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Certification of suitability of Monographs of the European Pharmacopoeia

Certificates of suitability for sterile active substances

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Certificates of suitability for sterile active substances

It is possible to apply for a certificate of suitability for a sterile active ingredient. The conditions and procedures for this option have been defined and are described below:

- The substance shall be sterile and shall comply with the test for sterility 2.6.1 described in the European Pharmacopoeia.
- The sterilisation process shall be described in detail in the application, together with full data on the validation of the sterilisation method.
- The company shall refer to suitable GMP rules. The *Good Manufacturing Practice for Active Pharmaceutical Ingredients* (ICH Q7A) only applies to the manufacture of sterile active pharmaceutical ingredients (APIs) up to the point immediately prior to the APIs being rendered sterile. The sterilisation and aseptic processing of sterile APIs are not covered by this guideline and shall be performed in accordance with GMP for medicinal products (Commission Directive 2003/94/EC of 8 October 2003, laying down the principles and guidelines of good manufacturing practice for medicinal products for human use and investigational medicinal products for human use, or equivalent). When a company applies for a certificate of suitability for a sterile active ingredient, declarations referring to appropriate GMP covering the sterilisation steps and subsequent aseptic handling are to be provided. Depending on the legislation in force in the country in which the manufacturer is located these steps may be subject to the holding of a manufacturing authorisation or establishment licence, and/or subject to regular inspections by a regulatory authority for medicinal products.
- Unless evidence is provided that the manufacturer is subject to routine inspections by a regulatory authority, the manufacturing site(s) involved in the sterilisation and aseptic handling of the sterile active substance will be inspected within the EDQM inspection program, (fee for inspection will also apply).
- If both sterile and non-sterile substances are produced, separate dossiers shall be submitted and separate CEPs will be granted.
- Additional fee for assessment of the sterilisation data will be required (3000 Euros).

When granted, the CEP will include the relevant subtitle (“sterile”), it will specify the sterilisation method used and will refer to the test for sterility. It will also be mentioned that the sterilisation process has been assessed and approved.

It should be noted that sterilisation of the active ingredient is generally regarded by the licensing authorities as part of finished product manufacture. Therefore data on the sterilisation process of the active substance (including validation data) should be submitted to the Marketing Authorisation applicant/holder for inclusion in the dossier submitted for the finished product and approval by the national licensing authority(ies).

For CEPs which have already been granted with the subtitle “sterile”, and for which the validation of the sterilisation process has not yet been assessed, the data have to be submitted to EDQM at the latest at the renewal of the CEP, or through a revision. The dossier will be treated as described above and the additional fee will also be applied. Failure to comply with these requirements will lead to the withdrawal of the information related to sterility aspects from the CEP.