PQM Program Technical Assistance for the WHO Prequalification Programme

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Promoting the Quality of Medicines Program
Outline

- Promoting the Quality of Medicines (PQM) Program good manufacturing practices (GMP) expertise
- PQM technical assistance (TA) statistics
- Example of PQM TA projects
- WHO prequalification on second-line tuberculosis (TB) medicines
- PQM TA
- How PQM TA works
- Lessons Learned in Russia and Commonwealth of Independent States (CIS)
- PQM TA on major issues
In-house experts experienced working with
- World Health Organization (WHO) Prequalification Programme
- Global Pharma Health Fund (GPHF)

Field consultants experienced working with
- WHO Prequalification Programme (PQ)
- US Food and Drug Administration (FDA)
- Australian Therapeutic Goods Administration (TGA)

Consultants experienced working with
- US FDA bioequivalence (BE) reviews
As requested by USAID, PQM provides TA on WHO PQ to manufacturers of first-line and second-line anti-TB medicines:

- 14 countries
- 12 active pharmaceutical ingredients (API)
- 14 finished pharmaceutical products (FPP)
- Over 55 projects total

Projects WHO Prequalified with PQM’s TA

- Zinc sulfate FPP from France (first and only zinc product prequalified; Maternal and Child Health funding)
- Cycloserine FPP from South Korea
- Isoniazid API from China
Projects that have received PQM TA:
- Capreomycin FPP GMP site inspection (WHO PQ)
- Capreomycin API Supplier I GMP site inspection (WHO PQ)
- Capreomycin API Supplier II GMP site inspection (WHO PQ)
- Streptomycin API Supplier GMP certificate (Spanish Government Agency) as a result of Corrective and Preventative Action (CAPA) on WHO PQ site inspection

Fastest turnaround from start of validation batches to passing WHO PQ GMP site inspection:
- Seven months for Capreomycin FPP
PQM Technical Assistance—Global Scope

PQM is currently providing TA on WHO PQ in 14 countries

- China
- Ghana
- India
- Indonesia
- Kazakhstan
- Kenya
- Nepal
- Nigeria
- Philippines
- South Korea
- Taiwan
- Tanzania
- Ukraine
- Zimbabwe

In addition, PQM has completed TA for France. In Russia, work under USAID funding stopped in 2012.
PQM Technical Assistance toward WHO PQ—Scope

- Provide reference standards
- Provide comparator products
- Provide CRO information on BE study to FPP producers
- Provide API supply info to FPP producers
- Dossier preparation
- Pre-dossier submission assessment
- Post-dossier submission assistance
- GMP gap analysis
- Mock audit
- Hands-on CAPA assistance
- CAPA document assistance
GMP Audit

- Conduct on-site GMP assessment to prepare manufacturer for WHO PQ inspection
- Validate integrity of data submitted
- Conduct full pharmacopeial monograph analysis and reporting
- Assist with CAPA implementation after WHO inspection, if needed
PQM began working in Russia in 2009, and in CIS in 2011

- Challenges encountered in process:
  - Engaging companies to express interest in submission for WHO Prequalification is difficult
  - Due to different stability requirements, company would need to invest more time and money to repeat stability testing
  - Infrastructure investment must be made to obtain GMP compliance
Challenges encountered in process, cont.

- Language: All documents submitted to WHO must be initiated in or translated into English; more time and effort for manufacturers
- Manufacturers are satisfied with local market, do not feel that time and money invested to obtain WHO PQ is a profitable decision
- Manufacturers are unaware of WHO PQ and its benefits
- Unreliable API source
- TA to manufacturers in Russia stopped in 2012 when the Russian government decided to end USAID activities
Lessons Learned (1)

- Risk approach to sterilized manufacturing
- Manufacturing media fill validation
- Environmental monitoring during sterilized powder-filling
- Validation master plan
- Equipment qualification protocols
- Warehouse sampling room
- Technology development report
- Process validation on critical process parameters and in-process controls (IPCs)
Lessons Learned (2)

- Gowning requirements for sterile manufacturing
- Sterilization and use of tools and equipment parts for manufacturing
- Behavior and workflow in Class A and Class B clean room environments
- Different quality and regulatory requirements
- Lack of understanding of GMP trends as required by WHO
Convince manufacturers that obtaining WHO Prequalification is a way to upgrade their GMP compliance, which will enable them to enter more stringent markets, e.g., those regulated by the EU or USA.
Thank You