

## Certification of Substances Division

FML/CB

### **PUBLIC DOCUMENT**

(LEVEL 1)

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## **Certification of suitability to Monographs of the European Pharmacopoeia**

### **Use of a CEP to describe a material used in an application for another CEP**

## 1. Introduction

A material which is the subject of a CEP (hereafter CEP X) may be used in the synthesis of a substance for which a separate CEP is requested (hereafter CEP Y) and may be an intermediate or a starting material in the process described for CEP Y. ICH Q11 includes information on the selection of starting materials and should provide the basis for the decision and justification of whether the material covered by CEP X is a starting material or an intermediate.

This document describes the practical aspects of a CEP submission where another CEP is referenced.

The use of CEP X in CEP Y is based on the fact that the manufacturing process and controls described in the application for CEP X have been assessed before CEP X was granted.

The applicant should make clear in the application whether the substance covered by the referenced CEP X is actually an intermediate in the manufacture of the substance covered by the new CEP Y or is a starting material.

## 2. CEP X covers a substance which is an intermediate in the synthesis described in CEP Y

### Conditions

The applicant should make clear in the submission that the substance covered by the referenced CEP X is an intermediate in the manufacture of the substance covered by the new CEP Y.

The substance which is an intermediate for the new CEP Y must be the substance which is covered by the CEP X being submitted. It is not acceptable to cross reference an existing CEP X for example, to cover an intermediate in the manufacture of the existing CEP X.

The CEP X application must have already been accepted by the EDQM and the corresponding CEP X **must have been granted and be valid**.

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

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

### Lifecycle Maintenance

Any regulatory activity on CEP X must be complemented by the appropriate regulatory activity on the CEP Y. Therefore if the referenced CEP X is revised then a copy of the revised CEP X must be submitted as a revision to the CEP Y, as described in the current version of the EDQM Guideline on Requirements for Revision/Renewal of Certificates of Suitability to the European Pharmacopoeia Monographs (PA/PH/CEP (04) 2).

If the CEP X is no longer valid (due to suspension, withdrawal or expiry etc.) then the CEP Y application which references it must be updated to either delete the reference to this CEP X (where there are multiple sources described) or replace the reference to this CEP X with details of another source of material. If the new source of material does not have a CEP then it will be necessary to define a starting material to an appropriate point earlier in the synthesis and update the CEP Y dossier accordingly.

### **Transparency of Manufacturing Supply Chain**

Where the materials covered by a referenced CEP X are considered as intermediates, the details of the manufacturing sites involved in the process for the referenced CEP X should also be mentioned in the application form and in the section "3.2.S.2.1 Manufacturers" of the submission dossier for the new CEP Y.

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

### **3. CEP X covers a substance which is a starting material in the synthesis described in CEP Y**

#### **Conditions**

The applicant should make clear in the submission that the substance covered by the referenced CEP X is a starting material in the manufacture of the substance covered by the new CEP Y.

The substance which is a starting material for the new CEP Y must be the substance which is covered by the CEP X being submitted. It is not acceptable to cross reference an existing CEP X for example, to cover an intermediate in the manufacture of the existing CEP X.

The CEP X application must have already been accepted by the EDQM and the corresponding CEP X **must have been granted and be valid.**

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

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

#### **Lifecycle Maintenance**

Any regulatory activity on CEP X must be complemented by the appropriate regulatory activity on the CEP Y. Therefore if the referenced CEP X is revised then a copy of the revised CEP X must be submitted as a revision to the CEP Y, as described in the current version of the EDQM Guideline on Requirements for Revision/Renewal of Certificates of Suitability to the European Pharmacopoeia Monographs (PA/PH/CEP (04) 2).

If the CEP X is no longer valid (due to suspension, withdrawal or expiry etc.) then the CEP Y application which references it must be updated to either delete the reference to this CEP X (where there are multiple sources described) or replace the reference to this CEP X with details of the source of starting material.

## **Transparency of Manufacturing Supply Chain**

Where the material covered by a referenced CEP X is considered as starting material, the details of the manufacturing sites involved in the process for the referenced CEP X should not be mentioned in the application form nor in the section "3.2.S.2.1 Manufacturers" of the submission dossier for the new CEP Y, but in the section "3.2.S.2.2 Control of materials".

The details of all manufacturing sites involved in the process described in the CEP X will not be mentioned in the annex 1 of the new CEP Y which describes the manufacturing sites.

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