

## Certification of Substances Division

HB/CB

### **PUBLIC DOCUMENT**

(LEVEL 1)

*English only/Anglais seulement*

**PA/PH/CEP (08) 17, R4**

Strasbourg, June 2014

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

## **SUSPENSION OR WITHDRAWAL OF A CERTIFICATE OF SUITABILITY, CLOSURE OF AN APPLICATION**

For implementation	July 2014
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This document describes the policy of the EDQM for suspension or withdrawal of a certificate of suitability (CEP) and for closure of a CEP application in accordance with the provisions of Resolution AP-CSP (07) 1 of the Council of Europe.

## 1. **DEFINITIONS**

- **CEP**: Certificate of suitability to the monographs of the European Pharmacopoeia, granted by the EDQM.
- **Suspension**: Temporary cancellation of a granted CEP made either upon request by the holder of the CEP or by a decision of the EDQM. Under certain conditions, the CEP may be restored.
- **Withdrawal**: Definitive cancellation of a granted CEP made either upon request by the holder of the CEP or by a decision of the EDQM.
- **Closure**: Cancellation of an on-going CEP application made either upon request of the holder of the CEP or by a decision of the EDQM.
- **Hearing**: A hearing provides an opportunity for the applicant or the holder of a CEP to submit a written request for re-consideration of a decision taken by the EDQM *Ad hoc* Committee (Terms of Reference section 2.6.) regarding the validity of a CEP or an application for a CEP, either in the context of the EDQM inspection programme or in the context of the evaluation of a CEP application.

## 2. **SCOPE**

This policy is applicable, but not limited to, the following situations:

### 2.1. **Suspension of a CEP**

2.1.1. The *Ad hoc* Committee may decide to suspend a CEP in the following situations:

- Inspection of a company, carried out in the framework of the EDQM Certification scheme, shows critical and/or major deficiencies leading to the conclusion that the company does not operate in compliance with EU GMP and, therefore, presents a potential risk for public health, and/or the inspection shows that the manufacturing process does not comply with the dossier submitted for the CEP.
- Inspection of a company carried out by an inspectorate of a European Economic Area (EEA) member state or a country with which the EU has a Mutual Recognition Agreement on GMP inspections of APIs (MRA) shows that the company does not operate in compliance with GMP and, where the company has submitted CEP application(s), their validity is likely to be affected by the conclusions of the inspection.
- A CEP dossier is not in compliance with the requirements of the Certification procedure and the holder has not submitted suitable information to maintain it.

2.1.2. The suspension of a CEP may also be requested by the holder of a CEP, *e.g.* if the CEP holder is not able to fulfil the commitments of the submitted CEP dossier. Typical examples are temporary cessation of production, upgrades or a partial destruction of the production site, or a temporary inability to meet the requirements of a revised Ph. Eur. monograph.

A suspension is limited to a period of 2 years. Failure to meet the conditions to lift a suspension leads to the withdrawal of the CEP if no justified extension to the suspension has been requested by the CEP holder and accepted by the EDQM.

## 2.2. Withdrawal of a CEP:

2.2.1. A CEP may be withdrawn by the EDQM *Ad hoc* Committee, for example, in the following situations:

- After an EDQM inspection, in cases where urgent action needs to be taken (a public health issue) and no corrective actions are considered possible.
- When an EDQM inspection has revealed that the CEP dossier consists of falsified data or when there is evidence of massive and systematic falsification of documents on site.
- After a CEP suspension, when the company is not able to fulfil the requirements of the Certification procedure with regards to the updating of the CEP dossier and compliance with GMP (*e.g.* repeated GMP non-compliance even if the inspections are not consecutive).
- If a CEP dossier is not in compliance with the requirements of the Certification procedure and the holder is not able to provide suitable information to maintain it.
- If the CEP holder no longer exists or has definitively ceased production of the substance without informing the EDQM.
- When a company refuses to be inspected, either at receipt of the EDQM notification, at the arrival of inspectors on site, or during the inspection. This includes any oral or written request from the company to discontinue an inspection, or delaying or restricting access to documents or areas which are considered part of the inspection scope.

2.2.2. A CEP may be withdrawn by the holder of the CEP due to, for example, cessation of production, closure of the site, or because the holder no longer wishes to retain the CEP.

A CEP that has been withdrawn cannot be restored. A new CEP application has to be submitted and will be treated as such.

## 2.3 Closure of a CEP application:

2.3.1 The EDQM *Ad Hoc* Committee may decide to close a CEP application in the following situations:

- Inspection of a company carried out in the framework of the EDQM Certification scheme shows critical and/or major deficiencies leading to the conclusion that the company does not operate in compliance with EU GMP and, therefore, presents a potential risk for public health, and/or the inspection shows that the manufacturing process does not comply with the dossier submitted for the CEP application.
- Inspection of a company carried out by an inspectorate of a European Economic Area (EEA) member state or a country with which the EU has a Mutual Recognition Agreement on GMP inspections of APIs (MRA) shows that the company does not operate in compliance with GMP and, where the company has submitted CEP application(s), their validity is likely to be affected by the conclusions of the inspection.
- Refusal by a company to be inspected in the framework of the EDQM Certification scheme, i.e. the CEP applicant does not fulfil its commitment of willingness to be subject to an inspection.

2.3.2 The assessors of the Certification procedure may decide to close a CEP application in the following situations:

- If, after assessment of the initial application and the reply to a deficiency letter, the information provided by the CEP applicant does not demonstrate compliance with the requirements of the Certification procedure, leading to the conclusion that a CEP cannot be granted.
- If the CEP applicant failed to provide an answer to a request for information in time.

2.3.3 A CEP applicant may also request the closure of an on-going CEP application. A letter should be sent by the applicant to EDQM asking for the closure. Fees are not refunded.

**Notes:**

- A CEP that reaches the 5-year validity period and for which the holder has not submitted a request for renewal expires automatically and is, therefore, invalid at the date of expiry. This case is considered outside of the scope of this procedure.
- In cases where several manufacturing sites are covered by a CEP and when an inspection of one site shows critical and/or major deficiencies leading to the conclusion that it does not operate in compliance with EU GMP or does not comply with the dossier submitted for the CEP, the EDQM requires that the CEP holder initiates a revision of the respective CEP deleting the concerned manufacturing site from the scope of the CEP.

### **3. DECISION-MAKING PROCESS AND COMMUNICATION TO THE CEP HOLDER**

#### 3.1 Suspension of a CEP

Any suspension of a CEP must be justified:

- When advised by the EDQM Certification of Substances Division in the situations described in point 2 (Scope No 2.1.1) above, by a justified recommendation from the relevant scientific officer (assessor or inspector).
- When requested by the CEP holder: by a letter sent to the EDQM asking for a suspension, explaining the reasons for the request and proposing a timetable for its restoration (Scope No 2.1.2).

In both cases, the Internal Decision Board (see Terms of Reference) reviews the recommendation for suspension and any supportive information and submits proposals to the *Ad hoc* Committee on the actions to be taken. The *Ad hoc* Committee decides on the suspension of the relevant CEP(s), as well as on the conditions for restoration and the information to be forwarded to the relevant authorities. The *Ad hoc* Committee renders its decision generally within two weeks after the end of the inspection campaign or the receipt of the request by the holder of the CEP(s). The detailed reasons (*e.g.* a list of critical and major deficiencies), the length of the suspension and the conditions for its restoration are given in the decision and communicated to the CEP holder.

#### 3.2 Withdrawal of a CEP

Any withdrawal of a CEP must be justified:

- When advised by the EDQM Certification of Substances Division in the situations described in point 2 (Scope No. 2.2.1) above, by a justified recommendation from the relevant scientific officer (assessor or inspector).
- Or by a letter from the CEP holder to the EDQM asking for the withdrawal of the CEP and explaining the reasons for the request (Scope No. 2.2.2).

In certain cases when a CEP holder requests a withdrawal of a CEP, the Internal Decision Board may review the request and any supportive information (*e.g.* public health risk or GMP non-compliance). If necessary the *Ad hoc* Committee endorses the actions to be taken.

When the withdrawal of a CEP is proposed by the EDQM Certification of Substances Division, the Internal Decision Board reviews the relevant recommendations for withdrawal, together with the supporting information. If there is a potential risk for public health or GMP non-compliance, proposals are submitted to the *Ad hoc* Committee on the actions to be taken. The *Ad hoc* Committee then decides on the withdrawal of the relevant CEP(s) and the information to be forwarded to the relevant authorities. The *Ad hoc* Committee renders its decision generally within two weeks after the end of the inspection campaign or receipt of the withdrawal request by the CEP holder.

The detailed reasons for withdrawal (*e.g.* a list of critical and major deficiencies) are given in the decision and communicated to the CEP holder.

### 3.3 Closure of an Application

Any closure of a CEP application must be justified:

- When advised by the EDQM Certification of Substances Division in the situations described in point 2 (Scope No. 2.3.1) above, by a justified recommendation from the relevant scientific officer (assessor or inspector).
- When advised by the assessors of the Certification procedure in the situations described in point 2 (Scope No. 2.3.2) above and where supported by a justified rationale.
- By a letter from the CEP applicant to the EDQM asking for the closure of the application and explaining the reasons for the request (Scope No. 2.3.3).

In certain cases when a CEP applicant requests the closure of their CEP application, the Internal Decision Board may review the request and any supportive information (*e.g.* public health risk or GMP non-compliance). If necessary the *Ad hoc* Committee endorses the actions to be taken.

When the closure of an application is proposed by the EDQM Certification of Substances Division, the Internal Decision Board reviews the request together with the supporting information. If there is any potential risk for public health or GMP non-compliance, proposals are submitted to the *Ad hoc* Committee on the actions to be taken.

The *Ad hoc* Committee then decides on the closure of the relevant CEP application(s) and the information to be forwarded to the relevant authorities. The *Ad hoc* Committee renders its decision generally within two weeks after the end of the inspection campaign or receipt of the request by the CEP applicant.

When proposed by the assessors of the Certification procedure, the responsibility for approving a request for the closure of a CEP application and informing the relevant authorities rests with the Head of the Certification of Substances Division (EDQM).

The detailed reasons for closure shall be given in the decision and communicated to the applicant.

#### **4. HEARING**

When the *Ad hoc* Committee or the EDQM has made a decision to withdraw or suspend a CEP, or to close a CEP application, the holder/applicant is given the possibility to submit a written request for re-consideration of the decision(s) (request for hearing) within two weeks of receiving the decision if they consider that the decision was not justified. The request for re-consideration should include information (supported by facts or figures) that demonstrates that the decision was unjustified.

Within two weeks of receipt of the request for re-consideration, the *Ad hoc* Committee reviews the request of the CEP holder/applicant and either rejects the request (*i.e.* maintains the original decision), or issues a new decision based on the written justification provided by the CEP holder/applicant.

#### **5. INFORMING CUSTOMERS AND AUTHORITIES**

Once a CEP has been suspended or withdrawn, the CEP holder must immediately inform its customers of the situation to allow them to take responsibility with regard to the substance concerned and any related marketing authorisation or marketing authorisation application.

Details on decisions to suspend or to withdraw a CEP, or to close a CEP application are communicated, in confidence, to the relevant authorities of the member states of the Convention on the Elaboration of a European Pharmacopoeia, as well as to the countries/organisations with which special agreements have been made, to enable them to take appropriate actions regarding the marketing authorisations or marketing authorisation applications concerned.

When confirmed, any change in the status of a CEP becomes publicly available on the EDQM website.

#### **6. EXTENSION OF A SUSPENSION**

A CEP is generally suspended for 2 years. In exceptional cases, the suspension may be extended, provided that the CEP holder submits a justified request for the extension for review by the Internal Decision Board before the end of the 2-year period.

The extension to the suspension may be accepted, but if the situation cannot be positively resolved, the EDQM may decide to withdraw the CEP as described in point 3 above.

#### **7. RESTORATION OF A SUSPENDED CEP**

After a suspension, a CEP may be restored as soon as the conditions for lifting the suspension are met by the CEP holder. The CEP restoration follows the same decision-making process as that for the suspension of the related CEP(s). In this case, a revised CEP is granted, which supersedes the suspended one. The CEP appears as valid in the public Certification database, together with its new revision number.

#### **8. RELATED DOCUMENTS**

- Resolution AP-CSP (07) 1 Certification of suitability to the monographs of the European Pharmacopoeia
- PA/PH/CEP (01) 1 Terms of Reference.