

Certification of Substances Division

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Certification of suitability to Monographs of the European Pharmacopoeia

TERMS OF REFERENCE

1. INTRODUCTION

The procedure for certification of suitability of 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 people:

- Steering Committee (SC)
- Assessors
- Inspectors
- Technical Advisory Boards (TAB)
- Certification Division 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. Persons who participate in the Certification Scheme acquire this status, and their 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 Scheme.

2.1. The Steering Committee (SC)

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 CVMP Immunologicals Working Party (IWP);
- The Chair of the Herbal Medicinal Products Committee (HMPC);
- The Chair of the GMP/GDP Inspectors Working Group (GMDP IWG);
- A representative of licensing authorities 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 Scheme 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 (from DG Health & Consumers/Pharmaceutical Unit);

- 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 who can be co-opted by the SC, as necessary.

The members of this committee may propose an alternate 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 elected/nominated, but are considered constitutive members by their status and title. As for any participant in the Certification procedure, they 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 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 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 Quorum

The deliberations/decisions of the SC shall be valid only if a simple majority (half of the members plus 1) participate (even via tele/videoconference).

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 application of the procedure;
- Ensuring that the needs of the licensing 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 and the CHMP/CVMP/HMPC and the relevant EMA Working Parties/Groups of any relevant issues;
- Advising the EDQM as required;
- Adopting the guidelines/policy documents within the Certification procedure;
- Adopting the EDQM inspection programme.

The SC establishes its own rules of procedure.

2.2 The assessors

2.2.1 Definition

Assessors are scientists with professional experience in the assessment of marketing authorisation or CEP applications, belong to or advise Official Medicinal Control Laboratories (OMCL) or competent authorities responsible for the evaluation of marketing authorisation applications, or are scientific administrators from the EDQM Certification of Substances Division (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 alone decides on the request (the criteria are described in a separate document, *Criteria for appointment of assessors by the SC*).

Assessors are proposed by the relevant authorities and are appointed for a period of three years, which is renewable. 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 same procedure applies to the appointment of scientific administrators to the DCEP when they are proposed by the EDQM.

A current 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 authority¹, 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.

2.2.3 Role

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

2.3 Inspectors

2.3.1. Definition

Inspectors taking part in the Certification scheme 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.
- for countries/organisations with which the EDQM has set up appropriate agreements, officials appointed by the competent supervisory authority of their respective country or by their organisation to carry out inspections according to their respective legislative framework.
- scientific administrators from the EDQM DCEP with the qualifications specified above.

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

2.3.2 Inclusion in the EDQM inspection programme

Inspectors are proposed by their competent supervisory authority/organisation to take part in the EDQM inspection programme. The proposal is supported by information on the official status of the candidate person. A curriculum vitae provided to the EDQM shall highlight their experience and their impartiality; any conflicts of interest they may have must be declared (using the declaration of acceptance of the Code of Practice for the Certification Procedure).

2.3.3 Role

The inspectors take part in the EDQM inspection programme, which is elaborated in the context of the mandate given to EDQM by the European Commission Pharmaceutical Unit in applying Directives 2001/83/EC and 2001/82/EC, as amended. They inspect the sites referred to in CEP applications or granted CEPs, write inspection reports and are in charge of any necessary follow-up actions. This includes:

- the issuance of GMP certificates or of statement of non-compliance (inspectors nominated by the competent supervisory authorities of EU/EEA member states)
- the issuance of attestations of inspection or information of suspension/withdrawal of CEPs or closure of CEP dossiers (EDQM inspectors).

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 are representative of the needs of both the licensing authorities and the European Pharmacopoeia Commission.

The TABs comprise three to ten members from different countries/agencies/organisations, and may include EDQM assessors. Members are proposed by their relevant authorities and are appointed by the SC for a period of 3 years, renewable twice. The Chair and, if necessary, the vice-Chair are elected by the SC for a period of three years, renewable twice. If there is more than one candidate, the Chair and vice-Chair are elected by a simple majority of the members present. The appointment of members and the election of the Chair and vice-Chair take place during SC meetings or by correspondence.

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 exceptions to this rule shall be submitted to the SC for approval.

In the absence of the Chair and vice-Chair for a meeting, the TAB shall elect an acting Chair from among the appointed 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 primary task for each relevant TAB is to assist assessors and the EDQM 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 EDQM 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.

If the Division 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 note highlighting the problem and seek further advice from the SC and, if relevant, the concerned licensing and/or pharmacopoeial authorities. Specific guidance for the assessors may be drafted on request and, if necessary, a proposal for amending the Resolution and/or any document concerned shall be prepared.

The TAB is consulted at the request of the EDQM DCEP and/or the assessors and elaborates technical documents (such as guidelines for the evaluation report), amendments or up-dates to be submitted for adoption by the SC.

TAB members also take part in hearings with applicants when a decision is made not to grant a CEP because the application is not in compliance with the requirements of the procedure, or in case actions are taken on CEPs or CEP applications following an EDQM inspection having a negative outcome, and where the applicant has requested a review of the decision, according to Resolution AP-CSP (07) 1.

2.4.4 Quorum

The deliberation/decisions of the TABs shall be valid only if a simple majority (half of the members plus 1) are present.

2.5. The Internal Decision Board (IDB)

The Internal Decision Board is a board within the EDQM DCEP, composed of at least one inspector from the EDQM, at least one officer from the EDQM involved in the evaluation of CEP applications and the Head of the EDQM DCEP.

This board:

- confirms positive outcomes as well as further actions for inspections carried out in the framework of the EDQM inspection programme, and
- 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, eg. in the case of EDQM inspections having a negative outcome as well as when CEP applications are not in compliance with the requirements of the procedure (administrative decisions).

2.6. The Ad Hoc Committee

The Ad Hoc Committee is a board that is appointed to take decisions 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.

It is composed of at least one officer from the EDQM involved in the relevant CEP application or one inspector involved in the relevant inspection, the Director of EDQM, the Head of the EDQM DCEP and, as needed, at least 2 representatives of the competent licensing and supervisory authorities that take part in the Certification Procedure (typically TAB members).

2.7 The EDQM Certification Division (DCEP)

2.7.1 Definition

The Secretarial support for the Certification Procedure is provided by the EDQM Certification Division (DCEP).

2.7.2 Role

The Certification Division:

- 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;
 - ensuring consistency of the assessment reports for similar products and adherence to the policy 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.

- shall liaise with the relevant national authorities (including inspectorates) and, where applicable, with European institutions 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 EDQM EPD (European Pharmacopoeia Department) 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 EDQM 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 normally meets at least once a year or, when necessary, upon invitation. The detailed summary of decisions and any relevant documents shall be circulated to the members of the Committee for approval within 5 weeks following the date of the meeting. When approved, the detailed summary of decisions is sent to the TABs, and any other person/group concerned, if necessary.

3.2. The TABs

Each TAB meets one to three times a year and, when necessary, upon invitation.

The minutes and any relevant documents shall be circulated to all members of the TAB for approval within 5 weeks following the date of the meeting. The final minutes are sent to the SC, to all assessors of the Certification Procedure and to any other concerned person/group if necessary.

3.3. The assessors

The EDQM 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 timetable set down in Resolution AP-CSP (07) 1.

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

3.4. The Inspectors

The EDQM DCEP invites the relevant inspectors to carry out the inspections, depending on the availability of the inspectors and in order to meet the EDQM inspection programme, or any urgent need identified in the framework of the Certification Procedure or by the national supervisory authorities, European institutions or international organisations (*e.g.* in the context of specific programmes of co-operation).

3.5 The Internal Decision Board

The Internal Decision Board meets as necessary and at least once after each campaign of inspections carried out by the EDQM.

3.6 The Ad Hoc Committee

The Ad Hoc Committee meets as necessary and generally by teleconference.

4. RELATED DOCUMENTS

Resolution AP-CSP (07) 1

Code of Practice for the Certification Procedure PA/PH/CEP (02) 4 as amended

Criteria for observership (non-public document)

Criteria for appointment of assessors by the EDQM (non-public document)