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Module 5
General overview of the CEP procedure

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8th December 2025

Overview

- ★ Background and legal framework
- ★ The CEP procedure
- ★ Comparison between CEP and ASMF procedures
- ★ How to apply for a CEP
- ★ Evaluation of applications and granting of CEPs
- ★ Key figures and information available on EDQM website

Overview

- ★ **Background and legal framework**
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Certification - Background

- CEP = Certificate of Suitability to the monographs of the European Pharmacopoeia
- The procedure for the CEPs was established in 1994 and was initially only applicable to pharmaceutical substances
- In 1999, the procedure was extended to include products with a risk of transmissible spongiform encephalopathy (TSE)
- The procedure was further revised to allow for the control of herbal drugs and herbal drug preparations

EU legislation and Regulatory background

- EU Directive 2001/83/EC (human) and amendment 2003/63/EC state that active substances should comply with the Ph. Eur monograph if there is one

EU legislation and Regulatory background

- EU Directive 2001/83/EC (human) and amendment 2003/63/EC state that active substances should comply with the Ph. Eur monograph if there is one
- The **Terms of Reference** are adopted by the Ph. Eur. Commission
- **Resolution AP-CSP (07) 1** on the "Certification of Suitability to the Monographs of the European Pharmacopoeia" adopted by the Public Health Committee of the Council of Europe

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A robust procedure which exists for 30 years

Open to
any manufacturer
regardless of
geographical origin

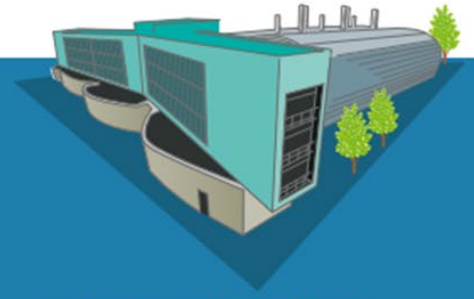
What is the CEP?

Certificate of Suitability

Assess and conclude that the quality of a substance* is controlled by the Ph. Eur.monograph and additional tests if needed

*except for biologicals

Check compliance with GMP at manufacturing sites



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The CEP procedure centralises the evaluation of the quality of pharmaceutical substances for the benefit of regulatory authorities and industry alike, thus saving time and resources and ensuring harmonisation in the assessment of data.

Regulatory Authorities accepting CEPs

Centralised assessment:
saves time and resources

CEP
Marketing Application evaluation

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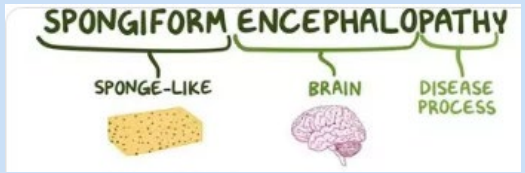
Scope and out of scope of the procedure

Scope

- Substances described in monographs in the Ph. Eur. (active substances, excipients, herbal drugs): "**Chemical**" or "**Herbal**" CEP

- Products with risk of TSE (starting materials, intermediates, reagents, etc.): "**TSE**" CEP



Out of scope

- Substances not included in Ph. Eur. (except TSE CEP)
- Substances which do not comply with the Definition section of the monograph
- Biologicals and products extracted from animal tissues
- Human tissues derivatives, blood derivatives, vaccines
- Finished products

What is a CEP

- A chemical or herbal CEP **certifies** that the quality of the substance is suitably controlled by the Ph. Eur. monograph and any supplementary tests deemed necessary in line with (V)ICH and EMA guidelines.
- A TSE CEP **certifies** that the substance complies with the Ph. Eur. General Chapter 5.2.8 on minimising the TSE risk. It **does not** certify that the quality of the substance is suitably controlled by a specific Ph. Eur. monograph.
- A CEP **does not** replace a certificate of analysis
- A CEP **is not** a GMP certificate

The CEP procedure

★ An international platform for:

- **Assessment of the quality of substances for pharmaceutical use** (mainly APIs), with reference to monographs of the Ph. Eur.
- Source of information to **update and revise Ph. Eur. Monographs**
- **Centralised assessment**
- Facilitates **management of MAAs** and variations
- Coordination and conduct of **GMP inspections** of API manufacturers

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CEP and ASMF procedures

★ Drug substance documentation is an integral part of a marketing authorisation application

★ Based on **EU NfG « Summary of requirements for active substances in the quality part of the dossier »**, the applicant can choose the way to provide data on the quality :

- Certificate of suitability (CEP)
- Active substance Master File (ASMF)
- Full details of manufacture in MAA

★ The data to be submitted are the same, regardless of the option selected

CEPs are not mandatory, but generally avoid any subsequent re-assessment

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Comparison between CEP & ASMF procedures

	CEP procedure	ASMF procedure
Purpose	• The CEP is independent from MAA • It confirms that the API complies with Ph. Eur. requirements	• The ASMF is submitted in the context of a specific MAA for medicinal products
Scope of material	Pharmacopoeial substances only: • Active substances or excipients • Any substance for TSE CEP	Active substances only: • New chemical entities • Existing substances
Dossier	• Content identical (CTD 3.2.S) • Full dossier sent directly by the manufacturer to EDQM (will generally be the holder of the CEP)	• Content identical (CTD 3.2.S) • AP sent to the marketing authorisation holder of medicinal product and the RP is submitted to the competent authorities (NCA / EMA)

Comparison between CEP & ASMF procedures

	CEP procedure	ASMF procedure
Evaluation	• **Single** evaluation centralised at EDQM • Assessment performed by assessors from NCA appointed by the Certification Steering Committee • The pool of assessors is a mix of EDQM and assessors from NCA	• **Multiple** evaluations • Assessment of ASMF by each NCA in the context of assessing a specific MAA or variation for medicinal products
Evaluation references and principles	Assessment against: • ICH/EU guidelines for quality • Ph. Eur monographs • EDQM specific guidance	Assessment against: • ICH/EU guidelines for quality • Ph. Eur monographs (if applicable)

Comparison between CEP & ASMF procedures

	CEP procedure	ASMF procedure
Deliverable	• The Certificate is granted to the CEP holder (usually API manufacturer) • CEP holder can provide a copy to their customers (users of the substance)	A Marketing Authorisation for the medicinal product using this particular API
Variations	• Changes to the CEP dossier centralised at EDQM • Submission of revised CEPs according to EU Variations regulation	Submission of changes to marketing authorisation applications, according to EU Variations regulation
Use	• Ph. Eur member states (including the UK) • Others (Australia, Canada, Tunisia, Morocco, Singapore, South Africa, Saudi Arabia, Brazil, etc)	• EU/EEA member states • UK • Australia and Canada

Worksharing and cooperation accross Europe

- ★ Holder's commitment / Annex 7 of the CEP application form foresees sharing EDQM assessment reports with:
  - National Competent Authorities of the Ph. Eur. member states
  - EMA including all CHMP and CVMP Members and their experts
  - Competent Authorities of countries with whom EDQM has a Memorandum of Understanding and/or Confidentiality Agreement in place (list on the EDQM website)

- ★ ASMF reports may also be made available for EDQM (see NfG ASMF procedure CHMP/QWP/227/02 Rev 3 corr).

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How to apply for a CEP

★ **Module 1**: application form (available on the EDQM website)

- Information on CEP holder / manufacturing sites
- Statements and declarations
- Request for a grade / re-test period
- Details on the marketing history (details on accepted ASMFs following October 2012)

★ **Module 2**: Quality Overall Summary
Template for Quality Overall Summary to be submitted for Certification applications

★ **Module 3**: quality part, submitted preferably in English (or in French)

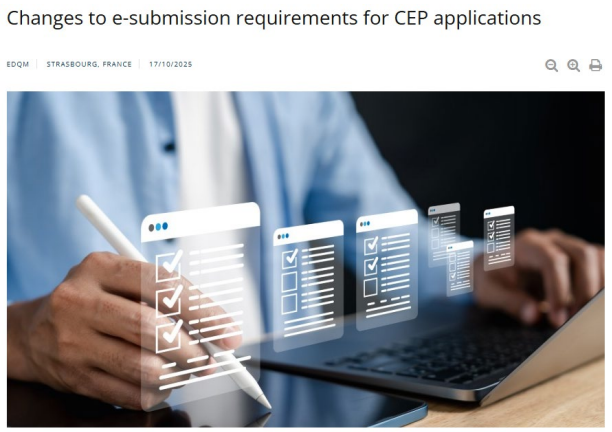
- EDQM guideline “Content of the Dossier for Chemical CEP”: comparable to ASMF or 3.2.S of CTD
- For TSE risk CEP: requirements from Ph. Eur. general text, 5.2.8 and “Content of the dossier for TSE risk”
- “Content of the dossier for herbal drugs/herbal drug preparations”
- “Content of the dossier for sterile substances”

How to apply for a CEP – electronic submissions

★ Electronic submissions for any applications in eCTD format via CESP (register for a CESP account on the Heads of Medicines Agencies website)

- Use of CESP to submit electronic documents to EDQM
- Guidance for electronic submissions for Certificates of Suitability (CEP) applications
- EDQM DCEP Sharing Tool - How to manage your account
- **NEW**: https://www.edqm.eu/en/-/changes-to-e-submission-requirements-for-cep-applications

As of 1st of November 2025, new requirements should be fulfilled (**eCTD validation report** must be provided)



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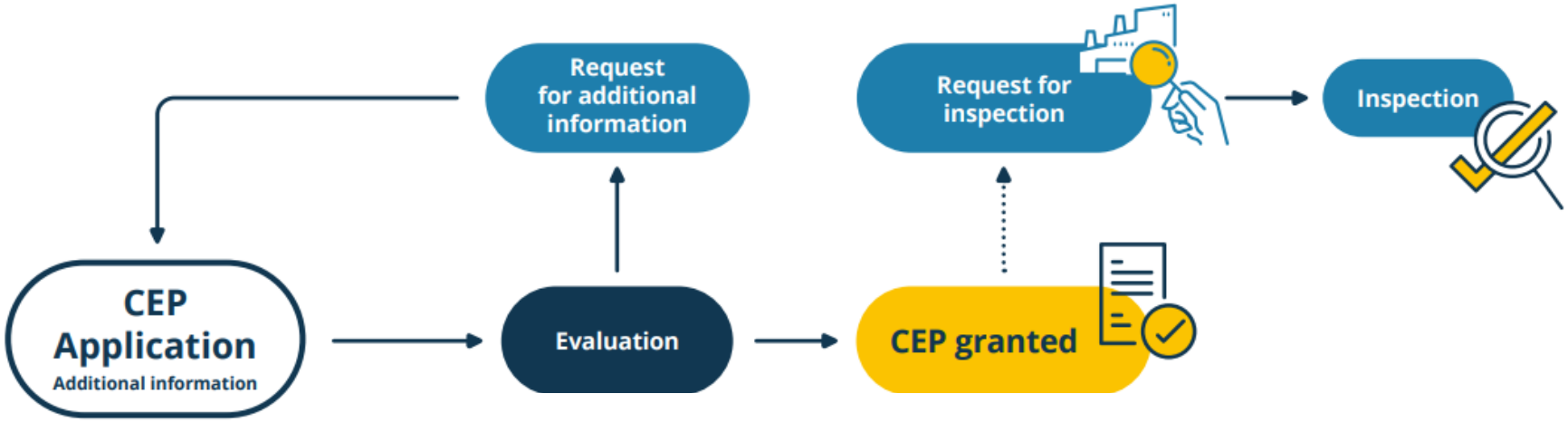
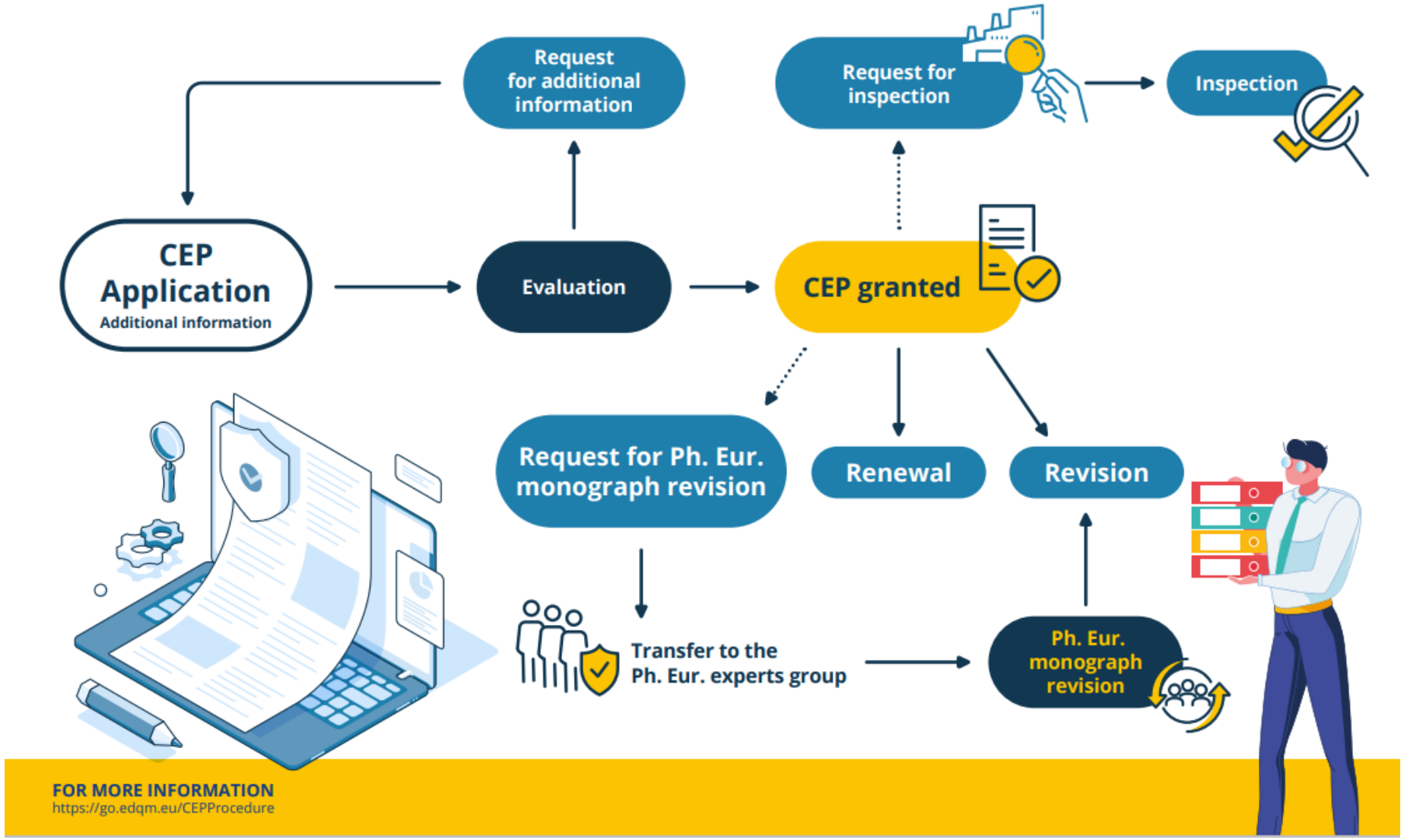
How does it work?



How does it work?



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Basic principles for maintaining a CEP

Once a new CEP is granted, the CEP holder should apply for revisions of their certificate to:

- ★ have changes in the process or in the controls **approved**;
- ★ be up to date with most recent **regulatory requirements**;
- ★ update the certificate with the **administrative changes**

Any change **must be reported** to EDQM **for approval**

- ★ Classification of changes are based on EU Regulations on Variations to Marketing Authorisations (being revised)
- ★ Specific EDQM guideline for revisions of CEPs, available on the EDQM website:

Application form "Request for Revision or renewal of Certificate of Suitability“

Guideline on Requirements for Revision/Renewal of Certificates of Suitability to the European Pharmacopoeia Monographs

Revisions of the CEPs

List of changes classified as:

- Notification: immediate **(IN)** / Annual **(AN)**
- Minor change **(MIN)**
- Major change **(MAJ)**

Non-classified changes are: **Minor by default**

CEP holders have to:

- Inform their customers of any changes made
- Send revised CEP to customers as soon as a revised CEP has been issued

CEP holders responsibilities towards their customers

4.II.1.1 Change in the manufacturer of a starting material used in the manufacturing process of the final substance	Conditions	Specific documentation	Type of change
a) The proposed manufacturer of the starting material is part of the same group as the currently approved manufacturer	1, 2	1, 2, 3, 4	IN
b) The proposed manufacturer of the starting material is not part of the same group as the currently approved manufacturer	1,2	1, 2, 3, 4	MIN
c) The proposed manufacturer of the starting material uses a different route of synthesis or manufacturing conditions which impact the specifications of the starting material		1, 3, 4	MIN
d) The proposed manufacturer of the starting material uses a different route of synthesis or manufacturing conditions which impact the specifications of the final substance			MAJ (*)
e) The proposed manufacturer of the starting material is used in the manufacturing process of a biological substance		1, 3, 5	MAJ

Conditions	
1.	The specifications of the starting material are identical to those already approved.
2.	The final substance is not a biological substance or a sterile substance.
Documentation	
1.	A declaration from the Certificate holder that the specifications of the final substance are the same as those already approved.
2.	A declaration from the Certificate holder that the specifications and the quality control procedures of the starting material are the same as those already approved. If a different route of synthesis is retained for the new supplier, the synthetic flowchart of how the starting material is obtained should be provided.

Sister files

- A company holding a CEP may wish to apply for another CEP for the same substance via the sister file procedure

- There are conditions to meet: the sister file should refer to the parent file and could be treated as a revision of the parent file

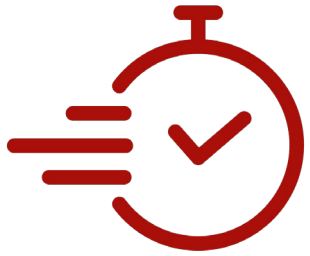
- Document available on EDQM website:

Guidance on applications for «sister files»

- Why applying for a sister file? To benefit from a faster assessment

Fast-Track and Reliance: two pillars for efficient procedure

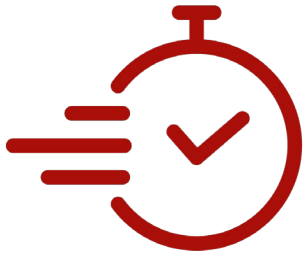
- ★ Support efforts to address shortages of substances
- ★ Support the principles of the Critical Medicines Act



Fast-track

Reliance

Fast-Track and Reliance: two pillars for efficient procedure



Fast-track

★ **What is it?**

Expedited assessment for some applications - e.g. (EU) Union List of critical medicines

★ **How**

- By considering requests from NCA / EMA
- By considering requests from CEP holders based on the Union List of critical medicines or reported shortages

Fast-Track and Reliance: two pillars for efficient procedure

Reliance

★ **What is it?**

Increased use of assessments of NCA to make best use of assessors' resources and enhance convergence of assessment

★ **How**

- CEP applicants declare in the application form whether their substance has been approved by means of an ASMF/DMF
- EDQM gets (confidentially) the relevant Assessment Report from the authority and uses it as a reference for own assessment

Fast-Track and Reliance: two pillars for efficient procedure

★ Support efforts to address shortages of substances on the Union List of Critical Medicines

★ Support the principles of the Critical Medicines Act

Fast-track

- Operational since September 2025
- Official procedures for fast tracked applications will be published in 2026

Reliance

Regulatory Reliance and Fast track assessment in the CEP procedure

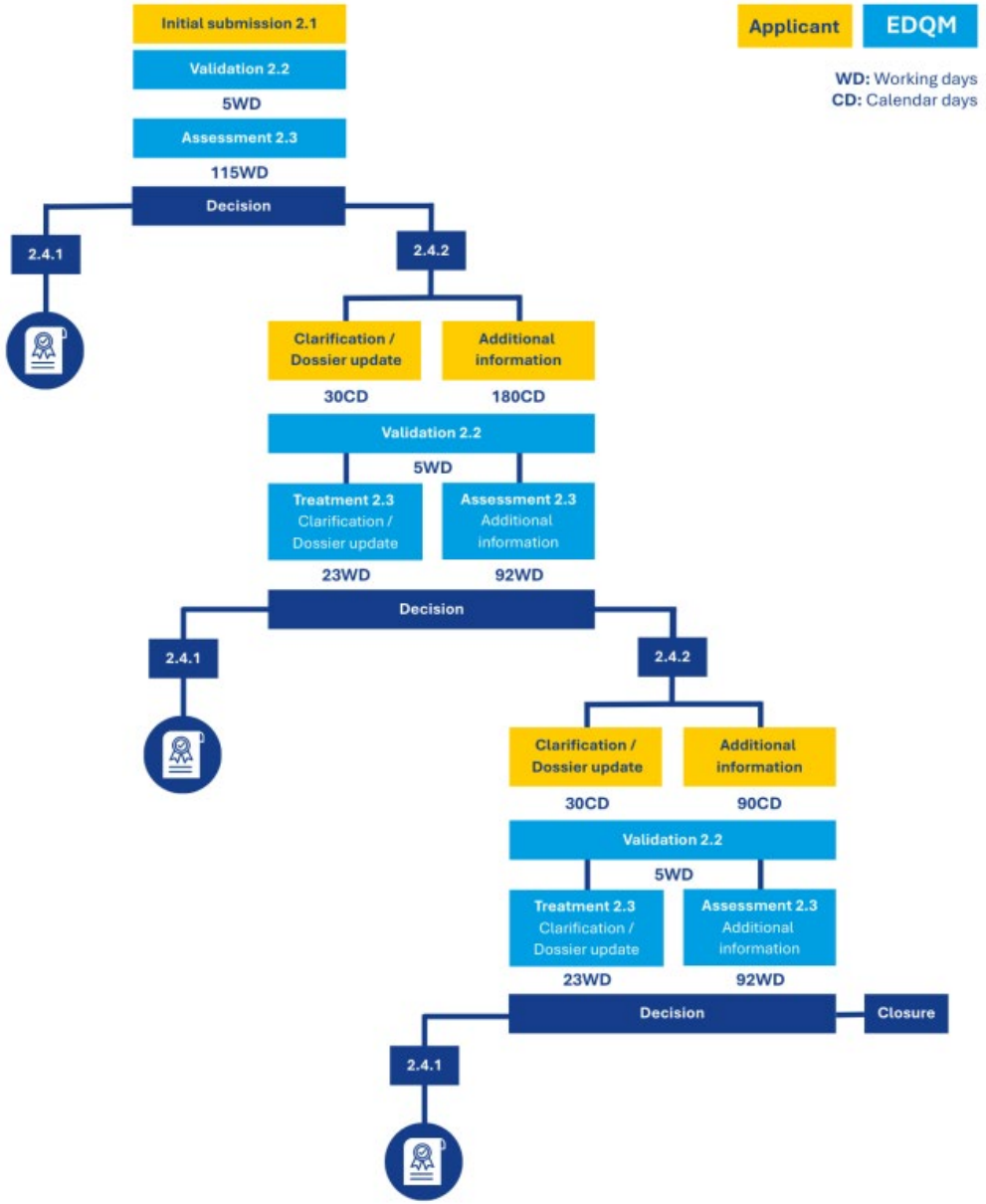
EDQM | 09/10/2025 | STRASBOURG, FRANCE

According to the World Health Organization (WHO), "Good reliance practices are anchored in overall good regulatory practices (GRP), which provide a means for establishing sound, affordable, effective regulation of medical products as an important part of health system strengthening. If...

How long does it take?

"Stepwise process to get a CEP or having a change approved"

For a new CEP application:



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Who performs the evaluation?

- ★ Assessors are proposed by NCA/EDQM and appointed by the CEP Steer. Co.;
- ★ New application are assessed by 2 assessors: most commonly one from EDQM and one from NCA from Ph. Eur member states and beyond
- ★ About 100 assessors from authorities from 25 countries:
  - Skilled in the relevant domain (chemical evaluation, TSE risk, herbal products, toxicologists)
  - Come regularly to EDQM premises for the evaluation of dossiers
  - Procedure for remote evaluations introduced in 2020 (due to Covid-19 pandemic)

The EDQM Inspection programme

★For active substances manufacturing sites covered by CEPs

★Applicants for a CEP commit:

- Manufacture is performed in compliance with GMP or a suitable Quality System (for non-API)
- Willingness to be inspected

★Selection of sites to be inspected based on evaluation of risks

★On-site inspections and Real-Time Remote Inspections:

- Performed mainly in Asia (India and China)
- Together with GMP inspectors proposed by authorities and appointed by the CEP Steer. Co.

Non-compliances to the CEP procedure

★ Non-compliances may be linked to:

- **GMP non-compliance**, following inspection carried out by EDQM or by an EU inspectorate, or refusal to receive an EDQM inspection
- **Failure to update** the CEP application in line with a revised Ph. Eur. monograph or a regulatory change
- Major **quality issue** (eg. Nitrosamines)

★ Need to consider risk for public health and actions to be taken:

- Formal Decision Making Process
- Actions taken on CEPs: suspension, withdrawal, etc..
- Communication to stakeholders + on the EDQM website

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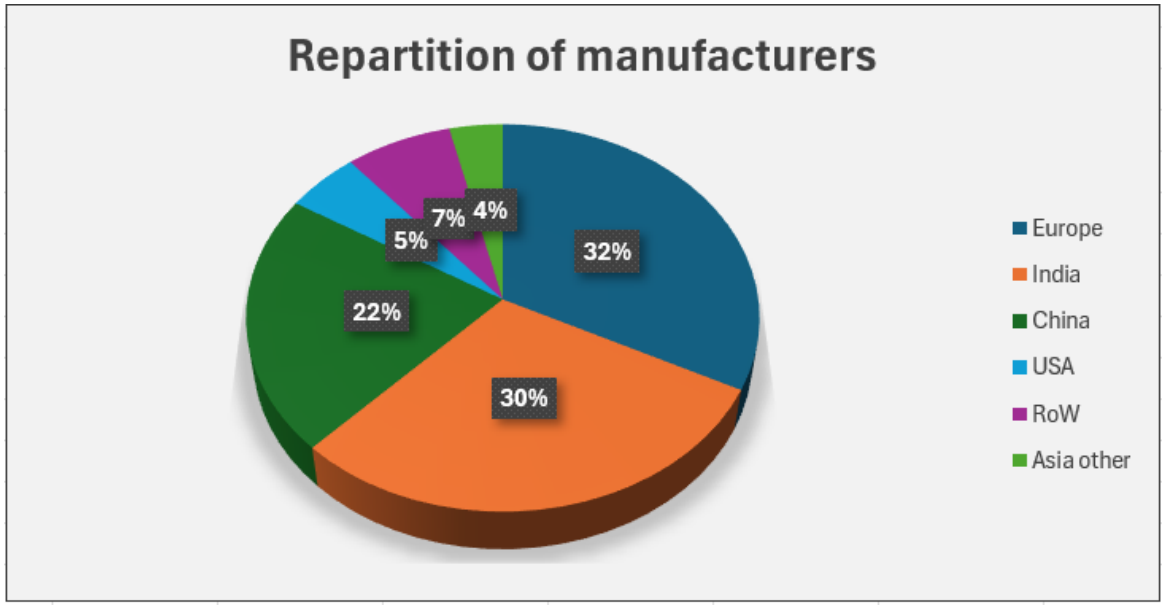
Key figures

- Since 1994, more than 10 000 CEP applications received for nearly 1500 different substances

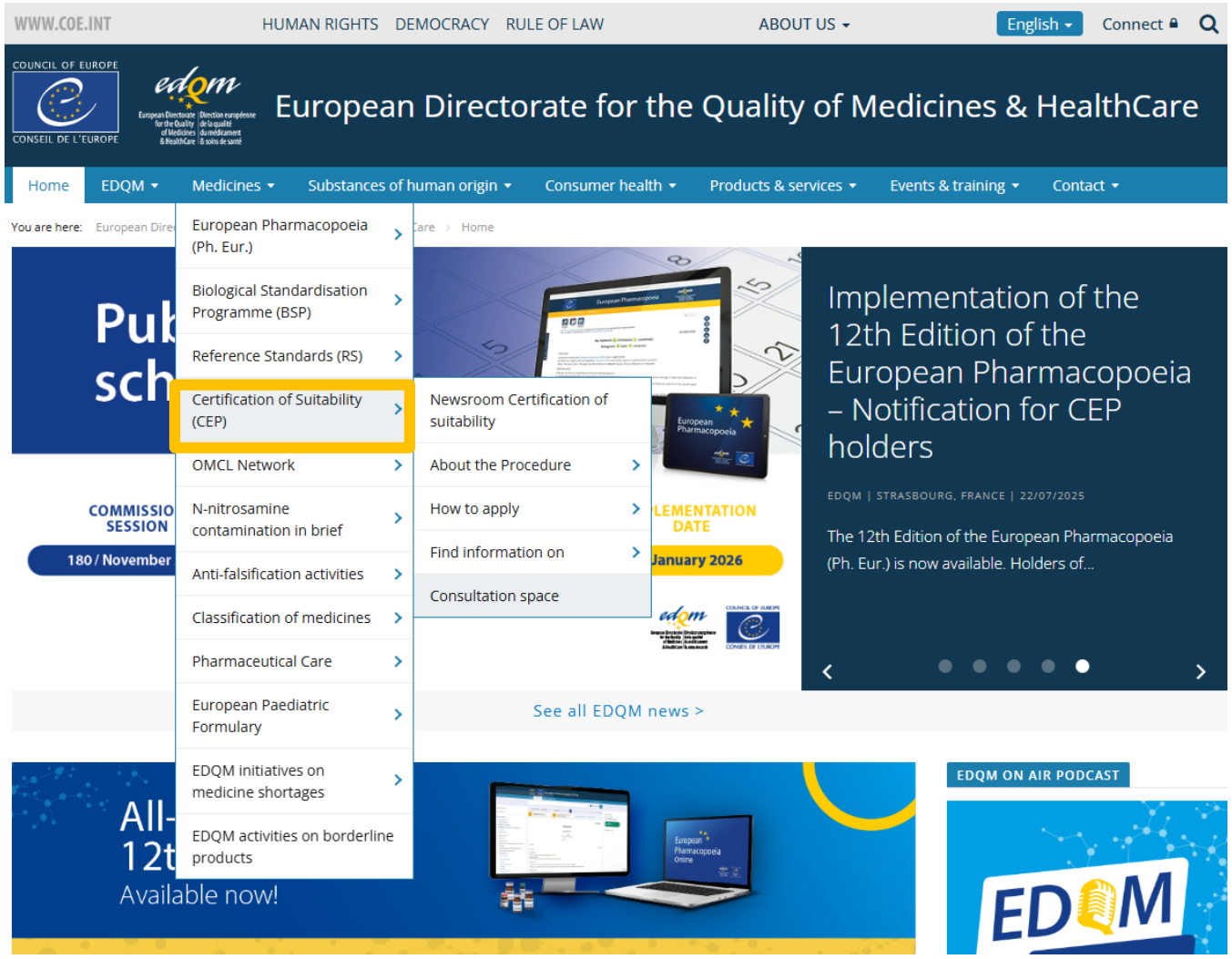
- Currently more more than 7000 valid CEPs

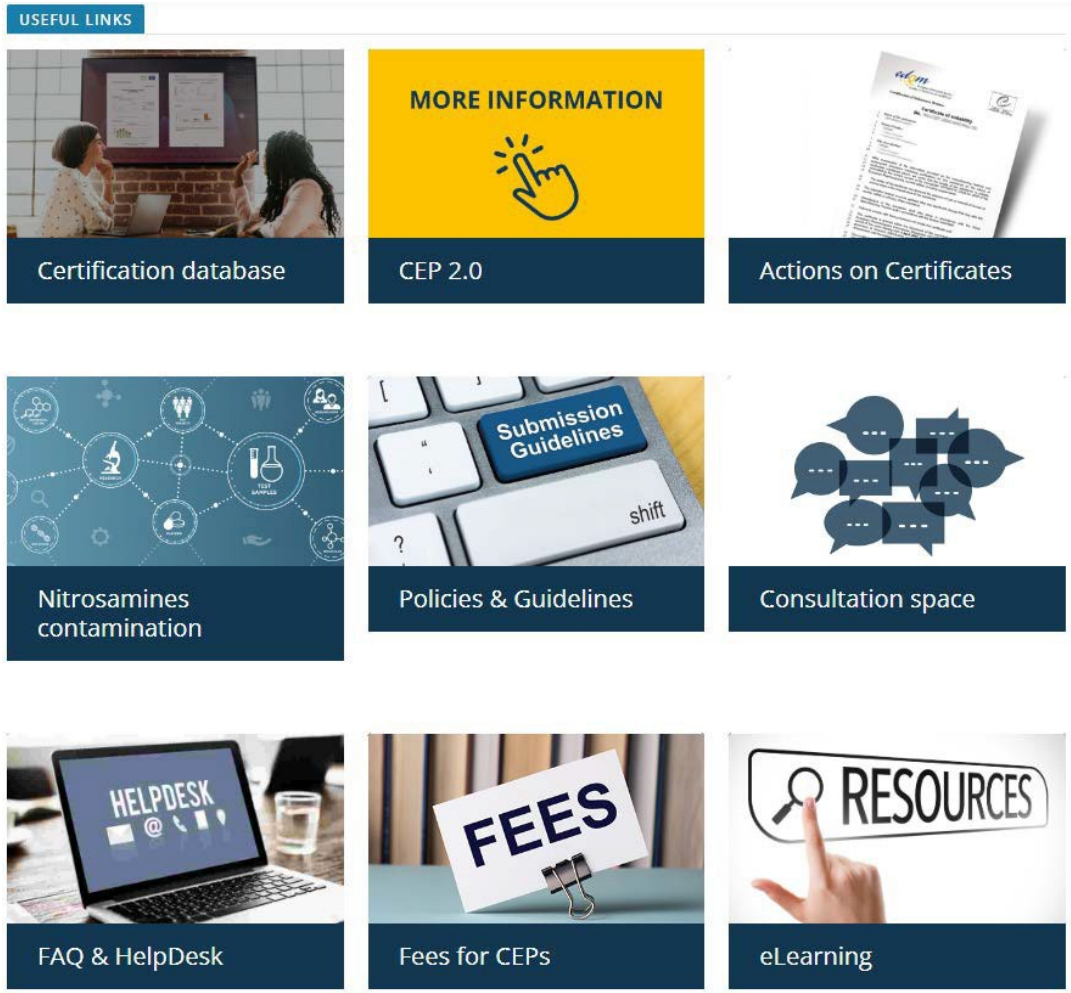
- About 1500 manufacturers from >50 different countries (50% in India and China)



Keep up-to-date with CEP activities

- EDQM Website (www.edqm.eu) > Medicines > Certification of Suitability





Communication with EDQM

- General questions on CEPs: look at the FAQs and if necessary use **EDQM Helpdesk**
- For queries specific to applications: via the email address included in EDQM communication
- Technical Advice: to meet the EDQM staff and get advice about applications (fee applicable)

Thank you for your attention

Anaïs Bouisseau – Certification of Substances Department

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