

Certification of Substances Division

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Certification of suitability to Monographs of the European Pharmacopoeia

Note for the applicants: Procedure for validation of new applications

This document presents the measures taken for the validation of new applications for a CEP that were put in place in 2007, and also the results obtained.

1. Procedure for validation of new applications:

All applications are screened at reception to check whether they are acceptable and can be validated. The main criteria that are checked for completeness are:

- administrative information: the application form and all the declarations filled in, the signed quality overall summary and the technical dossier in CTD format are present.
- the dossier contains all the relevant sections of the CTD as described in the relevant document "Content of the dossier" (PA/PH/CEP 04 1 4R, or PA/PH/CEP (06) 2).

The evaluation clock can start only once the application has been validated. Otherwise, it is blocked and a deficiency letter is sent to the applicant together with a deadline for providing the missing documentation.

The clock will start only if the required information is received in time. Failing to provide the missing information will result in the definite closure of the procedure without reimbursement of the fees.

2. How to avoid a blockage of the application at receipt:

38% of the applications received in 2007 have been blocked at receipt. The requirements and the corresponding information which should be submitted for a new chemical application are listed below.

- in the case a complex starting material is declared, its route of synthesis should be described and its specifications suitably defined. This has been the first reason for blocking an application in 2007 (45% of the blocked applications)
- in case of an active substance, the company should provide a declaration that the manufacture of the substance takes place in accordance with the dossier presented and according to Good Manufacturing Practice for Active Substances used as Starting Materials as published in the Rules governing Medicinal Products in the European Union, Volume 4, EU Guidelines to Good Manufacturing practice for Human and Veterinary use, Part II, and Annex 1 in case of sterile substances, (10% of the blocked applications in 2007)
- the dossier should contain information showing that all solvents used during synthesis have been either properly removed or suitably limited in the specification of the final substance. The methods used to demonstrate the absence of residual solvents should be properly described and validated. (9% of the blocked applications in 2007)
- all the potential impurities of the process with their origin should be listed, correspondence with the transparency statement of the monograph should be established and individual impurity results should be provided. (8.5% of the blocked applications in 2007)
- the company should refer to the current European Pharmacopoeia monograph (6.5% of the blocked applications in 2007)
- if the substance is claimed to be sterile, the applicant should provide a description and the complete validation data for the sterilisation process.
- if a Class I solvent is used, a proper justification for doing so and suitable control of this solvent should be made,
- in case there is a non-specific TLC method in the European Pharmacopoeia monograph, the applicant should propose an alternative quantitative method.

The attention of the applicants is drawn to these points in order for them to submit applications complying with requirements and not to delay the process.