件和专家报告中进行讨论，并证明其合理性（见下文），

- Quality control during manufacture; description of all in-process controls in place; action limits and quality assurance system.

- 生产过程的质量控制；所有现行中间控制描述；行动限和质量保证体系。

- Validation of the process regarding TSE (refer to paragraph 3.3 Process validation of the general chapter of the Ph. Eur. 5.2.8); any deviation is to be discussed and justified in the dossier itself and in the expert report.

- 有关TSE工艺的验证（参见欧洲药典5.2.8第3.3段“工艺验证”）；所有不符合上述药典规定的情况都应在申报文件和专家报告中进行讨论，并证明其合理性

- Procedures in place in case of undesired material entering the manufacturing plant, including decontamination of the plant if infected material entered into the manufacturing, or decontamination of the production area when a different grade of the substance (eg industrial grade) is produced on the same line.

- 异物进入生产车间后的现行操作规程描述，包括传染物质进入制造过程后的污染清除操作规程，或者同一生产线生产不同级别产品（如工业级）之后的除污染措施。

4. TRACEABILITY
4. 可追踪性

- schematic presentation of the system in place to ensure traceability
  • traceability for the raw materials used in the production process
  • traceability for intermediates and final products

- description of the code numbering system (used internally/externally to distinguish from other types of products or batches produced in the same production site using different production processes)

- 保证生产具可追踪性的现行图解式流程
  • 生产过程使用的原料的可追踪性
  • 中间体和成品可追踪性

- 代码编制体系的描述（内部/外部使用的，区别其它类型产品的代码；或区别同一场地按不同工艺生产的产品的代码）

5. AUDITING SYSTEM
5. 审计体系

- Description of the system in place for auditing the suppliers of the raw materials: SOP and auditing scheme

- Description of the system in place for self-auditing: SOP and auditing scheme

- 现行原料供应商的审计体系描述:
  标准操作规程（SOP）和审计大纲

- 现行自检体系描述: SOP 和审计大纲

Expert report
专家报告

A critical evaluation of the content of the dossier should be given in the form of an expert report. The expert report should discuss the ability of the system in place to minimise the risk of TSE for the substance with particular reference to general chapter of the Ph. Eur. 5.2.8. A short curriculum vitae should be provided highlighting the experience of the expert in this field.

Particular attention is given to justifying cases where the information given differs from that requested in the Ph Eur monograph Products with risk of transmitting agents of animal spongiform encephalopathies and general chapter of the Ph Eur 5.2.8.

应以专家报告形式对申请书内容做出关键性评估。专家报告应按EP5.2.8总章要求，评价现存体系减少申报物质中疯牛病因子传播风险的能力。应提供一份专家简历，着重介绍专家在该领域内的经验。

应特别关注不同于欧洲药典“有疯牛病因子传播危险产品”和欧洲药典 5.2.8规定的信息，并证明其合理性。