Certification of Substances Department

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Certification of suitability to the Monographs of the European Pharmacopoeia

Outcome of the public consultation on the "CEP of the future"

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1. <u>Background</u>

The content and layout of the current Certificate of Suitability (CEP) remains very similar to the original created in 1992. The EDQM is nonetheless well aware of the far-reaching effects that globalisation, the rise of digital technology and many other major regulatory and scientific developments have had on the pharmaceutical industry and competent authorities over the last three decades. In response, the EDQM launched a project to design the CEP of the future. The aim is to develop a modern CEP that will better fit the current needs of stakeholders, offer both greater transparency of the information conveyed and enhanced user-friendliness, increase the acceptance of CEPs and ease the registration activities performed using CEPs.

2. <u>Methodology</u>

The first step was to gather feedback via a large public consultation using an online survey that was available on the EDQM website from 31 August 2020 to 31 December 2020 and addressed three major topics: content, layout and use/distribution of the CEP.

At the end of the consultation period, a total of 150 responses had been received by the EDQM. The respondents were divided into two groups, with Industry accounting for 107 respondents and Authorities accounting for 43 respondents.

3. <u>Results of the survey</u>

Overall, stakeholders expressed their satisfaction with the CEP procedure and document.
No major divergent views were expressed by Authorities and Industries with respect to the topics covered in the survey.

Highlights from the feedback received:
- There was a strong demand to include more information in CEPs, including statements on what is approved and what is not approved, to increase transparency and clarity for users, but also to avoid questions from both authorities and marketing authorisation holders (MAHs).
- The majority of respondents indicated that they would like more of the information included in CEP files to be approved by the EDQM and covered within the CEP document in order to avoid questions or assessment of marketing authorisation applications (MAA).
- There were strong calls to find ways to reduce revisions of CEPs.

The responses also showed there was a lack of knowledge of the current EDQM policies on the content of the CEP (e.g. policy document "How to read a CEP", use/route of administration considered during the assessment of the CEP), as well as a lack of knowledge and understanding of the responsibility and duties of CEP holders/API manufacturers vs MAH/drug product manufacturers and also on current regulatory requirements involving CEPs.

The stakeholders made the following specific suggestions regarding the content of CEPs:
- To include more details on all sites involved in manufacturing in order to understand the supply chain and roles of each site.
- To be more transparent regarding the specifications of the substance covered by the CEP.
- To include statements on the CEP with regard to risk assessment of nitrosamine and mutagenic impurities and also on the maximum daily dose and route of administration

considered during assessment.
- To include information on physical treatments and related grades and controls (e.g. polymorphisms, PSD), or alternatively to include a statement that this aspect was not approved by the EDQM.
- For stability, respondents would appreciate the mandatory inclusion of a re-test period on the CEP, with the possibility of covering more climatic zones, together with statements on the need and absence of need for specific storage conditions.

With regard to the layout and format of the CEP:
- A clear preference was expressed for an electronic CEP (e-CEP) rather than a paper document.
- The need to present the information mentioned on the CEP (additional tests, re-test period, elemental impurities, etc.) in tabular form for easy consultation was raised by many respondents.

The aspects most frequently mentioned related to the use of the CEP were:
- To report the status of applications in the online "certification database" (e.g. requests for revision approved, change log with a general description of the changes included in the dossier and/or the CEP).
- To no longer issue revised CEPs for administrative changes (e.g. changes to names/addresses of companies).
- To no longer issue revised CEPs for changes not impacting the quality of the substance or not impacting the content of the CEP.
- There was still a need to check the authenticity of a CEP, either in the online "certification database" or through the introduction of a QR code.
- To revise the current declaration of access box (e.g. to have more space, to be aligned with the letter of access for ASMFs).

4. <u>Conclusions</u>

Based on all the comments and feedback received, the following 5 areas of work have been identified to design the "CEP of the future":

Review information to be reported on CEPs
- Increase transparency and clarity to give a better understanding of the aspects which are approved and also those which are not approved (on grades and subtitles, approved specifications, etc.).
- Fill in gaps with information reported on CEPs.

Reduce revisions of CEPs and facilitate handling of changes
- Avoid revisions of CEPs linked to administrative changes, such as changes to names and addresses of companies.
- Avoid revisions of CEPs not impacting the quality of the substance covered.

Enhance digital tools and public databases
- Implement a digitally signed electronic CEP.
- Use IT tools to facilitate the preparation and use of CEPs and also reference to CEPs in marketing applications.

- Update EDQM databases to include more features and to disclose more information.

Foster information sharing between CEP holders & medicines manufacturers
- Disclose more information in the CEPs and in the online "certification database".
- Identify ways to enforce and verify information sharing.

Train users on content and use of CEPs
- Provide more training and use the full range of EDQM communication tools to explain what is covered by CEPs and how CEPs should be used.
- Enhance information and improve visibility on the EDQM website to facilitate easier access to all relevant data.

5. <u>Next steps:</u>

- The design of the CEP of the future will be prepared during the first half of 2022.
- During the second half of 2022, the proposals will be discussed with the relevant stakeholders and decision-making bodies. A large communication campaign will be initiated to explain the proposed changes.
- At the beginning of 2023, the CEP of the future should be deployed and available to users.