

## Certification of Substances Department

HB/CB

### **PUBLIC DOCUMENT**

(LEVEL 1)

**PA/PH/CEP (01) 1, 12 R**

Strasbourg, September 2021

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

## **TERMS OF REFERENCE AND RULES OF PROCEDURE**

Implementation date	1 October 2021
---------------------	----------------

**Revision history of the document**

Revision N°	Revision date	Reason
12 R	2021	Clarification of title. Update of IDB following changes to the EDQM CEP Department structure, and clarifications on working procedures

## 1. INTRODUCTION

The procedure for Certification of suitability to the monographs of the European Pharmacopoeia as defined in the Resolution AP-CSP (07) 1, is based on the participation of the following bodies and persons:

- Steering Committee (SC)
- Assessors
- Inspectors
- Technical Advisory Boards (TAB)
- Internal Discussion Board (IDB)
- *Ad Hoc* committee (AHC)
- Certification Department of the EDQM (DCEP).

## 2. THE PARTNERS IN THE PROCEDURE

Independence and impartiality are fundamental principles imposed on any public authority or institute, or any persons working for those bodies with a public health duty. For persons who participate in the Certification Procedure, the same ethical principles and impartiality are essential elements of the quality, legitimacy and credibility of the system. This is also highlighted in Resolution AP-CSP (07) 1, which establishes in particular that assessors that examine applications for a certificate of suitability (CEP) are persons without direct or indirect interests that may compromise the protection of the confidential trade information they have access to. This applies equally to inspectors participating in the inspections of related manufacturing sites as well as to any person participating in the Certification Procedure.

### 2.1. The Steering Committee (SC)

The SC establishes its own rules of procedure, as laid down below.

#### *2.1.1 Composition*

The composition of the Steering Committee should reflect the authorities involved in the Certification procedure, such as European licensing authorities and inspectorates, and representatives of the member states of the Convention on the Elaboration of a European Pharmacopoeia. Members of the SC are:

- The Chair of the CHMP/CVMP Quality Working Party (QWP);
- The Chair of the CHMP Biologics Working Party (BWP);
- The Chair of the Herbal Medicinal Products Committee (HMPC);
- The Chair of the GMP/GDP Inspectors Working Group (GMDP IWG);
- A representative of a licensing authority from a country that is a member of the Convention on the Elaboration of a European Pharmacopoeia, but is not a member of the EU/EEA, and which actively participates in the Certification Procedure by sending assessors;
- A representative of an inspectorate from a country that is a member of the Convention on the Elaboration of a European Pharmacopoeia, but is not a member of the EU/EEA, and which actively participates in the EDQM inspection programme;
- The Chair of the European Pharmacopoeia Commission;
- The Chairs of the Technical Advisory Boards (TAB);
- A representative of the European Commission;
- A representative of the European Medicines Agency (EMA);

- The Director of the European Directorate for the Quality of Medicines & HealthCare (EDQM);
- Expert(s) from relevant authorities or other independent experts who can be co-opted by the SC, as necessary. Their number in the SC should not exceed 50% of the total number of members.

With the exception of co-opted members, the members of this committee may appoint an alternate representing the same group/organisation to replace them in exceptional cases when they cannot attend a meeting.

The SC can accept the presence of representatives of a country/organisation as observers in the context of facilitating/developing recognition of the CEP procedure. The extent of this participation is defined by the SC on a case-by-case basis and as indicated in the document *Criteria for observership*.

#### *2.1.2 Nomination and appointment*

Except co-opted experts and representatives of non-EU countries, SC members are not appointed, but are considered constitutive members by their status and title. As for any participant in the Certification procedure, members and co-opted experts must declare their acceptance of the Code of Practice for the Certification Procedure.

The mandate of appointed members of this Committee (co-opted experts and representatives of non-EU countries) is for 3 years, renewable once. Representation of the non-EU/EEA countries should preferably be on a rotational basis. Appointments should be made by consensus. If no consensus can be reached, a secret ballot is held where a simple majority of the members present in a meeting decides the outcome.

The SC appoints a Chair for three years, renewable once, amongst its members. The appointment should preferably be made by consensus. If no consensus can be reached, a secret ballot is held where a simple majority of the members present in a meeting decides the outcome. In the absence of the Chair for a meeting, the SC shall elect an acting Chair from amongst the members present.

#### *2.1.3 Decisions*

Quorum: The deliberations/decisions of the SC shall be valid only if at least a simple majority (half of the members plus 1) participate in a meeting (including via tele/videoconference).

The decisions of the SC should preferably be made by consensus. If no consensus can be reached, a vote takes place and the simple majority (half of the members plus 1 from those who participate in the meeting) decides the outcome.

Decisions may be taken in writing, and the same rules apply.

#### *2.1.4 Role*

This Committee is in charge of:

- Monitoring the procedure;
- Giving appropriate advice on all regulatory or administrative problems associated with the implementation of the procedure;
- Ensuring that the needs of the licensing and supervisory authorities, the European Pharmacopoeia Commission and the applicants are satisfied and making proposals for the adaptation or updating of current regulations, guidelines, monographs or chapters, as necessary;

- Appointing assessors;
- Deciding on the composition of the TABs and appointing its members and chairs;
- Informing the European Pharmacopoeia Commission, the relevant EMA Working Parties/Groups and the relevant licensing or supervisory authorities of any relevant issues;
- Advising the EDQM as required;
- Adopting the guidelines/policy documents within the Certification procedure;
- Adopting the annual EDQM inspection programme.

Any document sent on behalf of the SC is signed by the SC chair (or any person designated by the SC chair).

## 2.2 The assessors

### 2.2.1 Definition

Assessors are scientists with professional experience in the assessment of marketing authorisation or CEP applications, who work for or advise competent authorities responsible for the evaluation of marketing authorisation applications, or are scientific officers from the EDQM DCEP. They have appropriate qualifications for the evaluation of dossiers in one of the fields covered by the Certification Procedure. These qualifications are evaluated based on objective criteria.

### 2.2.2 Appointment

The appointment and re-appointment of assessors is under the responsibility of the Steering Committee and is delegated to the EDQM, except in some cases where the SC itself decides on the request (the criteria are described in a separate document, *Criteria for appointment of assessors by the SC*).

Assessors are formally proposed by the relevant authorities and are appointed for a period of three years, which is renewable every 3 years (for an unlimited number of terms). A curriculum vitae provided to the EDQM must highlight their experience in the field of the evaluation of dossiers. Their impartiality and any conflicts of interest must be declared using the declaration of acceptance of the Code of Practice for the Certification Procedure.

The list of assessors is regularly up-dated and published by the EDQM.

The mandate of each assessor expires at the end of their period of appointment, unless a renewal is requested by their respective nominating authority<sup>1</sup>, and re-appointment is decided. Where an assessor has not participated in any assessment session for more than 2 years without justification (*e.g.* illness, leave, etc.) he/she will not be eligible for renewal for the next term.

Scientific officers of the DCEP are formally proposed by the EDQM and are appointed by the SC for an unlimited period, as long as they are DCEP staff and meet the criteria to be an assessor.

### 2.2.3 Role

The assessors perform the scientific assessment of applications submitted by manufacturers and produce an evaluation report, as described in the Resolution AP-CSP (07) 1 and in the guidelines for evaluation reports for the Certification procedure.

---

<sup>1</sup> The authorities are asked by the EDQM DCEP to send a request for renewal sufficiently early before the end of the period of appointment.

## **2.3 Inspectors**

### *2.3.1. Definition*

Inspectors taking part in the Certification procedure are:

- officials appointed by the competent supervisory authority of their respective country: member states within the EU/EEA or countries that have a mutual recognition agreement (MRA) with the EU in the GMP sector to carry out inspections according to Article 111.1 of Directive 2001/83/EC as amended.
- DCEP staff, with the qualifications specified above at the time of their recruitment.

### *2.3.2 Inclusion in the EDQM inspection programme*

Inspectors are nominated by their competent supervisory authority/organisation and take part in the EDQM inspection programme for a period of three years, which is renewable every 3 years (for an unlimited number of terms). The nomination is supported by information on the official status of the candidate person. A curriculum vitae provided to the EDQM shall highlight their experience. Their impartiality and any conflicts of interest must be declared using the declaration of acceptance of the Code of Practice for the Certification Procedure. The documents supporting the nomination are reviewed by the EDQM.

### *2.3.3 Role*

The inspectors take part in the annual EDQM inspection programme adopted by the SC. They inspect the sites referred to in CEP applications or granted CEPs, write inspection reports and contribute to any necessary follow-up actions. This includes:

- the recording of planned inspections in the EUDRA GMDP planning module (inspectors nominated by the competent supervisory authorities of EU/EEA member states)
- the issuance of GMP certificates or of statement of non-compliance in the EUDRA GMDP database (inspectors nominated by the competent supervisory authorities of EU/EEA member states).

## **2.4 The Technical Advisory Boards (TAB)**

### *2.4.1 Definition*

A TAB is established in each scientific/technical field of the Certification Procedure where a need is identified. The Board can be created, as necessary, upon approval by the SC.

### *2.4.2 Composition*

The TABs are composed of members from the list of appointed assessors and from the EDQM DCEP (preferably an assessor). They deal with technical issues related to the Certification procedure.

The TABs comprise three to ten members from different countries/agencies/organisations (including up to 1 DCEP member). Members are formally proposed by their relevant authorities (or by EDQM for the EDQM representative) and are appointed by the SC for a period of 3 years, renewable once. The Chair is elected by the SC for a period of three years, renewable once. As an exception, for the TSE and Herbal TABs, the SC may decide to renew and/or extend the mandates of the members and the chair.

In case of absence from all meetings and evaluation sessions for more than one year without proper justification (*e.g.* illness, temporary leave, etc.) a TAB member will not be eligible for renewal for the next term. Any exception to this rule shall be submitted to the SC for approval.

In the absence of the Chair for a meeting, the TAB shall elect an acting Chair from among the members present.

Inspectors, observers or experts may be invited to participate in part(s) of a TAB meeting to discuss specific items.

#### *2.4.3 Role*

The tasks for each relevant TAB include the following:

- to assist assessors and the DCEP in decisions on technical matters and in case of doubt or disagreement between assessors. Whenever possible, each relevant TAB should ensure consensus in the outcome of discussions with assessors and the DCEP. However, if this is not possible, the final decision is the sole responsibility of the relevant TAB. Such decisions and their justification must be recorded in writing.
- The TAB is consulted at the request of the DCEP and/or the assessors and elaborates technical documents (policies, guidelines), amendments or updates relevant for the assessors participating in the Certification procedure, to be submitted for adoption by the SC.
- If the DCEP and/or the TAB in their respective areas of work become aware of problems within the Certification Procedure that are not addressed in Resolution AP-CSP (07) 1 or the guidelines for evaluation, they shall prepare a proposal and seek further advice from the SC and, if relevant, the concerned working group/party at the EMA, licensing and/or pharmacopoeial authorities.

#### *2.4.4 Decisions*

Quorum: The deliberations/decisions of the TAB shall be valid only if at least a simple majority (half of the members plus 1) participate in a meeting (including via tele/videoconference).

Decisions of the TAB should preferably be made by consensus. If no consensus can be reached, a vote takes place and a simple majority (half of the members plus 1 from those who participate in a meeting) decides the outcome.

Decisions may be taken in writing, and the same rules apply.

### **2.5. The Internal Discussion Board (IDB)**

#### *2.5.1 Composition*

The Internal Discussion Board is a board composed of DCEP staff as follows: the Head of the DCEP (or a staff member representing him/her), one member representing the EDQM evaluation teams, one member representing the EDQM inspection team a , and the staff member in charge of the liaison between evaluation and inspection teams within the DCEP.

The DCEP staff members involved in the relevant CEP applications or in the relevant EDQM inspections are invited to the meetings of the IDB and present the case(s) to be treated. If necessary, other DCEP staff members may be invited.

#### *2.5.2 Role*

The IDB:

- ensures that inspections carried out in the frame of the Certification procedure are performed according to established procedures and that outcomes are harmonised

- Ensures that CEP holders maintain their applications according to established procedures and handles exceptions (e.g. administrative decisions, in case production of a substance is stopped for a defined period, etc.)
- Makes proposals to the *Ad Hoc* Committee on actions to be taken regarding granted CEPs or on CEP applications in the framework of the Certification Procedure, e.g. in the case of inspections having a negative outcome or when CEP applications are not in compliance with the requirements of the procedure (e.g. quality issues, impurities above acceptable limits, failure to update an application when a monograph is revised, etc).

In case of absence of a member of the IDB in a meeting, delegation takes place according to internal DCEP procedures.

## **2.6. The *Ad Hoc* Committee**

### *2.6.1 Composition*

The *Ad Hoc* Committee is composed of:

- the Director of the EDQM,
- the Head of the DCEP,
- at least one assessor from a competent licensing authority who takes part in the Certification Procedure (volunteer selected amongst the panel of assessors),
- at least one inspector from a competent supervisory authority who takes part in EDQM inspections (volunteer selected amongst the panel of inspectors).

The DCEP staff members involved in the relevant CEP applications or in the relevant inspections are invited to the meetings of the *Ad Hoc* Committee and present the case(s) to be treated. If necessary, other assessors or inspectors involved in a specific item may be invited.

### *2.6.2 Inclusion in the *Ad Hoc* Committee*

*Ad Hoc* Committee members are taken from the lists of assessors and inspectors taking part in the Certification procedure. Calls for candidates are made by the DCEP when needed and volunteers are included in the *Ad Hoc* Committee for a period of three years, which is renewable (for an unlimited number of terms).

### *2.6.3 Role*

The *Ad Hoc* Committee decides on actions to be taken regarding granted CEPs or on CEP applications, and on the information to be circulated to the relevant authorities, in the framework of the Certification Procedure, including the EDQM inspection programme.

In addition, when an applicant has requested a review of such a decision (hearing), according to Resolution AP-CSP (07) 1, the *Ad Hoc* Committee takes the final decision after examination of the request and its justification.

## **2.7 The EDQM Certification Department (DCEP)**

### *2.7.1 Definition*

The support for the Certification Procedure is provided by the DCEP.

### 2.7.2 Role

The DCEP:

- is in charge of administration, co-ordination and execution of the Certification Procedure including:
  - handling and follow-up of dossiers;
  - notifying the applicants of the conclusions of the assessment;
  - granting CEPs;
  - ensuring consistency of the assessment reports for similar products and adherence to the policies of the Certification Procedure;
  - assisting the assessors in their evaluation;
  - participating in the assessment of dossiers in collaboration with the relevant assessors;
  - establishing the inspection programme in collaboration with the relevant competent supervisory authorities;
  - organising and participating in inspections according to the approved programme
  - issuing attestations of inspection
  - informing authorities of decisions taken by the Ad Hoc committee, in particular in case of actions taken on CEPs or CEP dossiers.
  
- shall liaise with the relevant national authorities (licencing authorities and inspectorates) and, where applicable, with European institutions (including the relevant EMA Working Parties and Working Groups) and international organisations and with marketing authorisation holders (MAH), manufacturers and industry associations in general within the framework of the activities related to the Certification Procedure.
  
- shall prepare and, when necessary, propose amendments to existing documents or create new documents in relation to the Certification Procedure that shall be submitted to the SC, with the prior approval of the relevant TAB when necessary (technical documents).
  
- shall inform the European Pharmacopoeia Department (EPD) at EDQM of any need for revision of the Ph. Eur. monographs.
  
- shall forward any proposal of the SC concerning amendments of regulations, notes for guidance, *etc.* to the appropriate bodies.
  
- shall organise with the Public Relations Division & Documentation of the EDQM any specific meetings or scientific symposia, in particular to promote and explain the Certification Procedure.

When relevant, the DCEP is assisted by other EDQM services for the specific analysis of samples or advice on the status and content of monographs.

### **3. MEETINGS**

#### **3.1. The Steering Committee**

The SC meets at least once a year and more frequently if necessary, on the EDQM premises, or by teleconference/videoconference.

The detailed summary of decisions and any relevant documents shall be circulated to the participants in the meeting for approval within 4 weeks following the date of the meeting.

#### **3.2. The TABs**

The TABs meet one to three times a year and more frequently if necessary, on the EDQM premises or by teleconference/videoconference. The TSE and Herbals TABs may meet less frequently or may stay dormant, depending on the needs.

The minutes and any relevant documents shall be circulated to the participants in the meeting for approval within 4 weeks following the date of the meeting.

#### **3.3. The Assessors**

The DCEP invites the relevant assessors to evaluate applications as often as needed, depending on the availability of the assessors, the number and the specificity of the applications received and in order to cope with the official timetables.

Meetings with assessors may be organised to discuss or present new policies based on a decision by the EDQM.

#### **3.4. The Inspectors**

The DCEP invites the relevant inspectors to carry out the inspections, depending on their availability and in accordance with the EDQM inspection programme.

#### **3.5 The Internal Discussion Board**

The Internal Discussion Board meets as necessary..

#### **3.6 The *Ad Hoc* Committee**

The *Ad Hoc* Committee meets as necessary by teleconference/videoconference.

### **4. RELATED DOCUMENTS**

- Resolution AP-CSP (07) 1 Certification of suitability to the monographs of the European Pharmacopoeia
  - PA/PH/CEP (02) 4 Code of Practice for the Certification Procedure
  - Criteria for observership (non-public document)
  - Criteria for appointment of assessors by the SC (non-public document).
-