Prequalification Team – Medicines (PQTm)

Update

Dr. Matthias Stahl,
Group Leader Medicines Assessments
PQ Medicines assessments 2018-2019

Some highlights

• High number of FPPs are expected to be prequalified in 2019 in part due to the tighter response timelines for applicants
• Early signs of reduced manufacturer time to prequalification (FPPs)
• More variations due to increasing number of prequalified products and requalification applications – still PQ is meeting its timelines
• Dramatic increase in the number of requalified FPPs during the last year – 52 vs. 7 products over the same period in 2017 – 2018 (due to risk-based approach, allocation of more resources and faster responses by manufacturers).
• Total time to acceptance of an APIMF has decreased, both for WHO and manufacturers (since 2017, by one-third for WHO time).
• Regulatory support to manufacturers has been strengthened
  • More advisory meetings, eg pre-submission meetings, in 2019
  • The Copenhagen workshop for manufacturers is now an annual event
Time to prequalification of medicines (FPPs, median, full assessment) 2010-2018

- WHO time
- Company time
- Total time to PQ

Copenhagen, Denmark      2 – 5 December 2018
Key performance targets for medicines assessments (full assessment)

- Screening: 80% of applications screened within 30 days (2018 – 98%)
- “First action” (first round of Q and S/E assessments) – completed for 80% of dossiers in less than 120 days (2018 – 89%)
- Total WHO time to PQ – less than 270 days for 70% of FPP and 30% of API applications (2018: FPPs – 42% less than 270 days, but for 70% it was less than 300 days; APIs – 35% less than 270 days)
- First action for variations to FPPs (including amendments to APIMFs) – completed for 80% within the timelines stated (2018 – 86%)
WHO and company time to prequalification of FPPs (days) – since 2013
New or updated guidances

• PQ Medicines develops guidances on an ongoing basis, many of them product-specific, eg BE study design, Q&As etc.

• Updated “Q&A on variation applications” (November 2019) – options for handling of unclassified changes, further update planned including clarification of API related changes

• Updated “General Notes on Biopharmaceutics Classification System (BCS)-based Biowaiver Applications” (March 2019) – adding misoprostol

• Updated Comparator products list (November 2019)

• Updated “Guidance on Bioequivalence Studies for Reproductive Health Medicines” (October 2019)

• New BE design advice, for example

  - Fexinidazole
  - Amphotericin B (liposomal)
  - Levofloxacin
  - Linezolide
  - Moxifloxacin

  - Oseltamivir
  - Ribavirin
  - Zanamivir
  - Abacavir

Note, e-mail your final draft BE protocols to us for review, before study start.
Recent additions to EOIs

- Tuberculosis
  - Pyridoxine (vitamin B6), tablet 50 mg (scored), tablet 10 mg (scored)

- Reproductive health
  - Heat-stable carbetocin, injection 100 microgram/ml - in 1 ml ampoule
  - Tranexamic acid 100 mg/ml - in 10 ml ampoule

- Malaria
  - Primaquine base 2.5 mg tablets (preferably dispersible for paediatric use)
  - Primaquine base 3.75 mg tablets (preferably dispersible for paediatric use)
  - Primaquine base 5 mg tablets (scored) (preferably dispersible for paediatric use)
  - Primaquine base 7.5 mg scored tablets (scored) (preferably dispersible for paediatric use)
**Pilot prequalification of BTPs/SBPs (rituximab, trastuzumab) - ongoing**

- Pilot in progress
- Biotherapeutic product experts mainly from UK and Spain
- Guidances (full assessment, abridged pathway), templates, screening check lists, Q&As on website

  - 25 dossiers received for pre-submission advice (as of 26 Nov 2019)
  - Pre-submission meetings are being held
  - So far almost all dossiers for full assessment have been too deficient to take further
  - Some dossiers for the abridged pathway are nearing prequalification.

- **Planned:** Publication of a PQ-specific addendum to the Risk Management Plan, publication of WHOPARs
- Recently EOI for human insulin published
Pre-submission meetings

• Pre-submission meetings are mandatory for applicants new to PQ
  - Generally when the applicant has generated at least 1-2 months stability data on submission batches
  - Important to have early interaction to plan the pre-submission meeting, or to address specific questions
• Pre-submission meetings are recommended for any applicant especially if unusual products/products with particular issues.
• PQ Medicines can provide advice at any stage before, or after submission - *PQ is accessible. You should use this opportunity!*
Facilitated prequalification of products supported by SRA assessment reports

- **CRP lite (pilot):** a collaboration between USFDA and WHO PQ whereby minimally redacted USFDA reports for tentatively approved products are shared with WHO PQ to facilitate its assessment and further registration in countries in the context of CRP
  - For applications not yet submitted to PQ, or submitted and in the initial stages of assessment
  - Possibly reduced total time to prequalification due to sharing and expected good quality dossier with fewer deficiencies
  - Two FPPs (ARVs) are currently under assessment in the pilot (closed)
- Concept of using SRA reports is not new (EMA)
PQTm collaboration with regulators and WHO clinical departments

• Increased collaboration with regulators to facilitate prequalification of FPPs and APIs
  • CRP-lite
  • Increased sharing of reports from EMA to assist in APIMF and FPP assessments
  • Increased sharing of reports from the EDQM, and to the EDQM to assist in APIMF and CEP assessment
  • PQ co-chairs the IPRP* QWGG (Quality Working Group for Generics) whose purpose it is to promote sharing of quality information between members

• Increased collaboration with WHO clinical departments to explore the possibility of inviting certain FPPs and APIs for prequalification at an earlier time point while treatment policy recommendations are being developed

*International Pharmaceutical Regulators Programme
PQT-M Quality Workshop for Manufacturers

• The 2\textsuperscript{nd} Quality Workshop for manufacturers was held in July 2019 – 60 participants from 30 companies.

• The 3\textsuperscript{rd} workshop is planned for 1-3 July 2020.

• To be announced on the PQ website in the spring of 2020.
Thank you!