Reliance on CEPs

South African, MCC Perspective

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Place of the Certification Procedure in the Global Regulatory Environment ,
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edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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MEDICINES CONTROL COUNCIL

Alternative API Evaluation

- CEP- Certificate of Suitability-EDQM
- CPQ-WHO

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Background to Acceptance of CEPs

- Duplication of assessment of the same API from same source (same DMF open part) is inefficient especially when confronted with large numbers of API source changes
- API source/synthesis changes reached 81% in 2013 Time
- Sometime same API sources evaluated during pre-registration stage for other products
- Many same API's from the same manufacturers are being applied for by the same and different applicants resulting in evaluation of the same DMF/ASMF/APIF repeatedly

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Provisions In The Regulatory System

- **3.2.R.3 Certificate(s) of suitability with respect the Ph.Eur. (CEPs)-*Not in Module 3.2.S ,as may be expected***
- A valid EU certificate of suitability (CEP) may be submitted if available.
- The CEP certifies the suitability of the relevant Ph. Eur. monograph to control the quality of the API produced by the manufacturer specified in the CEP.
- The Ph. Eur. must be used for API specifications and procedures if a CEP is submitted

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Important Notes For Applicants

- that the CEP is accompanied by any annexes mentioned in the CEP.
- -additional requirements indicated in the CEP
- and the methods described in the annexes are officially part of the API specification and therefore should be submitted.
- ensure that the declaration of access is completed. i.e- impurities and residual solvents listed in the CEP should be included in the API specifications (3.2.S.4.1).

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Important Notes For Applicants

- It is the responsibility of the applicant to be aware of changes in the status of CEPs that are used for their products and to notify Council accordingly.
- It is also the responsibility of the applicant to ensure that the revised CEP is obtained from the CEP holder when applicable and to submit such updated CEP
- If the CEP is withdrawn or suspended for whatever reason a DMF or APIF should be submitted within six months, in accordance with 3.2.S.

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Additional Information Required

- 3.2.S.1.3 General properties -. solubility and polymorphs as per guidance in this section.
- 3.2.S.3.1 polymorphs (exception: where the CEP specifies a polymorphic form) and particle size distribution, where applicable, as per guidance in this section.
- 3.2.S.4.1 Specification - the specifications of the FPP manufacturer and additional tests for polymorphs and/or particle size distribution.
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Additional Information Required

- 3.2.S.4.2 / 3.2.S.4.3 Analytical procedures and validation – for any methods used by the FPP manufacturer in addition to those in the CEP and Ph.Eur. monograph.
- 3.2.S.4.4 Batch analysis -
- 3.2.S.5 Reference standards or materials – information on the FPP manufacturer's reference standards.
- 3.2.S.6 Container closure system -.
- 3.2.S.7 Stability - exception: where the CEP specifies a re-test period

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What Benefits Does The CEP Offer To The Regulator, MCC?

- CEP provides an assurance that the API concerned is of good quality,
- Sometimes also provide confidence that API manufactured in accordance with Good Manufacturing Practices (GMP) –MCC, currently do not inspect API manufacturing sites.
- Reduced product dossier assessment time – reduced API source change assessment time
- Less data required as opposed to DMF/ASMF/APIMF submission (e.g detailed route of synthesis not required)

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Benefits to API manufacturers

- CEPs can be issued independent of an FPP application.
- Public recognition as a source of quality API, manufactured in compliance with GMP.
- Opportunities to compile, revise and refine their regulatory documentation, leading to quicker acceptance by other national regulatory agencies.
- MCC, South Africa has recognised and accepted CEPs **before 2007** -Manufacturers could investigate on other regulatory agencies that recognise CEPs.

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Benefits To Applicants & FPP Manufacturers

- Ease of identifying potential sources of quality API complying with compendial STDs, e.g Eur.Ph.
- Identifying API manufacturers with robust quality systems in place, GMP
- Identifying API manufacturers that maintain good regulatory documentation, which may be used in regulatory submissions.
- Reduced API assessment requirements
- Reduced post-registration variations (changes) requirements.
- Saves time, resources and costs in finding reliable manufacturers
- Less information is required as compared to ASMF/APIMF/DMF evaluation

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Validity of CEPs

Search Database online | Certification edqm

1 records matching your search string: " ethambutol".
Click on the hyperlink(s) in column"Substance Number" below to obtain a more detailed information on the substance monograph.

Issue date - Indicates date of issue of the Certificate number listed.'

Type - The type of certificate is given as TSE or Chemical or Double and indicates whether a certificate is concerned by TSE risk evaluation ('TSE') or evaluation of chemical and microbiological quality ('Chem.') or both ('Double').'

New Search

Substance Number	Substance	Certificate Holder	Certificate Number	Issue Date	Status	Type
553	Ethambutol hydrochloride	Lupin Limited IN 400 098 Mumbai	R1-CEP 2000-019-Rev 02	30/09/2008	VALID	Chemistry

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How To Submit When CEPs Is Use

- As per Amendment guideline requirements i.e 1.0; 1.1; 1.2.1; 1.5.2.1; 3.0; 3.1;
- 3.2.S (limited information);
- 3.2.R.3-CEPs is complete and accompanied by the accepted
  - annexes -specifications, additional
  - *retest period and storage conditions*.
  - Also ensure that the authorisation box of the CEPs is filled out by the API manufacturer in the name of the manufacturer or applicant seeking to use the document.

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Some Challenges

- Unable to verify the validity of the CEP
- Some CEP declarations section not completed and signed- Manufacturer/applicants
- Storage instruction not reflected on CEP,
- An additional API source with a CEP,
- Notification of amendments (including the nature of the amendment) to the regulator

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THE END!

Thank You

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