DIRECTION EUROPÉENNE DE LA QUALITÉ
DU MÉDICAMENT & SOINS DE SANTÉ

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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Certification of suitability to the Monographs of the European Pharmacopoeia

Changes implemented with the CEP 2.0

What is the CEP 2.0?

The CEP 2.0 is a "new look" CEP that better meets the current needs of stakeholders and offers both enhanced user-friendliness and greater transparency of the information conveyed, without, however, increasing the regulatory burden related to revisions of CEPs.

CEP 2.0: which changes have been implemented?

The changes linked to its implementation cover the following 9 areas:

- Area 1: CEPs and information reported
- Area 2: Changes regarding assessment of CEP applications
- Area 3: On-line public certification database
- Area 4: Authorities database
- Area 5: Fostering information sharing between CEP holders & MAH
- Area 6: Reduction of revisions of CEPs
- Area 7: Impact of changes and their implementation
- Area 8: Trainings for CEP holders and CEP users
- Area 9: Revising documents available on the EDQM website

A specific CEP 2.0 FAQs section on the EDQM website is regularly updated and gives more details on the changes implemented:
https://faq.edqm.eu/display/FAQS/CERTIFICATION+OF+SUBSTANCES+FOR+PHARMACEUTICAL+USE

At any time, stakeholders may contact the Certification Department via the EDQM HelpDesk to get more information: https://www.edqm.eu/en/faq-helpdesk-certification-and-ceps. Please choose CEP-Certificates of suitability then 'CEP 2.0'.

The CEP is now an electronic document with a digital signature. It can be downloaded as a pdf or printed by CEP holders to share with their customers, for inclusion in Marketing Authorisation Applications (MAA).

The CEP numbering system has been modified due to a change in the renewal procedure for CEPs (see area 6).

The declaration of access box on the CEP document has been replaced by a separate letter of access for which a template is available on the EDQM website.

The company details (name and address) now appear with the EMA SPOR/OMS Organisation (Org) and Location (Loc) ID (more information on EMA website). These validated organisation data are now mandatory for the submission of CEP applications.

Information provided on the CEP for chemical purity and herbal drugs/herbal drug preparations that is related to the quality of the substance has been revised. The main changes to the content are:

- The "Technical" information (such as additional controls for impurities or solvents) has been replaced by annexing the specification applied by the CEP holder (section 3.2.S.4.1) and the additional methods needed to control the quality of the substance (not methods that are alternative to Ph. Eur. methods) as approved during the assessment of the CEP dossier.
- The quality of water used in the last steps of the synthesis of the substance is now also listed on the CEP.
- Some sentences and statements have been updated and the expiry date of the certificate is no longer mentioned.

Area 2: Changes regarding assessment of CEP applications

Some changes have been introduced regarding the content of the CEP dossier and the associated assessment, which apply to CEPs for chemical purity and herbal drugs/herbal drug preparations. The recommendations on how to present data are listed in document PA/PH/CEP (23) 21: New requirements for the content of the CEP dossier for chemical purity and for herbal drugs/herbal drug preparations according to the CEP 2.0. These requirements should be implemented in any new CEP application, sister file and also at renewal.

The process description and the specification sections of the CEP dossier should only contain information corresponding to the quality claimed (data on micronisation, particle size, microbiological controls, etc. should not be included in the dossier if no corresponding specific grade is requested).

The CEP dossier, the assessment performed and the approved specifications are now fully aligned. As a result, any information not approved is to be deleted from the dossier.

Applicants are encouraged to claim a re-test period and to include stability data in their CEP applications. In addition, the assessment of stability data has been extended by proposing the option to submit data referring to additional climatic zones (III and IV).

During the initial phase of the implementation of the CEP 2.0, CEP holders are not required to update the content of their dossier according to CEP 2.0 new requirements for their existing CEPs except at renewal.

However, companies have the possibility to ask for a CEP revision (minor by default) to switch to the CEP 2.0, state clearly in the request for revision that they wish to switch and update their dossier in line with the new requirements.

Area 3: On-line public certification database

The public CEP database available on the EDQM website now includes additional features:

- The tabulated data include additional columns showing SPOR ORG and LOC-ID information for the holder where this is available* as well as the renewal date for the CEP (where not yet renewed) and the closure date of the last procedure. Users will also be able to view and print a tabulated history of a selected CEP** that provides information on the revision type, and on the outcome and closure date of completed procedures.
- These changes are intended to increase transparency and encourage communication between CEP holders and the users of CEPs.

  * In the EDQM Certification of Substances databases

  ** History of procedures is available for procedures opened as of 1 January 2020

Area 4: Authorities database

New features have also been added to the Authorities database. The database is currently accessible by the licensing authorities of the member states of the Ph. Eur. Convention. It contains confidential information related to the lifecycle of CEP applications as well as copies of the current CEPs and CEP assessment reports. The EMA SPOR/OMS Org and Loc ID are mentioned for CEP holders and manufacturing sites. The CEP number and CEP document corresponding to each procedure of a dossier (if any) are now available.

Regulatory authorities beyond Ph. Eur. member states that accept CEPs, have been granted access to it, under suitable confidentiality agreements or Memoranda of Understanding (MoU). The EDQM

website describes the list of authorities that have access to the Authorities database. The CEP holder's declarations on the CEP application form have been updated to cover this aspect.

Area 5: Fostering information sharing between CEP holders & MAH

As published in January 2022 on the EDQM website, CEP holders have responsibilities towards their customers. For example, they must provide them with suitable information in addition to the CEP and it is up to the CEP holder and the marketing authorisation holder (MAH) to agree on the information shared and its format. To raise awareness of this aspect, CEP applicants must provide a commitment to share information with their customers as part of the CEP application form. In addition, this obligation is specifically mentioned in the CEP document and compliance with these requirements is enforced and checked during GMP inspections. The history of procedures (opened after January 2020) for CEP dossiers is transparent in the public certification database, so users are aware of changes and can ask for the details they need from the CEP holders (see area 3).

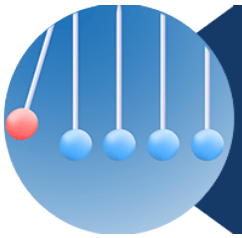
Area 6: Reduction of revisions of CEPs

The CEPs are no longer revised if their content has not changed. Therefore, a revised CEP is no longer granted after changes (even when major) that do not impact the CEP content are approved.

Renewal process:

The renewal process has been kept but does not result in a "renewed" CEP unless changes are introduced in the renewal application which impact the content of the CEP (in which case a revised CEP is granted). As a result of this change, the numbering of certificates has changed.

For CEPs issued before the implementation date of CEP 2.0 (1st September 2023), CEP holders should update their dossier in accordance with the CEP 2.0 requirements at renewal and a CEP 2.0 would be granted. If the valid version of a CEP is hybrid, holders may also request to switch to CEP 2.0 format at renewal if they wish. This should be clearly mentioned in the renewal application.



Area 7: Impact of changes and their implementation

As the project has a major impact on all users, a stepwise approach was foreseen for its implementation. The major impact is linked to the fact that the specification for the substance applied by the CEP holder is now appended to the CEP. To implement the CEP 2.0 smoothly, an appropriate balance had to be achieved between updating the existing CEPs to the "new look" and the burden this generated for the holders, the EDQM and other users.

The "new look" corresponds to the CEP 2.0 with the specification (3.2.S.4.1) and additional methods appended.

"New look" CEPs are issued for any new CEP granted and after renewal procedures if applicable. For ongoing new and renewal files, some updates of dossiers are requested if needed before the CEP is granted (in particular sections 3.2.S.4.1 and 3.2.S.4.2 should reflect what has been approved during the assessment of the dossier).

The "hybrid look" CEP is granted after approval of revision applications and after notifications, for existing CEPs where the content of the CEP is impacted. The "hybrid look" CEP has the new numbering, SPOR/OMS Loc ID for companies, the declaration of access removed and an e-signature, but the substance specification is not appended to the CEP.

The "old look" corresponds to CEPs as granted till the implementation of CEP 2.0 (1st September 2023), meaning that while no CEPs with the "old look" have been granted since the implementation of CEP 2.0, CEPs granted before this date are still valid until they are revised.

Training material addressing the "old", "new" and "hybrid" looks of CEPs and explaining what they are and in which case which one is issued is available .

"Old look", "hybrid look" and "new look" CEPs will coexist for some time and experience will show whether additional measures should be taken in the future.

Area 8: Trainings for CEP holders and CEP users

A number of webinars were organised before the implementation of the CEP 2.0 to present an overview of the changes and others will be organised after a few months of experience.

Guidance on the changes to the content of CEP dossiers and CEPs is given during conferences and events in which the EDQM is involved. Recordings of these events are available online.

Area 9: Revising documents available on the EDQM website

Most of the documents published on the EDQM website under "Certification policy documents and guidelines" are impacted. These are being revised progressively in line with the different changes and the information is also shared via news and specific documents.