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Certification of suitability to Monographs of the European Pharmacopoeia

Use of a CEP to describe a starting material in an application for another CEP

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Introduction

As described in the EDQM guideline, Content of the dossier for chemical purity and microbiological quality, PA/PH/ CEP (04) 1 current version, "for starting materials described in the European Pharmacopoeia certificates of suitability can be provided , if available" to replace the information on the manufacture and control of the starting material.

The use of certificates of suitability (CEPs) for starting materials in an application for a chemical CEP is applicable where there is a monograph of the European Pharmacopoeia for the substance identified as a starting material as the availability of such a monograph is a pre-requisite to the issue of a CEP. Typically the substances concerned are therefore active substances and if the CEP were not available would usually be regarded as intermediates in the synthesis. The CEPs can be accepted as the manufacturing process and controls being applied have been assessed before the CEP has been granted for the starting material.

It is therefore appropriate to clarify the practical aspects of the use of one CEP for a starting material in an application for another CEP.

Conditions

The starting material must be the substance which is covered by the CEP being submitted.

The CEP application for the starting material must have already been approved by the EDQM and the corresponding CEP **must have been granted and be valid.**

A copy of the CEP for the starting material must be included in the submission for the new CEP and the box of access for the CEP must be completed appropriately.

The full specification described on the CEP for the starting material must be applied to the starting material to allow release for use in the manufacturing process for the new CEP.

Lifecycle Maintenance

Any regulatory activity on the CEP for the starting material must be complemented by the appropriate regulatory activity on the new CEP. Therefore if the CEP for the starting material is revised then a copy of the revised CEP must be submitted as a revision to the new CEP.

The submission of a revised or renewed CEP for the starting material is considered as an annual notification except in the following cases:

- The specification of the substance (starting material) covered by the revised or renewed CEP is changed, in which case a minor revision by default should be submitted.
- There is a change to the manufacturing sites mentioned on the CEP for the starting material (but no change in the specification of the starting material), in which case an immediate notification should be submitted.

If the CEP for the starting material is no longer valid (due to suspension, withdrawal or expiry) then the CEP application which references it must be updated to either delete the reference to

this CEP (where there are multiple sources of starting material described) or replace the reference to this CEP with details of another source of material. If the new source of material does not have a CEP then it will be necessary to redefine the starting material to an appropriate point earlier in the synthesis and update the CEP dossier accordingly.

Transparency of Manufacturing Supply Chain

Since the starting materials covered by a CEP are typically active substances and would usually be regarded as intermediates in the synthesis if a CEP were not available, the details of the manufacturing sites involved in the manufacturing process described in the CEP for the starting material should also be mentioned in the section "3.2.S.2.1 Manufacturers" of the submission dossier for the new CEP.

The details of all manufacturing sites involved in the manufacturing process described in the CEP for the starting material will also be mentioned in the annex 1 of the new CEP which describes the manufacturing sites.