SAPRAA Meeting

Alternative API evaluation processes e.g. Confirmation of WHO API Prequalification - CPQ

Silverani Padayachee

30 October 2015
Bytes Conference Centre-Midrand

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

Alternative API evaluation processes

- **CEP- Certificate of Suitability-EDQM**
- **CPQ - Confirmation of WHO API Prequalification**

What happened following the inclusion of the CPQ information in the P&A guideline??

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

About CPQ

- **What is CPQ?**
- **What benefits does CPQ offer?**
- **How to submit when a CPQ is used ?**
- **What information is required in addition to CPQ?**
- **What is the difference between CPQ and CEP in terms of submission?**
- **Finding API's and API sources that have CPQ's**

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

What is CPQ?

The CPQ is a confirmation document provided by the WHO prequalification (PQ) of Medicines Programme/Team indicating that the relevant API has been evaluated and conforms to the WHO requirements for prequalification of APIs.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

When a CPQ is issued?

A CPQ (Confirmation of Active Pharmaceutical Ingredient Prequalification document) is issued by WHO PQ medicines programme to the successful API-PQ applicant

This document may be provided at the discretion of the API manufacturer to other parties, such as FPP manufacturers.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

mcc
MEDICINES CONTROL COUNCIL

What does the CPQ contain?

Provided to the API manufacturer for distribution at their discretion

- The assigned WHO application number.
- The INN name of the active pharmaceutical ingredient.
- API manufacturer company name.
- The API specification version number.
- A copy of the API specifications.
- The assigned re-test period.
- The recommended storage conditions.
- A copy of the assay and related substances test methods.

Intended for: UN agencies, National medicine authorities, FPP manufacturers

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

WHO requirements for PQ API's

The requirements for submission of an API to WHO for PQ is located *Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product (FPP): Quality part* (TRS 970, Annex 4)

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

What benefits does the CPQ offer?

Applicant & Regulator

- API prequalification provides an assurance that the API concerned is of good quality and manufactured in accordance with WHO Good Manufacturing Practices (GMP) –recognised MCC
- The prequalification guidelines are inline with the guidance of the stringent regulatory agencies
- 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)

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

mcc
MEDICINES CONTROL COUNCIL

Benefits to API manufacturers

- API's can be prequalified independent of an FPP application.
- Public recognition as a source of quality API, manufactured in compliance with GMP.
- Serves as a point of difference between good quality and poor quality APIs.
- Opportunities to verify compliance with GMP.
- Opportunities to compile, revise and refine their regulatory documentation, leading to quicker acceptance by other national regulatory agencies.
- There is currently no fee.
- Investigations are being made how API PQ can be recognised by National authorities. MCC South Africa has recognised and accepted CPQ (API) in Aug 2014. Other regulatory agencies that recognise CPQ are Malaysia; The East African Community and Zimbabwe

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

(Courtesy: WHO prequalification of Medicines Programme-Dr A Fake)

Benefits to FPP manufacturers

- Ease of identifying potential sources of quality API.
- Identifying API manufacturers with robust quality systems in place.
- Identifying API manufacturers that maintain good regulatory documentation, which may be used in regulatory submissions.
- Reduced API assessment requirements (PQP)
- Reduced post-prequalification variation (changes) requirements.
- There is no fee.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

(Courtesy: WHO prequalification of Medicines Programme-Dr A Fake)

What benefits does the CPQ offer?

Applicant

- API PQ helps identify acceptable sources of quality APIs manufactured in compliance with GMP
- Saves time, resources and costs in finding reliable manufacturers
- Less information is required as compared to ASMF/APIMF/DMF evaluation

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

Validity of CPQ

Third parties receiving copies of a Confirmation of Active Pharmaceutical Ingredient (API) Prequalification Document can confirm the validity of this document in two ways:

•First, the confirmation document includes an authorization box. This box should be filled out by the API manufacturer in the name of the manufacturer or agent seeking to use the document.

•Second, the validity of the Confirmation of Active Pharmaceutical Ingredient (API) Prequalification document can be determined by comparing the date of the document with that published on the List of prequalified APIs.

Please note: A revised Confirmation of Active Pharmaceutical Ingredient (API) Prequalification document will be issued every time there is a change in the API specifications, retest or storage condition, assay or related substance test method.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

mcc
MEDICINES CONTROL COUNCIL

How to submit when CPQ is used

Process is similar to that of CEP

- 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- CPQ is complete and accompanied by the accepted
  - specifications,
  - assay and related substance methodology,
  - retest period and storage conditions.
  - Also ensure that the authorisation box of the CPQ is filled out by the API manufacturer in the name of the manufacturer or applicant seeking to use the document.

Difference in CEP & CPQ submissions

CEP	WHO CPQ
Assessment by EDQM	Assessment by WHO PQ team
Certificate of suitability issued	Confirmation of prequalification document
May or may not include GMP inspection	Always include GMP inspection
API conforms with Ph.Eur monograph (note annexes)	Accepted tests and methods as per CPQ
May or may not include re-test period	Includes retest period and storage conditions
Specifications based on monograph and annexes	Copy of specification (vers & date) included
Declaration of access by holder of CEP	Authorisation box by holder of API CPQ
Minimal additional information required	Minimal additional information required
Includes assessment of any API included in Ph. Eur (limited to Ph.Eur monograph)	Includes only ARV; TB; Malaria; reproductive health; anti-diarrhorea; neglected tropical diseases i.e limited to therapeutic areas but not to a single pharmacopoeia

Finding API's with CPQ's

The date of prequalification is the date when the API is published on the WHO List of Prequalified Active Pharmaceutical ingredients.

http://www.who.int/prequal/info_applicants/API_PQ-List.htm

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

Prequalification of Medicines website

Prequalification of Medicines Programme - Windows Internet Explorer

http://apps.who.int/prequal/

World Health Organization

Search OK

WHO Medicines
Quality & Safety
Prequal home
About us
A-Z Listing of Documents
Information for applicants
Dossier assessments
Prequalification of APIs
Inspections
Quality Control Laboratories
Quality Monitoring
Training material, workshops and meetings
Press and media

Home - Prequalification: Active Pharmaceutical Ingredients - Information for applicants

Prequalification of Active Pharmaceutical Ingredients - Information for applicants

General information

- An introduction to WHO prequalification of active pharmaceutical ingredients (APIs)
- Who can participate
- What information is required
  - Application form
- Where this information should be submitted
- What requirements and standards must be met in order to be prequalified
- What information is published in the WHO List of Prequalified Active Pharmaceutical Ingredients
- The Confirmation of API Prequalification Document
- What happens if an API master file (APIMF) has already been submitted in relation to a finished pharmaceutical product (FPP) that has been prequalified
- Disclaimer
- Confidentiality

Active pharmaceutical ingredients (Pilot project) - Expression of Interest

- Invitations for Expression of Interest (EOI)

Prequalification guidelines related to active pharmaceutical ingredients

- Guidance on technical content of an APIMF

Information for national medicines regulatory agencies (NMRAs)

- For NMRAs seeking further information on the assessment of prequalified APIs

http://www.who.int/prequal

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

WHO List of Prequalified APIs

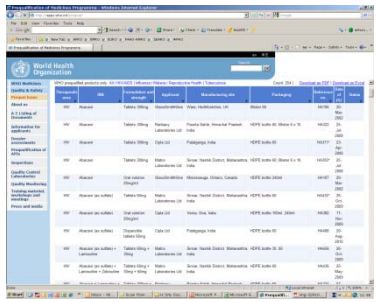
Publically available

- WHO application number.
- INN name.
- Date of prequalification.
- Name of the applicant
- Sites of API manufacture.
- The APIMF version number.
- The API specification version number.
- The primary and secondary packaging components.
- The assigned re-test period.
- The recommended storage conditions.
- Confirmation of API PQ document issue date

Intended for: UN agencies, National medicine authorities, FPP manufacturers, public

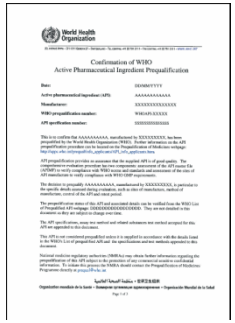
health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Publishing



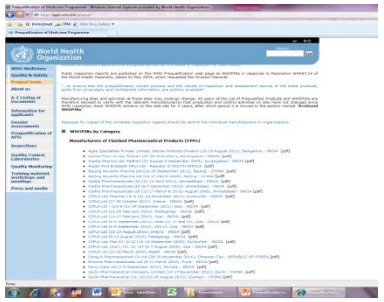
List of PQ APIs
Website (Public)

+



Confirmation of WHO
Active Pharmaceutical Ingredient Prequalification

Confirmation Document (Private)



WHOPIRs
Website (Public)

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Abbreviations

- API – Active Pharmaceutical Ingredient (*drug substance*)
- CPQ- confirmation of prequalification (API)
- FPP – Finished Pharmaceutical Product (*drug product*)
- APIMF – Active Pharmaceutical Ingredient Master File (*DMF)*
- PQ-APIs – Prequalification of Active pharmaceutical Ingredient
- SRA – Stringent Regulatory Authority
- GMP – Good Manufacturing Practice

Acknowledgements

WHO prequalification of medicines programme/team

Dr Mathias Stahl

Dr Antony Fake

Ms Isabel Ortega-Diego

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL

Questions ??