Promoting the Quality of Medicines

Promoting the Quality of Medicines(PQM) Program Technical Assistance

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U.S. Pharmacopeial Convention

Workshop for NMRAs and Manufacturers of Medicines for Treatment of Tuberculosis and Neglected Tropical Diseases

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USP U.S. Pharmacopeial Convention

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Outline

- Overview of the USP PQM Program
- Overview of USP PQM technical assistance to manufacturers and national regulatory agencies
- USP PQM contributions to improving standards of practice in LMICs and the resulting public health impact
- Conclusion

Promoting Quality of Medicines Program

- PQM is the result of a cooperative agreement between US Agency for International Development (USAID) and United States Pharmacopeia

- In fulfillment of USP and USAID missions, PQM serves as a mechanism to help USAID-supported countries strengthen their quality assurance systems to better ensure the quality, safety and efficacy of medical products that reach patients

- This collaboration between USP and USAID is a 25-year long partnership!

PQM Results Framework

Goal: Strengthen quality assurance systems to sustainably ensure the quality and safety of medical products, and thereby protect public health

IR1: Medical products quality assurance systems strengthened

- **IR 1.1** Quality assurance policies, legislation, guidelines and procedures improved
- **IR 1.2** Registration, inspection and licensing functions of medicine regulatory agencies sustainably improved (Pre-market)
- **IR 1.3** Standard of practices at national quality control laboratories sustainably improved
- **IR 1.4** Institutional capacity for regulatory workforce sustainably improved
- **IR 1.5** Capacity for post-marketing surveillance of medical products sustainably improved

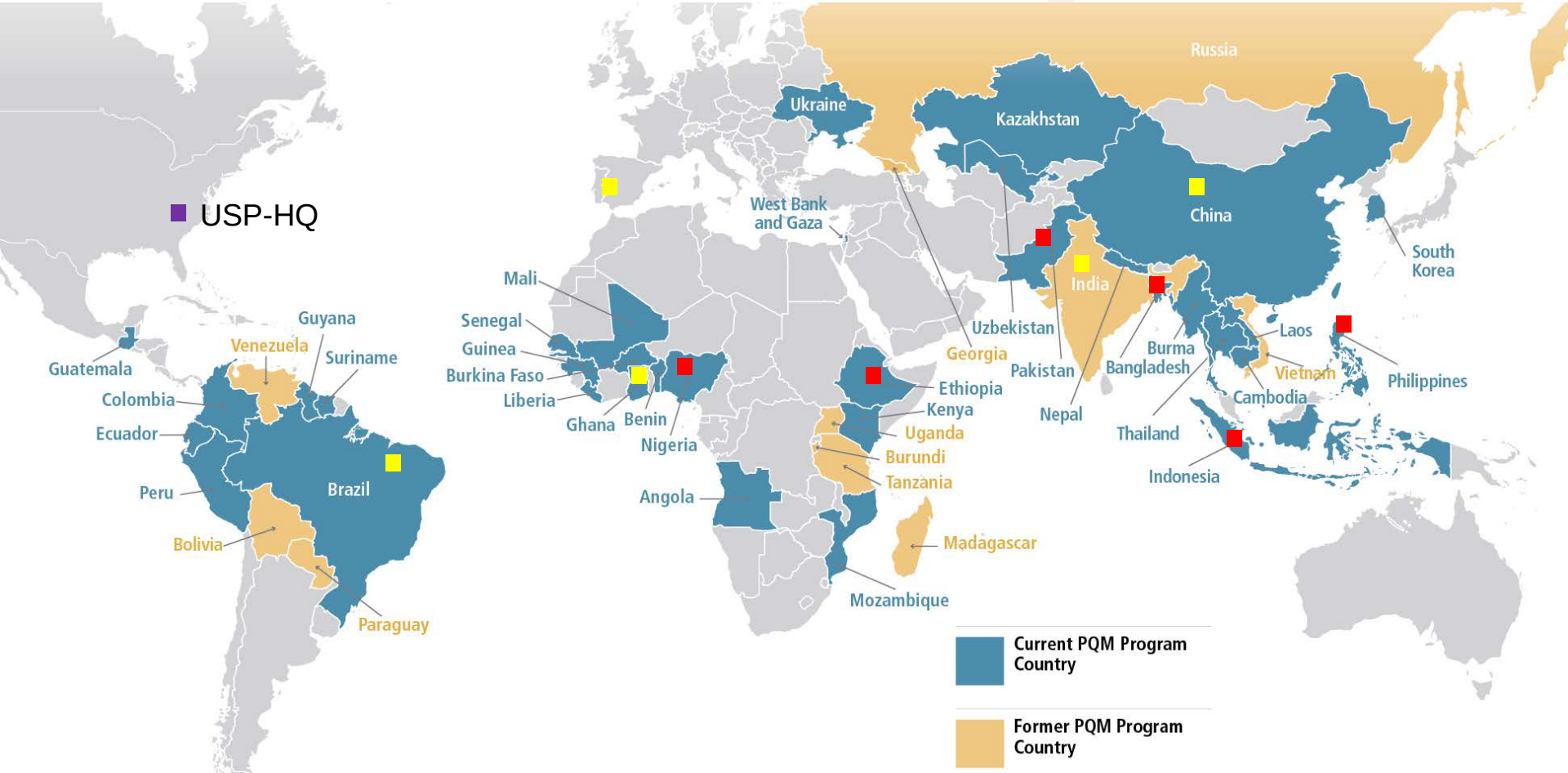
IR2: Supply of quality assured priority medicines increased

- **IR 2.1** Quality assured priority medicines produced locally increased
- **IR 2.2** Quality assured priority medicines produced globally increased
- **IR 2.3** CROs compliance with Good Clinical practices and Good Laboratory practices increased
- **IR 2.4** Sources of quality assured API and FPP diversified and supply secured

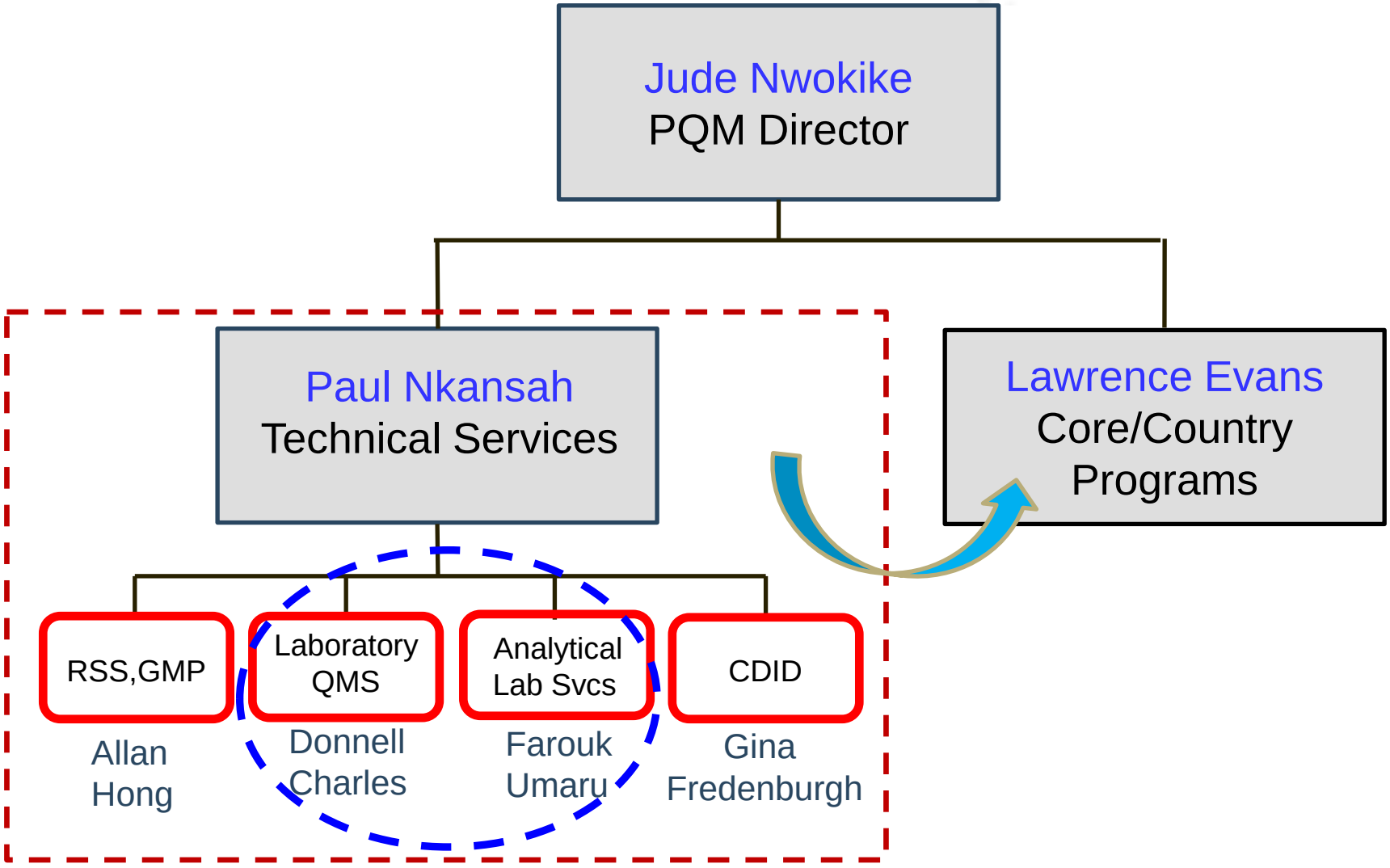
IR3: Utilization of medical product quality information for decision-making increased

- **IR 3.1** Availability of information related to quality of medical products increased
- **IR 3.2** Enforcement actions against falsified, substandard and unapproved medical products increased
- **IR 3.3** Information on quality assurance of medical products used for advocacy increased

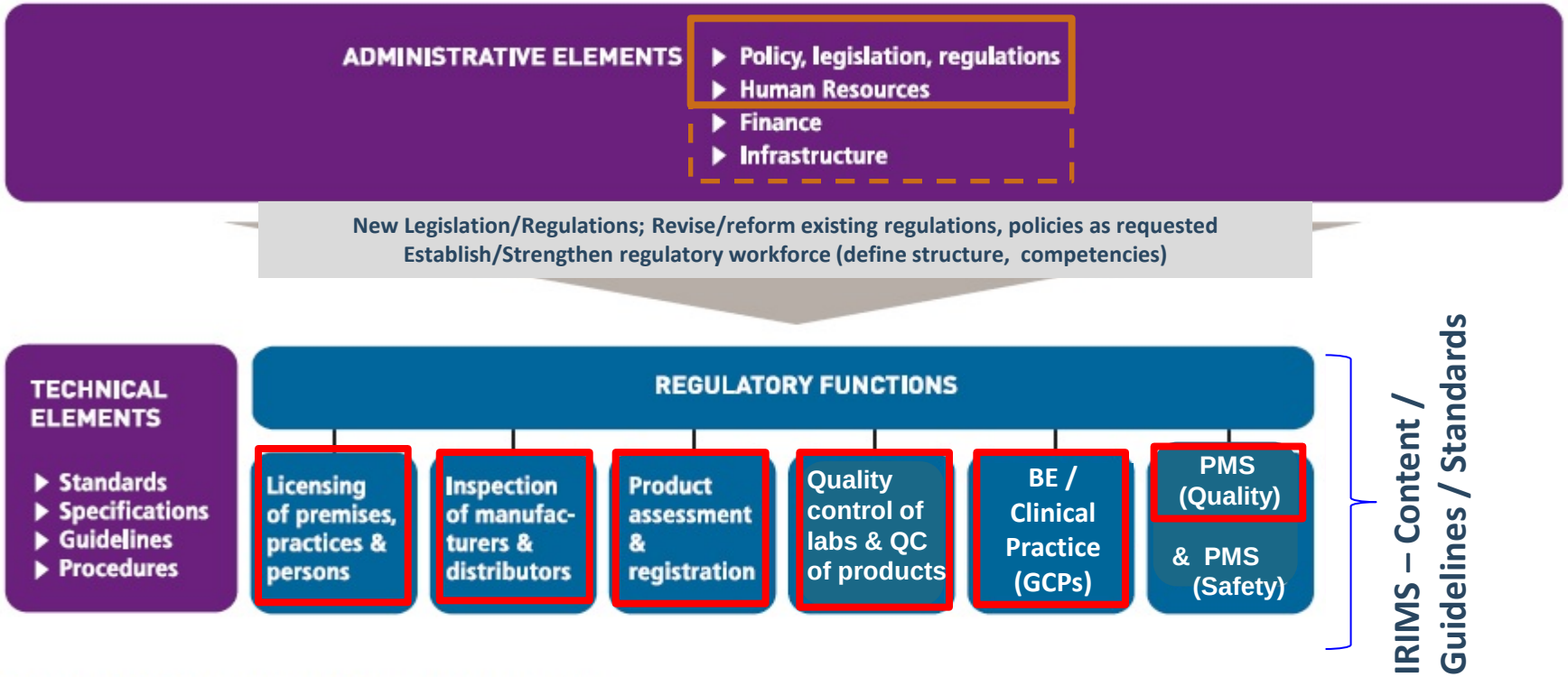
USP-PQM Global Footprint



USP-PQM Organizational Structure



Regulatory System Quality Assurance



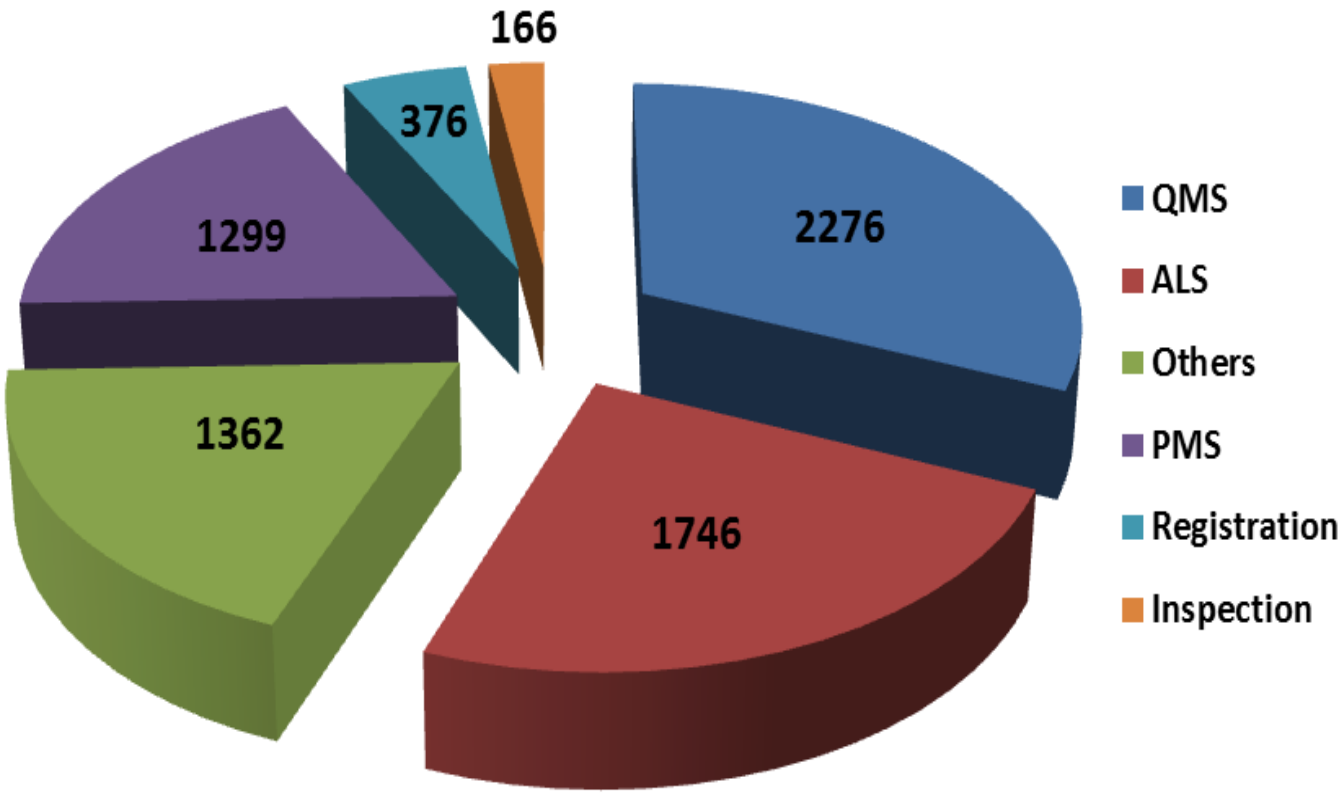
Source: Modified from Ratanawijitrasin/Wondemagegnehu 2002, 12.

Support GMP Licensing of manufacturers , distributors, warehouse and other pharmaceutical premises	Build Capacity of inspectorates GMPs, GLPs, GDPs, GSP, and GCPs Inspections	Training in Good dossier review practices (GDRev)	Training in QMS, GLPs, Testing, etc. toward WHO PQ ISO 17025	Training in GCP Reqs. & Inspections	Help develop PMS program (Guidelines and protocol) Help train on PMS

Red boxes: Primary areas of primary PQM mandate

Training by regulatory technical area 2009 - Present

(**7225** Individuals - 51% female)



30 National Regulatory Agency
(Africa, MENA, Asia, LAC, CIS)

Laboratory Services

Laboratory Quality Management Services

- Works collaboratively with NQCLs to build/strengthen Quality Management Systems to international standards of practice
  - Systems for facility, equipment, management, personnel
  - Guidelines, procedures and processes
  - Good Laboratory and Documentation Practices
  - Proficiency in quality control testing
  - Internal audit
  - Corrective and Preventive Actions

- Supports NQCLs to comply with international standard for laboratories, leading to ISO/IEC 17025 accreditation and/or WHO Prequalification

PQM Analytical Laboratory Services

- Provide full capacity building laboratory services, including design, qualification, maintenance, calibration and metrology
- Provide hands-on technical training in quality control testing of medicines, to strengthen NQCL and local manufacturers towards ISO/IEC 17025 and/or WHO Prequalification
- Perform analytical tests for NQCLs who lack capacity, or for partners (UNICEF, USAID, WHO, NIH) prior to medicines procurement, clinical trials, etc.
- Support development of monographs for public health – Zinc Sulfate, Zinc Gluconate, Zinc Acetate, Vitamin-A liquid, CHX gel, MiniLab, etc
- Evaluate new field-based medicines detection tools, and train on existing tools such as MiniLab, CD-3, TruScan™

PQM Contributions to improving laboratory standard of practice in LMICs

(2009 – Present)

82 laboratories across **30** LMICs

20 Africa
1 in MENA
50 in Asia
5 in CIS
6 in LAC

20 Labs ISO accredited or WHO PQ'ed

4,022 laboratory personnel from **30** LMICs received training

(Laboratory QMS, Analytical testing, Instrument maintenance and calibration)

Good Manufacturing Practice (GMP) Services

Technical Assistance to Manufacturers

Provide hands-on training and consultation to manufacturers on pharmaceutical development and manufacturing

- Provide guidance on API process development and scale-up
- Provide guidance on drug product development and scale-up
- Troubleshoot API and formulation issues

Support for product dossier

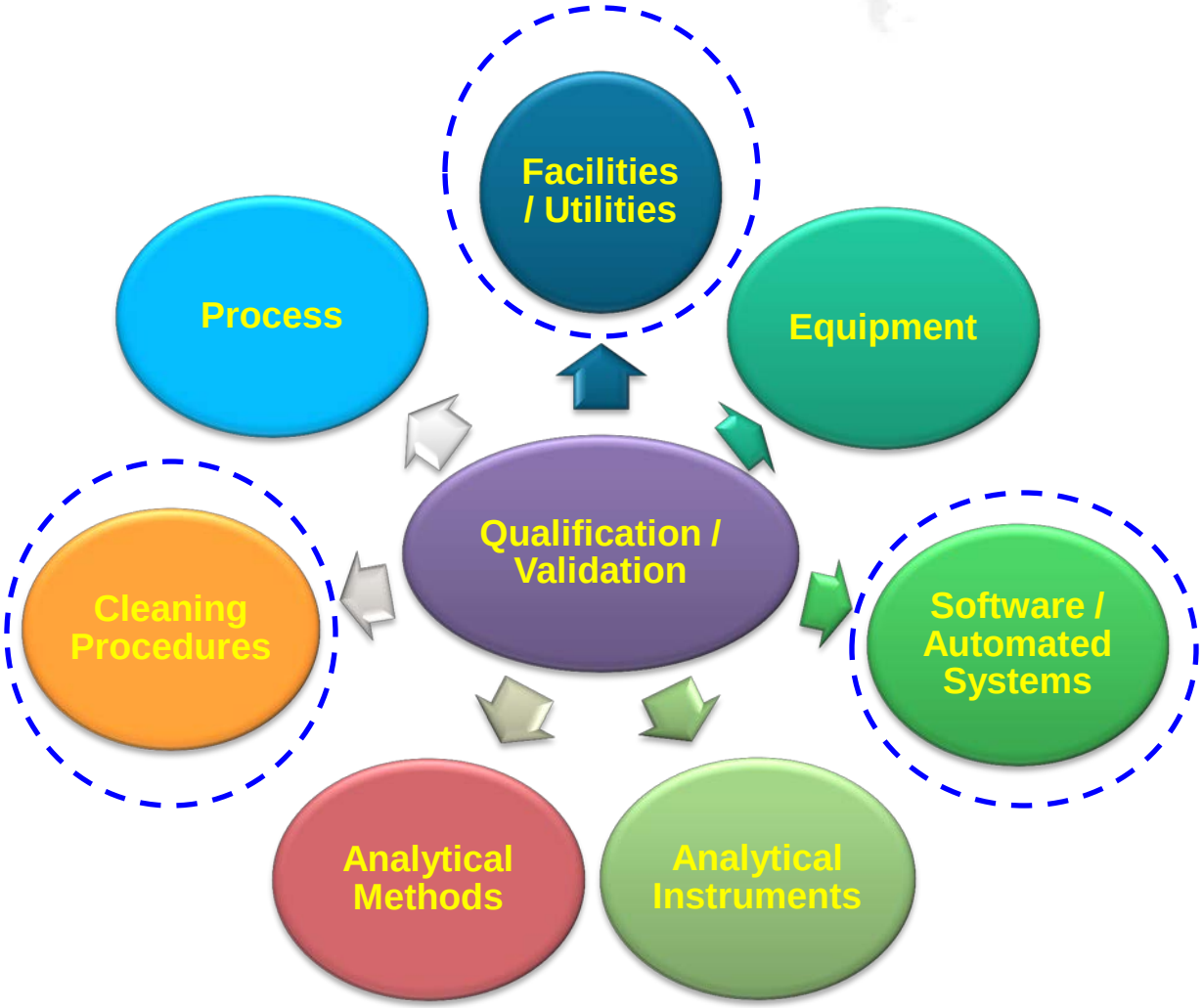
- Assist with dossier compilation according to CTD format
- Guide critical research to fulfill dossier requirements

Support for facility GMP and BE/GCP compliance

- Manufacturing facility GMP compliance
- Contract research organization (CRO) GCPs and GLPs in support of bioequivalence studies

Continuous follow-up and support until product approval

Validation/Qualification Support

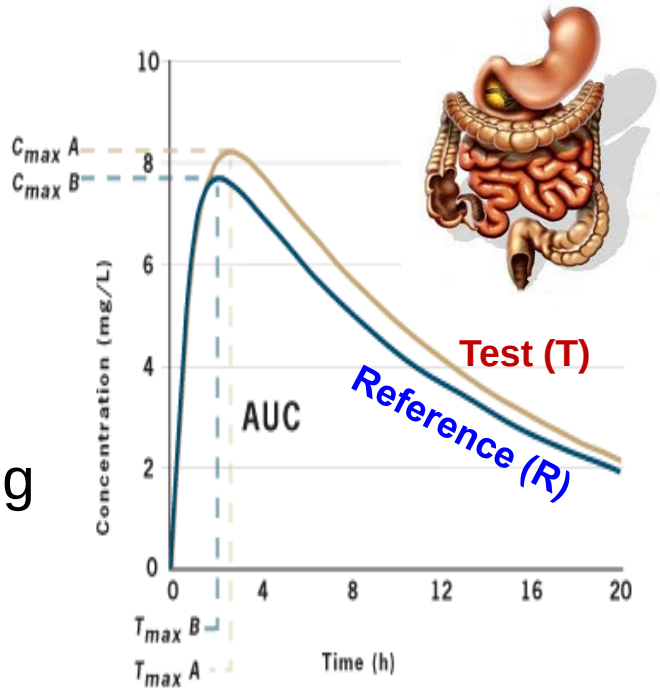


Support for BA/BE and CRO Inspections

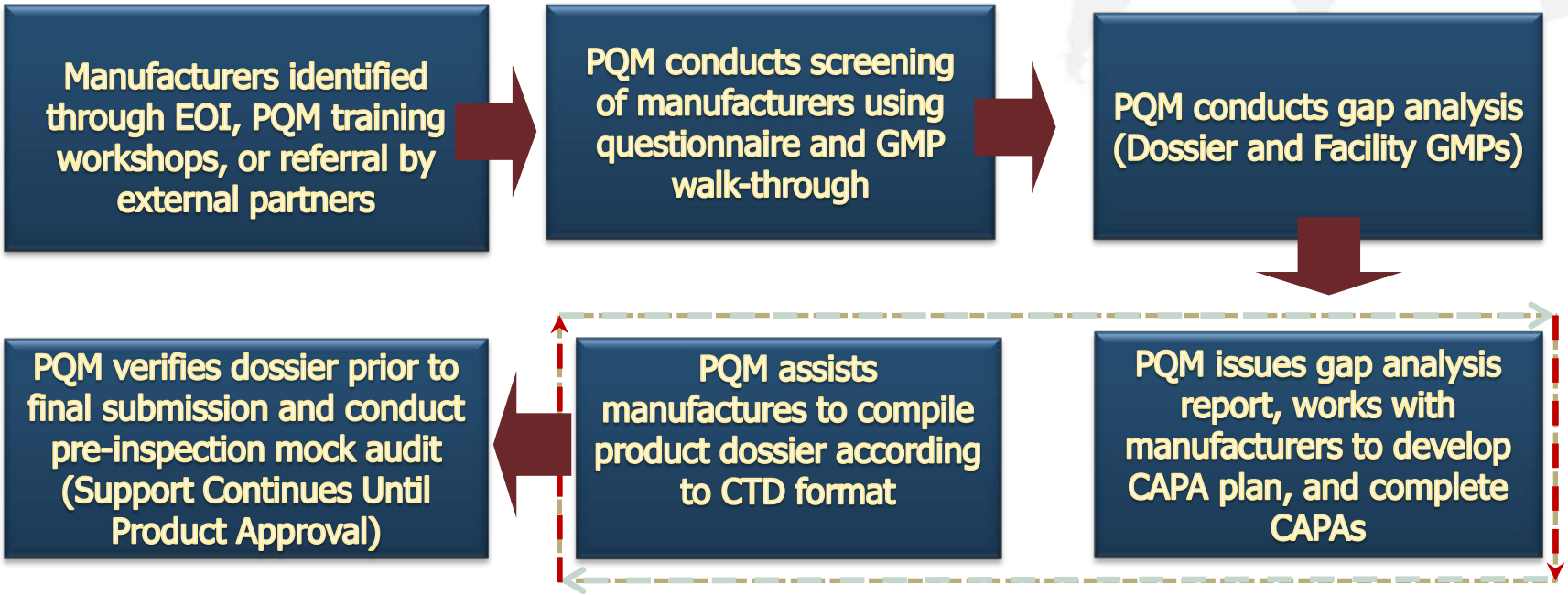
- High BE failures, high cost of BE studies, and surge in notices of concern make this a critical area for intervention
- PQM provides technical support to regulators and CROs in support of BA/BE studies according to GCPs and GLPs

Training of regulators, sponsors, CROs

- BA/BE guidelines and requirement
- BE study protocol review
- CRO GCP support pertaining to study conduct, monitoring, termination, self-auditing, PK/Statistical analysis, reporting and documentation
- GLPs (ISO/IEC 15189,17025)



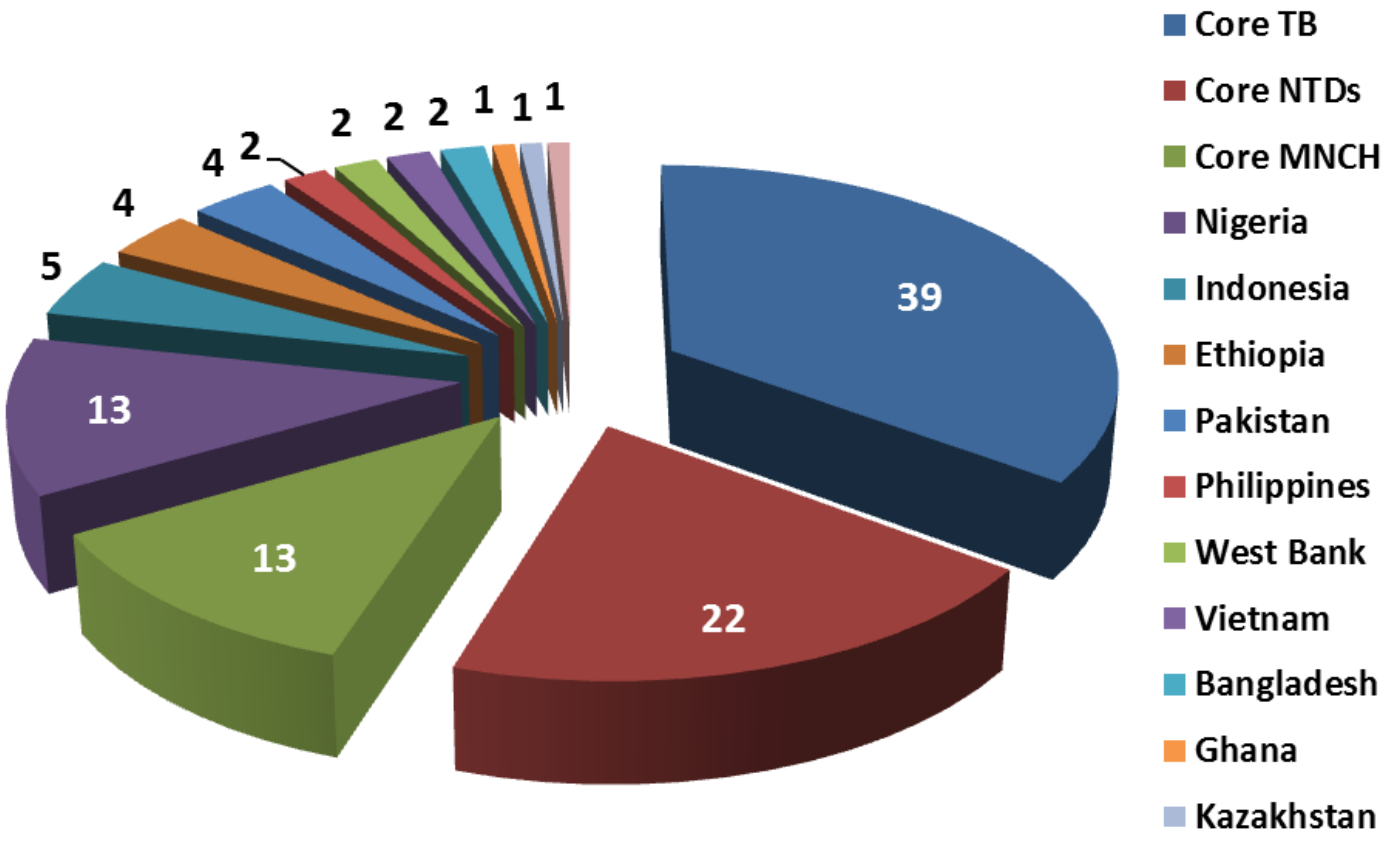
Workflow for Technical Assistance to Manufacturers



- PQM assists pharmaceutical manufacturers and regulator in low- and middle-income countries in achieving compliance with WHO PQ, as well as the regulatory requirements of stringent authorities such the USFDA, EU/EDQM, TGA, etc.
- Medicines regulatory authorities and manufacturers are trained in all aspect of dossier and cGMPs.
- By obtaining the approval of WHO or a stringent regulatory authority, quality-assured priority medicines become available to the public health market.

Manufacturers Supported October 2009 to Present

(**1971** Individuals - 55% female)



111 manufacturers, 22 countries

Results – WHO PQ, USFDA , EU, Global Fund ERP, UNICEF

1	Zinc Sulfate FPP	Lab Pharma Rodael	WHO PQ	2012
2	Cycloserine FPP	Dong-A Pharma	WHO PQ	2012
3	Streptomycin API	Shengxue Pharma	Spanish RA	2013
4	Isoniazid API	Second Pharma	WHO PQ	2013
5	Capreomycin API	NCPC Pharma	WHO PQ	2014
6	Capreomycin API	Hisun Pharma	WHO PQ	2014
7	Levofloxacin API	Langhua Pharma	WHO PQ	2014
8	Mebendazole API	Yabang Phama	CEP	2014
9	Azithromycin FPP	HEC Pharma	WHO PQ	2014
10	BE CRO	PT Equilab	MHRA	2014
11	Capreomycin FPP	Hisun Pharma	WHO PQ	2015
12	Moxifloxacin API	Hisun Pharma	WHO PQ	2015
13	Kanamycin API (non-sterile)	Fuzhou Fuxin	USFDA	2015
14	Kanamycin API (non-sterile)	Fuzhou Fuxin	WHO PQ	2015
15	Zinc Sulfate FPP	Chi Pharma	UNICEF	2015
16	Moxifloxacin API	HEC Pharma	CEP	2015
17	Kanamycin FPP	Interpharma/SHP	Global Fund ERP	2015
18	Kanamycin API (Sterile)	Fuzhou Fuxin Pharm	WHO PQ	2016
19	Mebendazole API	Changzhou Yabang Pharma	WHO PQ	2016
20	Cycloserine API	Dong-A Pharma	WHO PQ	2016
21	Streptomycin API	NCPC Huasheng Pharma	WHO PQ	2016
22	Rifampicin API	Shenyang Antibiotic Manufacturer	WHO PQ	2016
23	Levofloxacin API	Shangyu Jingxin Pharma	WHO PQ	2016
24	Praziqauntel API	Shanghai Jiayi Pharma	CEP	2016
25	Cycloeserine	Hisun Pharma	WHO PQ	2016

USP-PQM Portfolio – USAID Priority Medicines By Disease Program

Tuberculosis	Neglected Tropical Disease	Maternal, Newborn, Child Health
High Priority: • Kanamycin Sulfate API, • Clofazimine API, • Clofazimine 100mg capsules • Linezolid API, • Linezolid 600 mg coated (scored) • Gatifloxacin API, • Gatifloxacin 200mg Tablet • Gatifloxacin 400mg Tablet • Moxifloxacin API • Rifapentine • FDC (Rifapentine with INH) • Pediatric first line fixed-dosed combination (preferably dispersible or crushable tablets): o Rifampicin(R) 75 mg/ Isoniazid 50mg / Pyrazinamide 150mg o Rifampicin(R) 75 mg/ Isoniazid 50mg Medium Priority • Capreomycin API • Terizidone API • Terizidone, tablet/capsule 250 mg • Terizidone, tablet/capsule 300 mg • Rifampicin API	High Priority: • Praziquantel API • Praziquantel 600mg Tablet Medium Priority: • Albendazole API • Albendazole 400mg tablet (chewable*, preferably scored) Low Priority: • Mebendazole API • Mebendazole 500mg tabet (chewable*)	High Priority: • Amoxicillin 250 mg scored DT • 7.1% Chlorhexidine digluconate (4%) gel • 7.1% Chlorhexidine digluconate (4%) sol Medium Priority: • Magnesium sulfate injection 500 mg/ml, in 2-ml and 10 ml ampoule • Gentamicin injection 10mg/ml and 40 mg/ml, in 2-ml vial Medium - low Priority: • Oxytocin, injection 10 IU, 1-ml Low Priority: • Misoprostol 200-ug tablet • Betamethasone injection 5.7 mg/ml (betamethasone sodium phosphate 3.9 mg/ml solution, or betamethasone acetate 3 mg aqueous suspension) • Dexamethasone injection 4 mg injection (4 mg dexamethasone disodium phosphate in 1-ml ampoule)

Conclusion

- PQM/USAID in organizing this workshop seeks to raise awareness about pharmaceutical quality and provide information to medicines regulatory agencies and manufacturers of TB and NTD medicines about opportunities for engaging PQM technical assistance

- PQM technical assistance to manufacturers and MRAs has helped to strengthen medicines quality-assurance systems globally, and contributed to ensuring that needed priority medicines are available to patients.

- **Wishing you a productive workshop and a wonderful time here in Thailand!**

Promoting the Quality of Medicines

Thank You

This document is made possible by the generous support of the American people through the United States Agency for International Development (USAID). The contents are the responsibility of the Promoting the Quality of Medicines program and do not necessarily reflect the views of USAID or the United States Government.

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Questions

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USP–USAID Cooperative Agreements