CEP 2.0: the EU regulatory authorities' perspective

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What is CEP from the regulatory perspective?

- One of the possibilities how to submit the information regarding the active substance during the MAA or MAV
  - Full dossier = complete Module 3.2.S
  - ASMF procedure – Applicant´s part + Restricted part sent separately from the registration dossier
  - **CEP**
- CEP certifies that the quality of a substance can be suitably controlled by the individual Ph. Eur. monograph for the substance in question and any supplementary tests deemed necessary in line with applicable (V)ICH and EMA guidelines

What is CEP definitely NOT?

- CEP is not a GMP certificate
- TSE CEP does not certify that the quality of the substance is suitably controlled by a specific Ph. Eur. monograph
- CEP is not automatically a complete replacement of the documentation on the active substance
- „sterile“ CEP does not mean that the applicant does not have to provide information on sterilization—sterilization is ALWAYS a step in the manufacture of the finished product → consequences for GMP

What is CEP 2.0?

- Result of the „CEP of the Future“ project = new-look CEP
- **Why CEP 2.0?**
  - Responding to evolving regulatory needs
  - Enhancing transparency and trust
  - Supporting innovation and global harmonisation
- **Key goals**
  - 🧩 Simplify regulatory processes
  - 🔍 Increase transparency for stakeholders
  - 📈 Improve efficiency in dossier evaluation
  - 🌍 Support international cooperation

Key Enhancements Over CEP 1.0

Feature	CEP 1.0	CEP 2.0
Submission format	Paper/eCTD, signed manually	Fully eCTD, signed electronically
Lifecycle management	Manual	Digital & Structured
Numbering	3-block code (e.g., R0-CEP 2020-123-Rev 01)	2-block code (e.g., CEP 2024-123-Rev 00)
Access Declaration	Box on CEP	Separate template
Expiry date	Mentioned (if any)	No expiry date, but renewal still required
Company details	Basic name/address	Includes SPOR/OMS ORG_ID and LOC_ID
Site roles	General	Detailed roles (e.g., production, micronization, sterilization)
Technical info	Limited to additional impurities and additional tests	Includes specification, additional methods, water quality
GMP integration	Limited	Strengthened Links

	CEP 1.0	CEP 2.0
Certificate number	R1-CEP YEAR-123-Rev 05	CEP YEAR-123-Rev 05
Name	No change	
Name of the holder	Complete address	Complete address + EMA SPOR OMS ORG_ID and LOC_ID
Site of production	See Annex 1 – complete addresses	See Annex 1 – complete addresses + EMA SPOR OMS ORG_ID and LOC_ID
Statement regarding the water (if applicable)	In the last step of synthesis, water is used as solvent.	In the last step of synthesis, purified water is used as solvent.
Impurities	List of impurities (with limits) which are additionally needed to be controlled to assure the quality of substance	Copy of complete specification in Annex 2
Residual solvents	List of residual solvents (with limits) which are needed to be controlled in the substance	Copy of complete specification in Annex 2
Elemental impurities	No change	
Container closure system and re-test period	No change	
Statement regarding Production section	No change	
Statement on method of sterilization	No change	

Submission Format and Lifecycle Management

- Submission format

- Mandatory eCTD format for new CEP applications

- Structured format for regulatory submissions - harmonized across ICH regions

- Lifecycle management

- Digital lifecycle tracking of CEPs

- Facilitates lifecycle management and review – easier updates, renewals, and revisions

Company details

- Alignment with current digitalization efforts
- Complete addresses remain on CEP for easy review but followed with SPOR/OMS information
  - ORG_ID
  - LOC_ID
- Roles for each site listed in more detail
  - Better transparency
  - Easier possibility to fill in the eAF for MAA and MAV

Specification, quality of water

- Copy of complete approved specification – from assessor´s perspective very welcomed
  - Transparent to the finished product manufacturer as well as to the assessor
  - Possibility to compare
    - actual Certificate of analysis with the approved specification
    - specification of active substance as used by finished product manufacturer with the specification used by active substance manufacturer
- Quality of water
  - „old CEP“ did not provide this information – often requested in the LoQ related to the MAA and MAV – separate declaration needed
  - CEP 2.0 – transparent, no need for additional question

GMP integration – Why Integrate CEP with GMP Inspections?

- Ensure consistency between quality documentation and manufacturing practices
- Strengthens regulatory oversight and compliance

- CEP lifecycle aligned with GMP inspection outcomes → inspection findings can trigger CEP updates or actions + CEP suspension or withdrawal based on GMP non-compliance

- *Benefits for regulatory authorities*

- Efficient resource allocation for inspections
- Better risk-based decision-making

- *Benefits for Industry*

- Clear expectations and accountability
- Reduced duplication of regulatory efforts
- Strengthened value of CEPs – improved global recognition of CEPs

How does CEP 2.0 help regulatory authorities compared to previous version of the CEP?

CEP 2.0 is a modernized digital version of the Certificate of Suitability (CEP), which brings **greater transparency, security, and interoperability**

For **regulatory authorities** (e.g., national medicines agencies), it offers several specific advantages:

1. Digital format with verification

- CEP 2.0 is a fully **digital document in PDF/A-3 format** with an embedded eCTD-compatible structure
- It includes an **EDQM digital signature**, which is **legally valid and verifiable**, making it easy to **confirm the authenticity** of the document without needing to contact EDQM

How does CEP 2.0 help regulatory authorities compared to previous version of the CEP? Cont.

2. Easier version tracking and change monitoring

- Each CEP 2.0 is **uniquely identified and dated**
- Regulatory authorities gain **clear oversight of updates** (e.g., manufacturing process changes, holder transfers, etc.)

3. Interoperability with eCTD and eSubmissions

- CEP 2.0 is **fully compatible with electronic submissions (eCTD)**, the standard used in EU medicines registration processes
- It simplifies **integration into regulatory dossiers** and review workflows

How does CEP 2.0 help regulatory authorities compared to previous version of the CEP? Cont.

4. Security and document integrity

- The use of **digital signatures and PDF/A-3 formatting** reduces the risk of document forgery or tampering
- Regulatory authorities can trust the **document's authenticity and integrity**

5. Improved communication across stakeholders

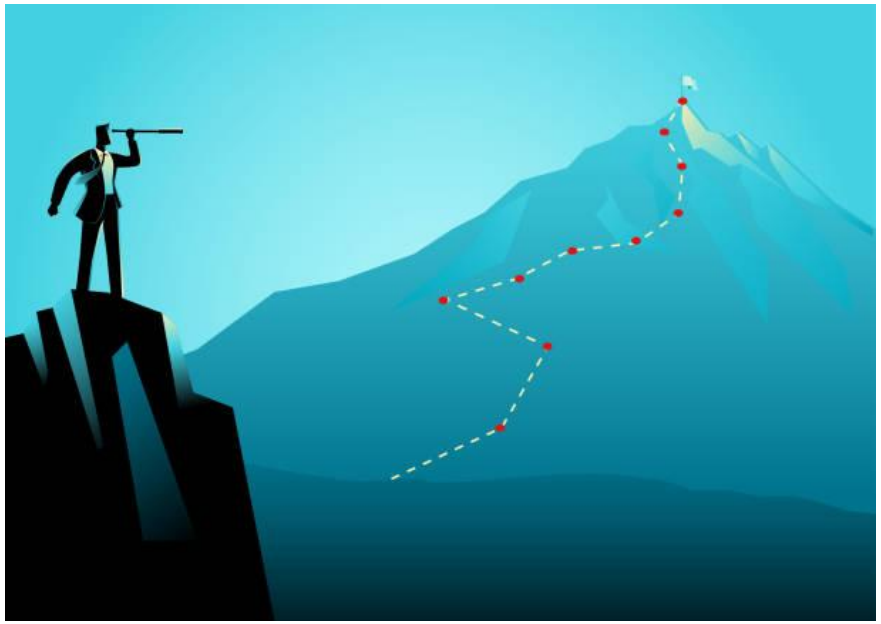
- CEP 2.0 facilitates **collaboration between EDQM, regulatory bodies, MAHs (Marketing Authorization Holders), and manufacturers**
- Structured information ensures better understanding and more efficient decision-making

Worksharing in practice

- Joint assessment of CEP applications
- Shared inspection outcomes
- Coordinated decision-making processes
- Benefits for Regulatory Authorities
  - Optimised resource allocation
  - Improved consistency in evaluations
  - Faster access to quality data
- Benefits for Industry
  - Streamlined submission process
  - Fewer redundant queries
  - Accelerated approvals across markets

Looking ahead

- **Future Vision for CEP**
  - Integration with AI-supported review tools
  - Challenges and opportunities for CEP scope expansion
  - Stronger links with international regulatory frameworks (e.g., ICH, WHO)



Quality assessor’s view

When we start the assessment of some application and see CEP …

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Current guidelines = basis for understanding

- EDQM Public documents

Revised guideline - How to read CEP.pdf

- Describes in details information conveyed on a Certificate of Suitability

01 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 (10).pdf

- Revised requirements as well as recommendations for the corresponding sections are described

- EMA Q/A

QWP Questions and Answers (Q&A): how to use a CEP in the context of a Marketing Authorisation Application (MAA) or a Marketing Authorisation Variation (MAV)

- This document aims to clarify existing guidance as a compilation of required data to be submitted in a MAA or in certain MAVs when a CEP is referred

Use of CEP in MAA and MAV

- Within the dossier copy of current version of CEP is provided
  - It can replace most of the parts of the Module 3.2.S
- The level of knowledge of the MAH/applicant in relation to manufacture and controls of the API should be such that it permits them to take responsibility for the quality of the active substance as incorporated into the finished product
- Any additional aspects not covered by the CEP, but relevant to a specific finished product, should be addressed by the applicant
- Compliance with GMP rules is declared by QP from the finished product manufacturer using „QP declaration“
  - Grades, specific routes of synthesis etc. need to be addressed when relevant
  - For „sterile“ CEPs it should not cover sterilization step

Specific challenges – „sterile“ CEP

- Public document:

Content of the dossier for sterile substances, PA_PH_CEP (23) 54, November 2024.pdf

- Sterilization of the active substance is regarded as part of finished product manufacture
- Sterilization process shall be described in detail in the CEP application, together with full data on the validation of the sterilization method.
- The SAME description should be available to the Applicant/MAH and provided in the MAA/MAV dossier together with a declaration that the same data were subject of the EDQM assessment
- QP declaration should not cover sterilization step → GMP certificate is necessary to be provided within MAA/MAV

Specific challenges – subtitles

- Small reminder for the case of parallel CEPs for one active substance from one substance manufacturer
  - micronized X non-micronized
  - route A X route B
  - …
- Always the correct CEP should be referred in the quality dossier corresponding to the substance quality that is really used
- The subtitle should be included in the QP declaration Part A as a part of substance name
  - To declare that the correct and complete synthesis was subject of audit of the MIAH

Lessons learned from CEP procedure – ASMF WS

- For CEPs there is well developed transparent process leading to one single dossier for the substance from one manufacturer – consistent quality → increased reliability
- Inspired by EDQM – ASMF WS – suitable for all substances not only where Ph. Eur. monograph exists
  - Avoid duplication of work and divergent decisions
  - More complex as the assessment is always connected with specific product and procedure
  - Could lead to complicated lifecycle

CMDh_308_2013_Rev.4_2024_05_-_ASMF_Worksharing_Procedure_User_Guide_-_clean.pdf

- From May 2024 – ASMF WS also allowed for already approved ASMFs under certain conditions

Upcoming EU Pharma Legislation

- So-called ‘pharma’ package constitutes the biggest reform to the EU’s laws on medicines in over two decades
- To optimise the use of resources for both applicants for marketing authorisations and competent authorities assessing such applications, a single assessment of an active substance master file should be introduced. The outcome of the assessment should be issued through a certificate. To avoid duplication of assessment, the use of an active substance master file certificate should be mandatory for subsequent applications or marketing authorizations.
- The Commission should be empowered to establish the procedure for the single assessment of an active substance master file

Closing & Q/A

CEP 2.0 is more than an update—it's a transformation.

Let’s shape the future of pharmaceutical quality together.

Questions?

SÚKL

THANK YOU FOR YOUR ATTENTION

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