



**Certification of Suitability of Monographs of
The European Pharmacopoeia**



CP/CB

PUBLIC DOCUMENT

(Level 1)

English only/Anglais seulement

PA/PH/CEP (06) 2

Strasbourg, August 2006

Certification of suitability of Monographs of the European Pharmacopoeia

**CONTENT OF THE DOSSIER FOR A SUBSTANCE
FOR TSE RISK ASSESSMENT**

CONTENT OF THE DOSSIER FOR A SUBSTANCE FOR TSE RISK ASSESSMENT

Content of the dossier

1. GENERAL INFORMATION

Nomenclature

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.

Complete name(s) and address(es) of intended holder, manufacturer(s) and manufacturing site(s)

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 authorised 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.

History of the product

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.

Declaration

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.

2. ORIGIN OF RAW MATERIAL AND TYPE OF TISSUE USED

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).

- 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,...).

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

3. MANUFACTURING PROCESS

- outline of the manufacturing process, accompanied by a flow chart including the starting materials and all intermediates,
- 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,
- 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),
- Quality control during manufacture; description of all in-process controls in place; action limits and quality assurance system,

- 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,
- 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.

4. TRACEABILITY

- 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)

5. AUDITING SYSTEM

- 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

Expert report

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.