The place of the Certification procedure in 2017 in the EU regulatory framework and beyond

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CEPs in the EU legislation

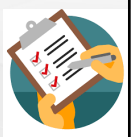
Directives 2001/83/EC and 2001/82/EC state that where the active substance is the subject of a monograph of the Ph. Eur, the applicant can apply for a certificate of suitability that, where granted by the EDQM, shall be presented in the relevant section of the CTD Module. Those certificates of suitability …are deemed to replace the relevant data of the corresponding sections described in the Module…

NfG CHMP/QWP/297/97 rev. 1 corr « Summary of requirements for active substances in the quality part of the dossier »

Gives 3 basic choices for providing information regarding the active substance

2.1. Certificate of suitability

"where applicable, option 2.1 has the advantage of generally avoiding any subsequent reassessment"



2.2. Active Substance Master File (ASMF)

2.3. Full details of manufacture in Marketing Authorisation Application

The information required is the **same** regardless of the procedure selected.

The procedure

- Official implementation in 1994
- An international platform for:
  - Assessment of the quality of substances for pharmaceutical use (APIs, excipients, herbals, TSE risk)
  - Coordination and conduct of GMP inspections of API manufacturers
- Keys for acceptance of CEPs:
  - Strong processes
  - Harmonisation of decisions
  - Transparency

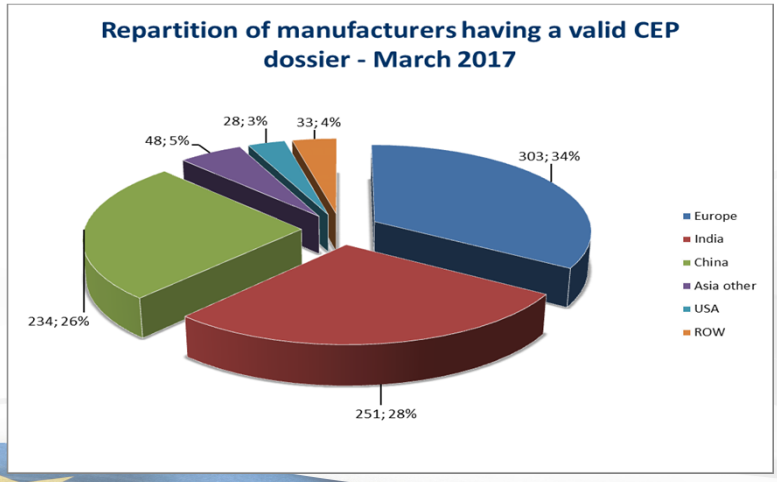
Assessment of CEP applications

- Scope: chemical substances, herbals, TSE risk materials
- About 350 new applications every year (mostly for chemical purity)
- About 1600 requests for revision every year
- More than 90% of applications treated within official deadlines ➔ performance published on a monthly basis
- Strict treatment of applications - 3-round policy for assessment
- #17 months to get a new CEP (min 6 months-max 3.5 years)

EDQM inspection programme

- Based on mandate from the EU commission
- Programme well established
  - ➢ More than 65 sites covered by the programme every year
  - ➢ Combination of on-site inspections and exchange of information with EU/EEA/MRA and international partners
  - ➢ Rate on non-compliance #20%
- >50% of sites involved in CEPs and located outside EU/EEA have been covered by the programme

Repartition of API manufacturers



Who is involved

- Steering Committee
  - 16 members, representing the main organisations & working groups in Europe and Ph. Eur member states
  - Takes decisions on scope, makes links with regulatory groups and adopts EDQM guidelines
  - Current chair: Dr Jean-Louis Robert
- Technical Advisory Boards (TAB)
  - Chemical, TSE, Herbals
  - Experienced assessors (n=10 for chemical TAB)
  - Prepare policies, guidelines, take decisions on technical issues…

Who is involved (2)

- Assessors from National competent authorities from Ph. Eur member states, and beyond
  - ➢ Skilled in the relevant domain (chemical evaluation, TSE risk, herbal products, toxicologists…)
  - ➢ Come regularly to EDQM premises for the evaluation of dossiers together with EDQM colleagues

101 assessors from 27 countries

Who is involved (3)

- 28 inspectors from supervisory authorities from 16 EU/EEA countries + Switzerland
  - ➢ Perform inspections with EDQM

- EDQM Certification Department
  #40 people: assessors, inspectors, scientific and administrative staff
  - ➢ Run the procedure, coordinate the activities and communication

CEPs and Ph. Eur. activities

- CEP procedure intended to provide information on the need to revise Ph. Eur. monographs
  - ➢ During assessment, "Report B"
  - ➢ When impurities present in a source of substance are not detectable by the monograph, or to propose improvements to the monograph
  - ➢ After agreement from the CEP holder, the report + some data from the CEP dossier are communicated to the group of experts
  - ➢ 27 requests in 2016

CEPs and Ph. Eur. activities

- Revision of monographs have an impact on CEP applications:
  - Need to update specification accordingly
  - Need to demonstrate suitability of the revised monograph to control a specific source of substance
- Systematic process: for each Ph. Eur Supplement, all affected CEP holders are contacted and asked if necessary to provide data for assessment
  - After assessment a revised CEP may be granted
- With this process, assurance that a CEP always refer to the current version of a monograph
  - About 200 dossiers updated in 2016

Cooperation with CHMP/CVMP Working Groups/Parties

- Close cooperation
  - EDQM observer to QWP, BWP, GMDP IWG, etc
  - Working groups chairs are members of the CEP SC
  - Bilateral reviews of draft documents
  - Some issues have been brought by EDQM to QWP (and vice-versa) eg. Manufacturers of intermediates, API-mix, etc
- Result = Facilitates harmonised implementation of policies

CEP and EU ASMF worksharing

- EU ASMF worksharing programme promotes worksharing for the assessment of ASMFs in the EU, under the authority of the CMD(h)
- Includes sharing of assessment reports amongst Authorities (cf. guideline for ASMF procedure CHMP/QWP/227/02)
  - Based on CEP holder declaration
  - EDQM may share reports with competent authorities of EU, of Ph. Eur. member states, and with EMA
  - ASMF reports may be made available for EDQM

➔Improved efficiency & harmonisation of decisions

CEPs beyond Europe

An increasing number of authorities outside Europe, and WHO, have decided to accept CEPs to support their work

- Eg. Australia, Canada, Morocco, Singapore, South Africa, TFDA, Saudi Arabia, etc …
- No official list of countries available
- CEP often accepted with additional documents, national requirements apply. A number of countries have published guidance on how to use CEPs

CEPs beyond Europe (2)

- Strengthened communication with authorities outside Europe
  - ➢ Bilateral confidentiality agreements to exchange information, including assessment reports and inspection reports
    - ✓ Based on holder's consent for assessment reports
    - ✓ In 2016-2017, assessment reports provided to ANVISA, TFDA, WHO, and EU authorities
    - ✓ In 2016-2017, inspection reports provided to ANVISA, HC, PMDA, USFDA, WHO
    - ✓ Recent MOU with ANVISA
- Participation in International Generic Drugs Regulatory Programme (IGDRP)

CEPs beyond Europe (3)

- Participation in PIC/S
- Participation in International API inspection programme
  - ✓ Exchange of information on planned inspections, inspection results and performing joint inspections
  - ✓ Worldwide impact of the work of this group
- Visits of agencies officials at EDQM
  - ✓ ANVISA (Brazil) and Saudi Arabia FDA in 2017

➔Increasing common understanding worldwide

THANK YOU !

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