

Promoting the Quality of Medicines (PQM) Program

FY 2017 Third Quarter Report
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About the Promoting the Quality of Medicines (PQM) Program

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The Promoting the Quality of Medicines (PQM) program is a Cooperative Agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to address critical pharmaceutical management challenges in developing countries. The earliest program, the Rational Pharmaceutical Management Project, implemented and evaluated country-specific drug information resource programs in selected developing countries. Subsequently, the Drug Quality and Information program focused on medicines quality control and quality assurance systems. The PQM program (2009–2019) provides technical assistance to strengthen medicines regulatory authorities and quality assurance systems and supports manufacturing of quality-assured priority essential medicines for malaria, HIV/AIDS, tuberculosis, neglected tropical diseases, and maternal and child health.

As of December 2016, USAID supports PQM's work in 20 countries, two Regional Missions, one Cross Bureau program, and four core health programs.

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Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance in partnering countries to strengthen quality assurance (QA) systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance supports countries build the capacity of medicines regulatory authorities (MRAs) and QA systems, supports the manufacture of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH), and provides support to increase the utilization of information for decision-making. The U.S. Agency for International Development supports PQM's work in 20 countries and in two regional programs in Asia and Latin America. This report summarizes results achieved during the third quarter of FY 2017, from April 1 to June 30, 2017.

PQM's first intermediate result area is to strengthen medical product QA systems. Quality is paramount to ensuring that the safety and efficacy of medical products are maintained from the moment a product is manufactured, across the entire supply chain, until it reaches the patient. By strengthening systems that help ensure quality—from developing effective and enforceable legislation, policies, and workforce capacity to helping implement regulations, guidelines, and standard operational procedures—PQM aims to reduce and eliminate substandard and falsified products that pose serious risks to patients' health and undermine global health investments. A key accomplishment this quarter can be seen in Ethiopia, where the implementation of the regulatory framework received a boost with the approvals of the pharmaceutical manufacturer good manufacturing practices (GMP) inspection directive, which provides legal provisions to enforce implementation of GMP requirements by the Ethiopian Food, Medicine, and Health Care Administration and Control Authority (EFMHACA). The EFMHACA also approved an enhanced marketing authorization strategy, developed with the support of PQM, and is progressing to complete development of a pharmaceutical recall directive. In Ghana, three quality control laboratories were visited by the ANSI-ASQ National Accreditation Board (ANAB) for an audit inspection to reaccredit the laboratories for International Organization for Standardization (ISO) 17025. Ghana Food and Drug Administration (GFDA) prepared for the audit visit with minimal support from PQM. This demonstrates GFDA has improved its technical capacity and is advancing towards complete ownership of its ISO 17025 accreditation maintenance and also testifies to PQM's success in building sustainable capacity and skills required to carry out this function effectively. In Nigeria, the National Agency for Food and Drug Administration and Control's (NAFDAC's) Kaduna regional laboratory has received official notification for ISO/IEC 17025:2005 accreditation. This accreditation will be the first of its kind in the northern region of the country; with this achievement, 100% of medicine quality tests in Nigeria will be conducted in ISO-accredited laboratories, ensuring accurate and reliable results.

The second intermediate result area of PQM is to increase the supply of quality-assured medicines. A continuous supply of quality-assured products—particularly for priority medicines for TB, NTDs, and MNCH—is necessary to address national health priorities. PQM works with manufacturers to improve compliance with international quality standards, helping them develop and submit dossiers for review and approval by the WHO Prequalification (PQ) Program. WHO PQ and stringent regulatory authorities' approval indicate that medicines meet acceptable international standards for quality, safety, and efficacy and can be purchased by procurement agencies. By increasing the number of suppliers and creating a competitive environment, PQM helps to shape the market for priority medicines and contributes to reducing their price. PQM also provides technical assistance and guidance to manufacturers for the local production of essential medicines. PQM supports local production of essential medicines where appropriate and feasible as it may decrease reliance on international donation, bring manufacturing closer to the burden of the disease, and help establish sustainable local supply. A local medicines manufacturer in Indonesia that receives technical assistance from PQM, Sanbe Farma/Caprifarmindo, achieved WHO prequalification for oxytocin injection and Expert Review Panel (ERP) approval for amoxicillin 250mg dispersible tablets, to be procured by the United Nations Children's Fund (UNICEF). PQM was essential in assisting to building the overall QC systems for Sanbe Farma/Caprifarmindo, as well as providing GMP support, which helped allow the company to reach WHO PQ and ERP approval for the products, respectively. These two priority products will lead to an increased supply of quality-assured products for maternal and child health on the global market. Also in Q3, two manufacturers that have been receiving technical support from PQM's Core TB program saw major accomplishments. NCPH Pharma received full WHO prequalification for streptomycin finished pharmaceutical product (FPP). Celltrion Pharmaceutical Company submitted an Abbreviated New Drug Application for linezolid FPP to the U.S. FDA and its dossier was accepted for review by WHO PQ. Streptomycin and linezolid are important anti-TB medicines, and these steps are expected to result in an increased supply of quality-assured products at affordable prices on the global market, potentially being supplied to low- and middle-income countries through the Global Drug Facility.

In Ethiopia, a manufacturer being supported by PQM, Cadila Pharmaceuticals, was audited by WHO to assess manufacturing practices for ethambutol 400 mg, a first line anti-TB medicine. The audit was concluded with no critical observations, and Cadila is working toward the corrective and preventive action (CAPA) response from the audit. Cadila is optimistic that it will attain WHO PQ status in the relatively near future. Attaining WHO PQ will be a great

step forward in creating local capacity for producing quality-assured ethambutol 400 mg. This will greatly contribute to increasing access to quality-assured medicine in the treatment of TB in Ethiopia and within the region. Within the quarter, Pakistan added two new sources for quality assured chlorhexidine 7.1% gel, approved by the Drug Regulatory Authority of Pakistan (DRAP) and at the recommended price of the Drug Pricing Committee. This brings to a total of four local sources of quality-assured chlorhexidine 7.1% gel, as a result of DRAP's commitment and the technical support for local production and regulatory capacity strengthening from the PQM program. It is expected that improved access to quality-assured, locally produced chlorhexidine may lead to a reduction in neonatal mortality due to umbilical cord infection. The manufacturers may also be able to export the products to neighboring countries in the region. Also in Pakistan, PQM's technical assistance assisted Pakistani manufacturer, Pacific Pharmaceuticals Limited, to receive a Certificate of GMP Compliance from the Medicines and Healthcare Products Regulatory Agency for ethambutol 400mg tablets.

The increased utilization of medical product quality information for decision-making is PQM's third intermediate result area. The collection, analysis, and use of data on medical products quality to support evidence-based decision-making are critical to reduce and eliminate substandard and falsified products. PQM supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory systems strengthening, as well as compliance and enforcement actions. PQM works with local, national, and international partners to bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, shape public policies on medical products, and support the attainment of public health objectives. Results in Ghana this quarter highlight PQM's contributions toward use of information for decision-making to eradicate falsified and substandard medical products. Following the Q2 initiation of post-marketing surveillance for zinc sulfate tablets in the supply chain in Ghana, the GFDA was able to finalize the report of the surveillance. Data from the surveillance indicated some samples did not meet the expected quality standards, and GFDA has proposed regulatory actions to ensure the quality and safety of products available to its population. This type of information is crucial for decision-makers within regulatory authorities to ensure proper actions are taken to remove poor-quality medical products from their markets and protect the lives of their citizens. In Liberia, an idea proposed by PQM of incorporating quality into the national malaria monitoring and evaluation (M&E) strategy was accepted by the National Malaria Control Program (NMCP) and included in the 2016–2020 M&E plan. For the first time, NMCP's M&E strategy will account for the quality of malarial medicines distributed to public health facilities throughout Liberia. Under the new arrangement, the Liberia Medicines and Health Product Regulatory Authority (LMHRA) will be charged with the responsibility of performing post-marketing surveillance (PMS) activities in accordance with established protocol developed in collaboration with PQM. While PQM will continue to support the strengthening of LMHRA's PMS capacity, for the first time, future PMS activities will be conducted at NMCP's five surveillance sites. Similarly in Indonesia, a stakeholders' planning workshop was convened in preparation for the upcoming 11-province Joint Sampling and Testing exercise between the Ministry of Health (MOH) and regulatory authority (BPOM) to initiate implementation of the MOH regulation Permenkes 75/2016, a new framework that allows for interagency information sharing on the quality of medicines in the government sector, including dissemination of quality testing data to relevant MOH partners in a timely manner. This is a crucial step toward a robust QC system in Indonesia

Acronyms

ACT	artemisinin-based combination therapy
ADE	adverse drug event
ANAB	ANSI-ASQ National Accreditation Board
ANDA	Abbreviated New Drug Application
API	active pharmaceutical ingredient
ARV	antiretroviral
BE	bioequivalence
BPOM	National Agency for Drug and Food Control [Indonesia]
CAPA	corrective and preventive action
cGMP	current Good Manufacturing Practices
CHX	chlorhexidine
CMO	contract manufacturing organization
CRO	clinical research organization
CTD	Common Technical Document
DFDA	Department of Food and Drug Administration [Burma]
DGDA	Directorate General of Drug Administration [Bangladesh]
DGPML	Director General of the Medicine Regulatory Authority [Burkina Faso]
DNPL	National Directorate of Pharmacy and Laboratories [Guinea]
DOH	Department of Health [Philippines]
DOTS	directly observed treatment, short-course
DPM	Directorate of Pharmacy and Medicine [Mali]
DRAP	Drug Regulatory Authority of Pakistan
DTL	Drug Testing Laboratory
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
EOI	Expression of Interest
EPCMD	Ending Preventable Child and Maternal Deaths
ERP	Expert Review Panel
FAA	fixed amount award
FDA	Food and Drug Administration
FDC	fixed-dose combination
FDQCC	Food and Drug Quality Control Center [Laos]
FDSL	Federal Drug Surveillance Laboratory [Pakistan]
FPP	finished pharmaceutical product
GCP	good clinical practices
GDF	Global Drug Facility
GDP	good distribution practices
GDSP	good storage and distribution practices
GF	Global Fund
GFDA	Ghana Food and Drug Administration
GLP	good laboratory practices
GPPQCL	good practices for pharmaceutical quality control laboratories
GMP	good manufacturing practices
GRP	good regulatory practices
GSP	good storage practices
GxP	good practice guidelines
HPLC	high-performance liquid chromatography
IRIMS	Integrated Regulatory Information Management Systems
ISO	International Organization for Standardization
KAN	National Accreditation Committee [Indonesia]
LIF	laboratory information file
LMHRA	Liberia Medicines and Health Products Regulatory Authority
LNCQM	Laboratório Nacional da Qualidade de Medicamentos [Mozambique]
LNS	National Laboratory of Health [Mali]
LNSP	National Laboratory of Public Health [Burkina Faso]
M&E	monitoring and evaluation
MDR-TB	multidrug-resistant tuberculosis

MNCH	maternal, newborn, and child health
MNTE	Maternal and Neonatal Tetanus Elimination
MOH	Ministry of Health
MOI	Ministry of Interior
MOP	Malaria Operational Plan
MQC	medicines quality control
MQDB	Medicines Quality Database
MQM	medicines quality monitoring
MRA	medicines regulatory authority
MRIS	medicine registration information system
NAFDAC	National Agency for Food and Drug Administration and Control [Nigeria]
NAP	National AIDS Program [Indonesia]
NCEM	National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan
NCL	National Control Laboratory [Bangladesh]
NHQC	National Health Products Quality Control Center [Cambodia]
NIPRD	National Institute of Pharmaceutical Research and Development
NMCP	National Malaria Control Program
NMI	National Metrology Institute [Ethiopia]
NMRL	National Microbiology Reference Laboratory [Kenya]
NQCL	national quality control laboratory
NTD	neglected tropical disease
NTP	National Tuberculosis Program
PD	Pharmaceutical Department
PDTRC	Pakistan Drugs Testing and Research Center
PE&R	Pharmaceutical Evaluation & Registration [Pakistan]
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIDS	Performance Indicator Database System
PIR	Public Inspection Report
PMI	President's Malaria Initiative
PMS	post-marketing surveillance
PPB	Pharmacy and Poisons Board [Kenya]
PQ	Prequalification
PQM	Promoting the Quality of Medicines
PT	proficiency test
PTBB	Therapeutic Products National QC Laboratory of BPOM [Indonesia]
PV	pharmacovigilance
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QMS	quality management systems
RBEC	Regional Bioequivalence Center [Ethiopia]
RDMA	Regional Development Mission for Asia
RDT	rapid diagnostic test
RFA	request for applications
SANAS	South African National Accreditation System
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SOP	standard operating procedure
SRA	stringent regulatory authority
TB	tuberculosis
TOR	terms of reference
TWG	Technical Working Group
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Development Organization
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WHO	World Health Organization

Result Highlights



Intermediate Result (IR) 1: Medical Products Quality Assurance Systems Strengthened

Overview of FY 2017 Third Quarter Achievements

Medical products are instrumental to any health system, but only if they are safe, effective, and quality-assured. Quality, in particular, is paramount to ensuring that the safety and efficacy of medicines and medical products are maintained from the moment a product is manufactured, across the entire supply chain, until it reaches the patient.

By strengthening systems that help ensure quality—from developing effective and enforceable legislation, policies, and workforce capacity to helping implement regulations, guidelines, and operational procedures—the Promoting the Quality of Medicines (PQM) program aims to address the end-to-end challenges that affect medicines quality. The ultimate goal is to reduce and eliminate substandard and falsified products that pose serious risks to the health of patients and undermine global health and development efforts.

Description of Sub-IRs

Sub-IR 1.1 Quality assurance policies, legislation, guidelines, and procedures improved

National medicines policies define the requirements that help ensure medicine access, quality, and rational use. A medicines policy also serves as the framework for developing sound pharmaceutical law, which provides the legal mandate for the creation of a national medicines regulatory authority (MRA). Working with in-country stakeholders at all levels, PQM helps to develop or revise policies, legislation and regulations, and guidelines by providing technical assistance to MRAs to ensure quality assurance topics are adequately covered and that the overarching regulatory framework is appropriate to their context and of internationally accepted standards.

Sub-IR 1.2 Registration, inspection, and licensing functions of medicine regulatory agencies sustainably improved (pre-market)

Among the key functions of an MRA, the registration or approval of medical products and the inspection and licensing of manufacturing facilities are crucial processes designed to ensure that only quality-assured products enter the market. PQM works with MRAs to build strong institutional capacity and support registration and licensing through hands-on training and technical assistance. By helping MRAs prioritize key issues through risk-based approaches, PQM guides regulatory agencies to focus their pre-market resources toward solutions that are value added and will result in high-impact and sustainable health outcomes.

Sub-IR 1.3 Standard of practice at national quality control laboratories sustainably improved

MRAs, national procurement agencies, and international donors require reliable and accurate data from quality control labs during the medicines registration process, when implementing corrective actions for poor-quality medicines identified following post-marketing surveillance (PMS), and to ensure that procured and donated products meet quality requirements. To help guarantee consistently reliable and accurate data, PQM builds the capacity of national quality control laboratories (NQCLs) to improve laboratory standards through assessments, hands-on training, and technical assistance. PQM places particular emphasis on strengthening quality management systems to help laboratories attain certifications of compliance with internationally recognized standards, such as ISO/IEC 17025:2005 and/or World Health Organization (WHO) prequalification (PQ).

Sub-IR 1.4 Institutional capacity for medical product quality assurance workforce sustainably improved

Building workforce capacity at central and decentralized institutions and facilities involved in maintaining operationally effective quality assurance (QA) systems is a core component of PQM's approach. PQM and U.S. Pharmacopeial Convention (USP) experts work in collaboration with WHO's global, regional, and national offices to provide hands-on trainings focused on a wide range of good practice guidelines (GxP), particularly bioequivalence aspects of good clinical practices (GCP), good manufacturing practices (GMP), good laboratory practices (GLP) including QC testing procedures and laboratory equipment maintenance.

PQM's in-service training programs, application of the Collaborative Learning Model, train-the-trainers approach, and hands-on support facilitates the turning of knowledge into practice, PQM supports the strengthening of quality assurance topics in pre-service programs in academic institutions as a critical part of the long-term solution for workforce development. Adopting a Collaborative Learning Model, PQM first gathers staff from multiple laboratories within each country and provides consolidated trainings to them. This ensures that the material delivered is consistent, reduces costs typically incurred from decentralized training operations, and promotes country ownership and collaboration among laboratory staff. In addition, if one laboratory experiences a high rate of attrition, new staff can be mentored by previously trained, tenured colleagues from neighboring laboratories, rather than relying on

foreign assistance again. By combining pre-service and in-service training interventions and the development of structures and processes necessary for effective quality management systems (QMS), PQM builds a sustainable in-country regulatory and QA workforce.

Sub-IR 1.5 Capacity for post-marketing surveillance of medical products sustainably improved

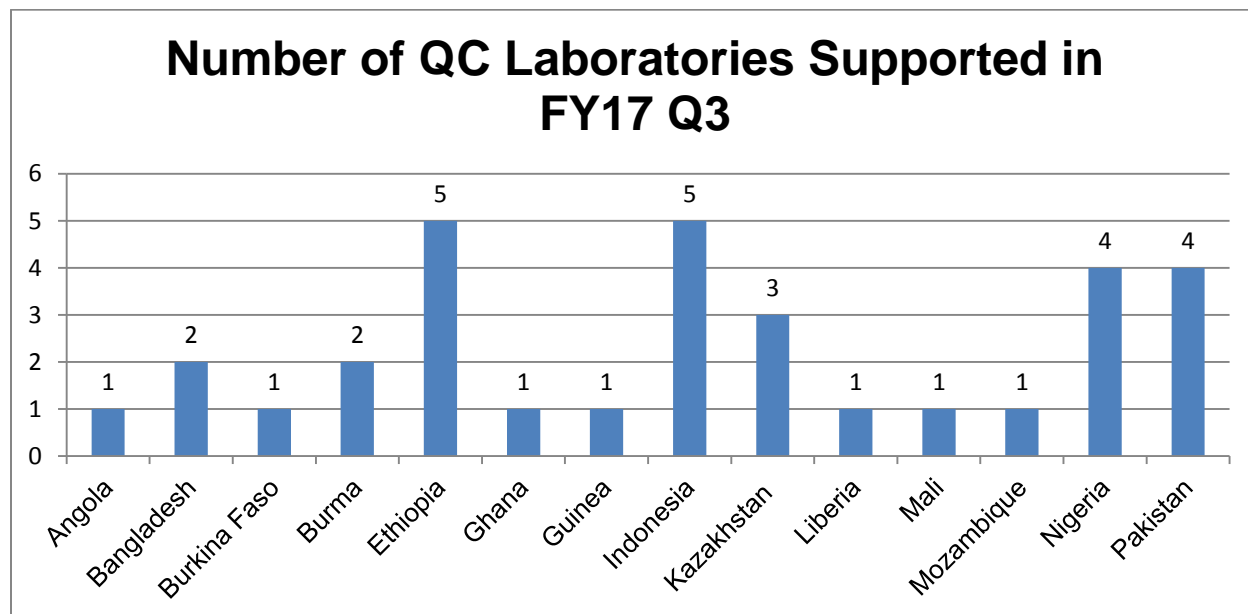
Ensuring the quality of medical products throughout the supply chain presents challenges that extend beyond the registration and procurement processes. Substandard medicines may occur due to poor manufacturing practices or as a result of poor storage conditions or practices. In addition, weak regulatory systems leading to unregulated distribution and sale of medicines and porous country borders facilitate the introduction of substandard, falsified, and unapproved medicines. To help address these challenges, PQM collaborates with MRAs to establish and strengthen PMS programs that regularly examine the quality of medicines throughout the supply chain.

PQM’s support to MRAs includes implementation of risk-based approaches that help prioritize scarce human and financial resources, assistance in strategic planning, and targeted sampling for products and locations where surveillance is most needed. PQM also provides training to field staff in sampling procedures, use of field screening tools and technologies (such as GPHF Minilab™), data management, and reporting. Field testing with screening methods and laboratory testing with complex and comprehensive compendial methodologies are integrated within the implementation of a risk-based framework for PMS.

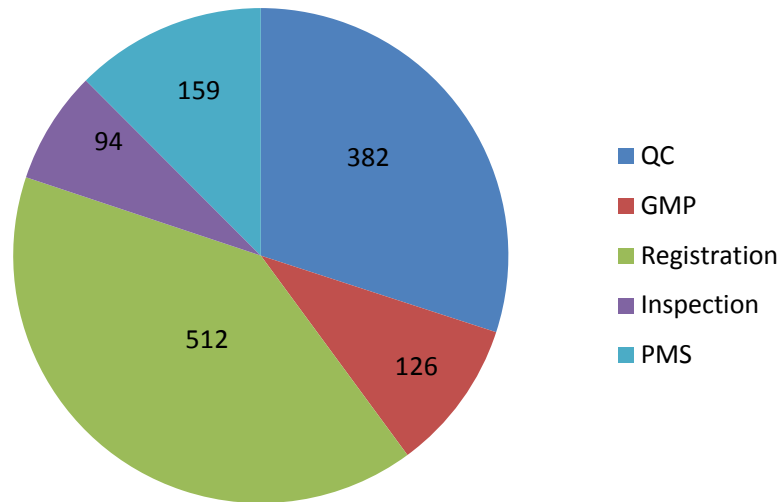
Key Results and Highlights

Select Q3 Data Points for IR1

Number of Individuals Trained in QA/QC Related Topics	1273
Number of QC Laboratories Supported	32
Number of QC Laboratories Participated in PT and Passed	1 – Agulu, Nigeria
Number of QC Laboratories Newly Accredited (ISO Accreditation or WHO Prequalification)	2 – Vietnam (WHO PQ); Kaduna, Nigeria (ISO 17025)



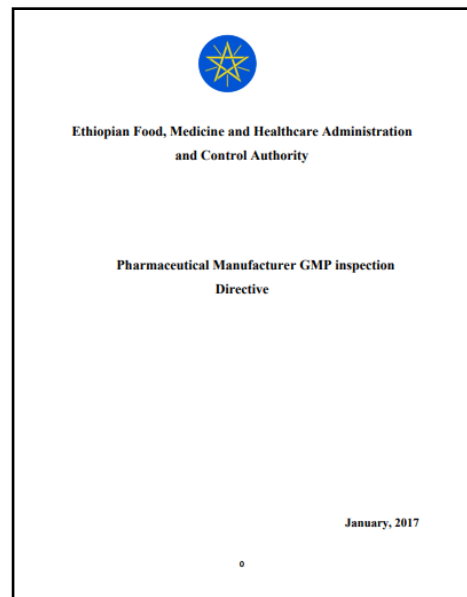
Number of Individuals Trained in FY17 Q3 by Topic



In Nigeria, the National Agency for Food and Drug Administration and Control's (NAFDAC's) Kaduna regional laboratory has received official notification for ISO/IEC 17025:2005 accreditation. This laboratory accreditation will be the first of its kind in the northern region of the country, and with this achievement, 100% of medicine quality tests in Nigeria will be conducted in ISO-accredited laboratories, ensuring accurate and reliable results.

Another key accomplishment within this result area can be seen in Ethiopia, where legal frameworks were developed and approved to strengthen the enforcement capabilities of the MRA. The Ethiopian Food, Medicine, and Health Care Administration and Control Authority (EFMHACA) approved and issued a Pharmaceutical Manufacturer GMP Inspection Directive, which has legal provisions to enforce implementation of GMP requirements (<http://www.fmhaca.gov.et/documents/GMP%20inspection%20directive.pdf>). EFMHACA management has also approved an enhanced marketing authorization strategy, developed with the support of PQM, and is progressing to complete development of a pharmaceutical recall directive. These directives are critical part of the EFMHACA's regulatory framework and will facilitate the implementation of regulations and improve compliance and enforcement actions for removing poor-quality medicines from the market.

In Ghana, three quality control laboratories (physical chemistry, pharmaceutical microbiology, and medical devices) were visited by the ANSI-ASQ National Accreditation Board (ANAB) for an audit inspection to reaccredit the labs for ISO 17025. Ghana Food and Drug Administration (GFDA) prepared for the audit visit with minimal support from PQM. This demonstrates GFDA has improved its technical capacity and is taking complete ownership of its ISO 17025 accreditation maintenance for its laboratories and also testifies to PQM's success in building the capacity and skills required to carry out this function effectively.



IR2: Supply of Quality-Assured Priority Medicines Increased

Overview of FY 2017 Third Quarter Achievements

A continuous supply of quality-assured products—particularly for essential priority medicines for tuberculosis (TB); neglected tropical diseases (NTD); and maternal, newborn, and child health (MNCH)—are necessary to address national health priorities and plans. However, the limited number of manufacturers weakens supply security and increases the vulnerability of supply chains to poor-quality medicines. Further exacerbating supply challenges is the lack of economic incentives for manufacturers to produce essential medicines. PQM works with manufacturers to improve compliance with international quality standards to meet local and global demand for quality-assured medicines. PQM assistance ensures a steady supply of essential medicines of assured quality, safety, and efficacy, thus strengthening countries' health systems to improve health outcomes.

Description of Sub-IRs

Sub-IR 2.1 Supply of quality-assured priority medicines produced locally increased

In support of key U.S. Agency for International Development (USAID) priority health programs, PQM provides technical assistance and guidance to manufacturers for the local production of medicines, including those used to treat newborn infections and child and maternal health products. Local production may decrease reliance on international donation and help establish a sustainable local supply. In addition, developing local manufacturing capacity and enhancing regulatory oversight can improve both national and regional capabilities for sustainable sourcing of quality-assured medicines.

Sub-IR 2.2 Supply of quality-assured priority medicines produced globally increased

To address global needs of essential medicines, PQM works with manufacturers to help them develop and submit dossiers for certification by the WHO PQ of Medicines Program for TB, malaria, and NTD medicines. Both WHO PQ and stringent regulatory authority (SRA) approval confirms that these medicines meet acceptable international standards for quality, safety, and efficacy, and can be purchased by international procurement agencies. In addition, by increasing the number of suppliers and creating a competitive environment, PQM helps shape the market for essential medicines and contributes to reducing the price of these essential products.

Sub-IR 2.3 CROs compliance with Good Clinical practices and Good Laboratory Practices increased

In the process of submitting an application to the WHO PQ Medicines Program or other SRA, manufacturers require access to clinical research organizations (CRO) to conduct bioequivalence (BE) studies when indicated. PQM engagement with CROs helps them to address compliance issues and timeliness and improve the cost-effectiveness of the services they provide in the approval process for priority medicines. PQM engagement aims to decrease the time needed for product approval as well as the actual cost of BE studies. PQM prioritizes support to CROs that can provide reliable data for timely approval of priority essential medicines.

Sub-IR 2.4 Sources for quality-assured API/FPP diversified and supply secured

In some instances, there is only one source of quality-assured essential medicine to supply the global public health market. This makes the medicine vulnerable to substantial price increases for both procurement agencies and countries purchasing the product. It also increases the risk for potential disruptions in supply if the manufacturer sustains any operational setbacks during production. PQM has witnessed companies that manufacture both the active pharmaceutical ingredient (API) and the finished pharmaceutical product (FPP) become the sole source of a quality-assured product on the market. Interrupting the supply of API to other FPP manufacturers allows for price increases in a monopolized FPP market. To prevent this, PQM works to identify API manufacturers that lack the capacity to produce FPPs but can ensure the API supply to multiple FPP manufacturers. This increases sources and competition within the market and helps reduce the prices of essential medicines. Additionally, by developing multiple sources of quality-assured FPPs, the risk of price gouging is averted and the vulnerability of the global supply chain to shortages is greatly reduced.

Key Results and Highlights

Select Q3 Data Points for IR2

Number of Manufacturers Supported toward GMP Standards	39
Number of Products Achieving WHO Prequalification	2 – streptomycin FPP; oxytocin injection FPP
Number of Dossiers Accepted for WHO Prequalification	1 – linezolid FPP

Number of Manufacturers Provided with Technical Assistance in FY17 Q3		
Countries/Core Programs	Number of Manufacturers	Product Types
Core TB	9	clofazimine API & FPP, gatifloxacin API, kanamycin API & FPP, linezolid FPP, PAS sodium API, streptomycin FPP, 4FDC (rifampicin/isoniazid/ethambutol/pyrazinamide)
Core NTD	7	praziquantel API & FPP, albendazole API & FPP
Core MNCH	5	magnesium sulfate FPP, chlorhexidine solution FPP, amoxicillin FPP
Nigeria	5	zinc dispersible tablet, chlorhexidine gel, oxytocin, magnesium sulfate, arthemether lumefertrine
Ethiopia	2	ethambutol, zinc sulfate, chlorhexidine gel
Indonesia	4	levofloxacin, 2FDC (isoniazid/rifampicin)
Pakistan	4	chlorhexidine gel
Bangladesh	1	chlorhexidine solution, zinc dispersible tablet
Kazakhstan	1	levofloxacin, moxifloxacin
Uzbekistan	1	levofloxacin, moxifloxacin

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In Ethiopia, a manufacturer being supported by PQM, Cadila Pharmaceuticals, was audited by WHO to assess manufacturing practices for ethambutol 400mg. The audit was concluded with no critical observations, and Cadila Pharmaceuticals is working toward the corrective and preventive action (CAPA) response from the audit. With the audit, Cadila is optimistic that it will attain prequalification status in the relatively near future. Attaining WHO PQ will be a great step forward in creating local capacity for producing quality-assured ethambutol 400mg, a first line anti-TB medicine. This will greatly contribute to increasing access to quality-assured medicine in the treatment of TB in Ethiopia and within the region.

Pakistan this quarter welcomed two additional chlorhexidine 7.1% gel products which were registered in the country and price recommended by the Drug Pricing Committee. Once these products are made available in the market, there will be a total of four local manufacturers supplying quality-assured chlorhexidine 7.1% gel, as a result of PQM's support. It is expected that improved access to quality-assured, locally produced chlorhexidine may lead to a reduction in neonatal mortality due to umbilical cord infection. The manufacturers may also be able to export the products to neighboring countries in the region.

IR3: Utilization of Medical Product Quality Information for Decision-Making Increased

Overview of FY 2017 Third Quarter Achievements

The collection, analysis, and use of data on medical products quality to support evidence-based decision-making are critical to reducing and eliminating substandard and falsified products. PQM supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory actions and are disseminated to all stakeholders. By working with local, national, and international partners, PQM helps bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, inform decision-making, shape public policies on pharmaceuticals, and support the attainment of public health objectives.

Description of Sub-IRs

Sub-IR 3.1 Availability of information related to quality of medical products increased

PQM assists national stakeholders with implementing medicines quality monitoring (MQM) programs to generate data on the quality of pharmaceuticals circulating in country. To increase the body of information generated by MQM activities in the countries, PQM advocates for the inclusion of priority essential medicines used in PMS programs, including medicines used for MNCH, HIV/AIDS, and TB.

The Medicines Quality Database (MQDB), developed and actively managed by PQM, is a free, web-based, and internationally referenced database of QC results for approximately 15,000 medicines sampled and tested in PQM-assisted countries in Africa, Asia, and Latin America. With the information available in the MQDB, PQM recently created the Poor-Quality Medicines ALERT feature. The ALERT provides rapid access to the most recent information on poor-quality medicines identified from PMS activities in PQM countries, including those performed independently of PQM assistance. Through collaborations with the World Wide Antimalarial Resistance Network and the newly-formed Infectious Diseases Data Observatory, PQM is exploring ways to integrate the information into these databases and expand the scope of medicines included.

PQM is undertaking a series of additional initiatives to increase the availability of data related to the quality of medical products, including working across regulatory functional areas; registration, licensing and inspection; and PMS to harness opportunities for data capture and sharing.

Sub-IR 3.2 Enforcement actions against falsified, substandard and unapproved medical products Increased

PQM works with in-country partners to detect and support action against cases of substandard and falsified medicines. When poor-quality medicines are detected, PQM collaborates with MRAs to facilitate enforcement actions and remove these medicines from the market. PQM also shares information to alert stakeholders and the public about the issue. By creating and supporting regional networks for sharing information, PQM also facilitates implementation of corrective actions in neighboring countries on poor-quality medical products sourced from the same manufacturers.

Sub-IR 3.3 Information on quality assurance of medical products used for advocacy increased

PQM raises awareness about the dangers of substandard and falsified medicines—it provides the information to the public and government stakeholders by supporting local, regional, and global initiatives on medicines quality. Activities often include hosting and attending partner meetings, developing regional databases and alert systems, advocating for allocation of resources for improving pharmaceutical quality systems, and encouraging collaboration among stakeholders. PQM develops e-learning courses on medicines quality assurance, participates in educational courses organized by international partners, collaborates with local universities to develop QA-related content for

pharmaceutical curricula, and supports studies and operational research on quality assurance and regulatory systems strengthening.

At the local level, PQM works with authorities and civil society to develop awareness campaigns and public service announcements. To share information with the global community, PQM participates in regional and international meetings, then develops printed and digital media materials to increase advocacy on matters related to medical products quality.

Key Results and Highlights

Select Q3 Data Points for IR3

Number of Active Sentinel Sites Supported for MQM Activities	197
Number of Samples Collected and Tested	1326 (66% antimalarials; 34% MCH products)

Results in Ghana this quarter highlight PQM's contributions toward use of information for decision-making to eradicate falsified and substandard medical products. Following the Q2 initiation of the PMS for zinc sulfate tablets in the supply chain, GFDA was also able to finalize the report of the surveillance. Data from the surveillance indicated some samples did not meet the expected quality standards, and GFDA has proposed regulatory actions to ensure the quality and safety of products available to its population.

In Liberia, PQM proposed the idea to the National Malaria Control Program (NMCP) of incorporating quality into the national malaria monitoring and evaluation (M&E) strategy. The idea was accepted in April 2017 by the Liberia Medicines and Health Product Regulatory Authority (LMHRA) and NMCP and was included in the 2016–2020 M&E plan. For the first time, NMCP's M&E strategy will account for the quality of malarial medicines distributed to public health facilities throughout Liberia. Under the new arrangement, LMHRA will be charged with the responsibility of performing PMS activities in accordance with established protocol developed in collaboration with PQM. PQM will continue to support the strengthening of LMHRA's PMS capacity. For the first time, future PMS activities will be conducted at NMCP's five surveillance sites. As part of overall health systems strengthening, LMHRA is planning to have one of its inspectors relocate to one of the sites to ensure that LMHRA inspections are conducted properly and to enforce any regulatory actions at the surveillance site. This activity will be conducted jointly with the National Drug Service, NMCP, and LMHRA.

This quarter, PQM convened a planning workshop with the National TB Program and 11 provincial health offices and laboratories on the "Joint Sampling and Testing of TB and HIV Medicines." This activity involved identifying the medicines to be sampled and tested, as well as the provincial and district warehouses from which samples would be taken. This is a joint activity between the Ministry of Health (MOH) and BPOM to encourage rapid implementation of the Permenkes 75/2016 regulation on ensuring medicines quality control activities in government-sector programs. Sampling will take place during Q4 FY 2017 at the provincial sites for Joint Sampling and Testing collaborative exercise between BPOM, Balai Besar POM (BBPOM), and MOH (provincial and district). A key outcome of these activities for joint sampling is to successfully implement the Permenkes 75/2016 regulation on the quality control of medicines in the government sector, including dissemination of quality testing data to relevant MOH partners in a timely manner. This is a crucial step toward a robust QC system in Indonesia.

Africa



Angola

I. Quarter 3 Highlights

PQM received a directive from USAID/Angola to put a hold on work plan activity implementation from June to August 2017 because of the upcoming country elections. All activities were put on hold for this quarter. However, PQM developed a Malaria Operational Plan (MOP) presentation on PQM activities for FY 2018 that was provided to the USAID/Angola Mission and used during the in-country MOP review meeting.

PQM was also informed by USAID/Angola about a meeting planned with Angola government counterparts this quarter to find out when a location/facility for the national quality control laboratory will be commissioned and when the new pharmaceutical law will be enacted. These two factors prevented PQM from implementing many of its FY 2017 work plan activities for Angola. After the meeting with government counterparts, USAID/Angola decided to discontinue funding for PQM based on the government's lack of current commitment to actualize the request, resulting in PQM's inability to implement any interventions without a structure in place to monitor and test medicines quality, as well as President's Malaria Initiative (PMI) budget cuts. USAID is exploring other ways to address this need, recognizing that medicine quality assurance is a very important gap area for Angola, particularly given the country's history of falsified medicines.

II. Country Context

Angola is a vast country sharing porous borders with the Democratic Republic of the Congo, Zambia, and Namibia, making Angola vulnerable to the threat of falsified and substandard medicines. This was evident in 2012 when large quantities of falsified Coartem® were seized by customs in Luanda.

To obtain a better understanding of the extent of the problem, the PMI in Angola sought PQM's technical assistance to conduct an antimalarial medicines (AMLs) quality study in the private and public sectors in selected regions of Angola. This study was conducted in October 2015 and provided a snapshot of medicines quality to the National Malaria Control Program (NMCP) and its partners, which addressed concerns about the presence of falsified and substandard medicines in Angola.

PQM collected additional antimalarial medicines in July/August 2016 from six provinces to obtain the information needed to design a PMS protocol for the country. The 2015 survey revealed that the proportion of failed samples for the specific products in the specific locations was 50%. However, it is important to note that the results are not representative of the overall quality of medicines in Angola. This revealed that additional surveys and collections must be conducted to ascertain the extent of the problem. For the purposes of focused PMS, samples from major provinces of Angola will still need to be collected to conclusively target the areas where malaria is endemic, but the current evidence from Luanda suggests significant antimalarial quality issues may be present in other areas of the country.

Benin

I. Country Context

Malaria is the leading cause of morbidity in Benin, which is a high malaria transmission country, according to WHO. In 2013, there were 1,078,834 reported and confirmed cases of malaria and 2,288 reported deaths. Benin adopted artemisinin-based combination therapy (ACT) in 2004 and began large-scale implementation of artemether/lumefantrine combination as first-line treatment in 2007.

PQM was selected by PMI and USAID/Benin to strengthen the QA/QC systems of AMLs in Benin. Activities focused on strengthening the capacity of the NQCL. Technical assistance in these areas supports PMI's Strategy for 2015–2020 Core Operating Principle #6 to ensure that all commodities provided to countries are of high quality and that systems are in place to continually improve the quality of services provided. It is also part of PQM's efforts to mitigate risk against current malaria control gains and limit the spread of ACT resistance. ACTs coming through the central medical store need to be tested prior to release into the market. However, the NQCL does not have the capacity to test these products following international standards.

II. Quarter 3 Progress by Objective

Objective 2 – Support sustainable local capacity to monitor the quality of medicines in the country

Facilitate one round of sampling and testing

Following USAID/PMI's recommendation to introduce other screening tools and help the NQCL use them in PMS of antimalarials, PQM supported the NQCL to procure a handheld Raman spectrometer. PQM staff will receive training on how to operate the device and will in turn train lab staff from NQCL.

Burkina Faso

I. Quarter 3 Highlights

In this quarter, PQM continued to strengthen technical capacity of the National Laboratory of Public Health's (LNSP) medicines quality control (MQC) services. Seven lab staff received training on the performance verification and preventive maintenance of high-performance liquid chromatography (HPLC). PQM gathered information about PMS activities in Burkina Faso and procured Minilab™ supplies for the next round of sampling and testing of antimalarials.

PQM finalized the hiring of a local consultant.

An abstract on the work of PQM in strengthening human resources of the local partners was submitted to 4th Global Forum on Human Resources for Health.

II. Country Context

In Burkina Faso, USAID's primary health sector focus is to expand the prevention and treatment of malaria. Working closely with the Burkinabe government, USAID aims to reduce morbidity and mortality due to malaria, primarily targeting children under 5 and pregnant women as the populations most vulnerable to this disease.

PQM was selected by the USAID/Burkina Faso Mission to strengthen the capacity of the country's national MRA, Director General of the Medicine Regulatory Authority (DGPML), NQCL, LNSP, and other major pharmaceutical systems with the primary goal of improving its QA/QC of medicines.

In February 2015, in response to the USAID Mission's request, PQM conducted a rapid assessment of the QA/QC capabilities of the country and met with key stakeholders involved in the regulation, control, management, and distribution of medicines. The results of the assessment showed that traditional medicines are widely used by patients in Burkina Faso and are included in the Ministry of Health's (MOH) Strategic National Plan. The assessment also revealed an immediate need to strengthen the capacity of DGPML and build the capacity of LNSP.

Strengthening these two pillars of medicines QA is essential to advancing the country from unregulated use of traditional medicines to use of regulated, modern medicines based on quality standards. To achieve this goal, it is critical to address the challenges that health programs are facing and to work closely with the Central Medical Store (CAMEG), DGPML, and LNSP to ensure that all medicines procured by USAID and the government are of good quality prior to release into the market and that their quality is maintained throughout the supply chain through to distribution.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

Facilitate qualification and calibration of lab equipment

Performance verification and preventive maintenance of laboratory equipment represent a challenge to laboratory staff and management. Laboratory equipment maintenance, performance verification, and qualification are costly. Developing laboratory staff skills in these areas will allow better control of laboratory equipment and reduced cost for their maintenance. Working toward this goal, PQM trained seven laboratory staff on performance verification and maintenance of HPLC and other critical laboratory equipment.

Objective 2 – Strengthen post-marketing surveillance of antimalarial medicines

Facilitate one round of sampling and testing

To prepare the first round of sampling and testing of antimalarial medicines, PQM reviewed DGPML's triennial PMS plan. PQM commenced work with DGPML to develop a sampling plan. Part of the preparation also included procurement of Minilab™ supplies for screening antimalarial samples.

Ethiopia

I. Quarter 3 Highlights

During Q3, EFMHACA approved and issued a Pharmaceutical Manufacturer GMP inspection directive that has legal provisions to enforce implementation of GMP requirements. PQM played a key role in the development of this directive. In addition, EFMHACA management has approved the enhanced marketing authorization strategy developed with PQM's support. EFMHACA is also progressing to complete the development of the pharmaceutical recall directive that was started during the past quarter. These directives are critical part of the EFMHACA's regulatory framework and will facilitate the implementation of regulations and improve compliance and enforcement actions for removing poor-quality medicines from the market.

Another remarkable milestone achieved through PQM support was the completion of Cadila Pharmaceuticals' GMP audit by WHO with no critical observations to address. This is a key success factor to secure WHO PQ for ethambutol 400mg tablet manufacturing. PQM contributed by conducting a mock audit and follow-up with a preparatory visit to the manufacturer prior to the WHO inspection.

The technical support provided to branch laboratories by PQM has resulted in continuous improvement of activities and has strengthened the capacity and skills of laboratory staff to carry out PMS on routine basis. The supportive supervision conducted at the four branch laboratories during Q3 showed that after the branch laboratory staff were trained on HPLC, they were able to conduct testing of samples using the instrument. Previously, due to insufficient capacity, the laboratories were limited to using only Minilabs™ for testing products they collected from the field. The branch laboratories are also now able to independently procure chemicals they need for PMS. These achievements highlight the move by the EFMHACA branch laboratories to become self-sustaining to ensure continuity and maintenance of their activities and functions. The lab analysts seconded by PQM at the branch labs for the interim period have helped the labs to be functional in testing of medicines. Meanwhile, PQM advocates that the staff need to be absorbed by EFMHACA soon to promote self-sustenance. In addition, PQM supported EFMHACA to complete the collection of about 500 antimalarial and MNCH medicines samples for PMS. Testing of these samples will follow, and results will be disseminated to stakeholders. PMS is currently considered a regular/routine activity by EFMHACA and has been effectively utilized as an evidence-based information source to identify products with quality defects and allow for follow-up regulatory actions that protect public safety.

PQM participated in a 1-day consortium meeting, jointly organized by WHO and MOH to discuss the capacity-building needs of the Regional Bioequivalence Center (RBEC). PQM was selected to be a member of the committee established during the meeting and assigned to prepare terms of reference (TOR) for the group.

PQM built the capacity and skills of staff from different agencies during this quarter. Twenty-seven staff were trained on medicine sample collection for PMS. One staff member from the National Metrology Institute (NMI) participated in training on calibration of dimensions, and 60 staff were trained on good distribution practices (GDP) and good storage practices (GSP). Of the 60 people, 15 were trained on registration of food supplements. PQM is increasingly leveraging funds with EFMHACA for these trainings. EFMHACA provided funds for the training expenses, while PQM provided technical assistance.

II. Country Context

Ethiopia aspires to achieve elimination of malaria from its mid- and lowlands in the eastern part of the country. While malaria control measures will be scaled up and sustained, the country has planned to implement several other strategies to pave the way for malaria-free Ethiopia by 2030.

The impact-level targets included under the Health Sector Transformation Plan (HSTP) by 2020 are to reduce measles, mumps, and rubella to 199 per 100,000 live births; reduce under-5, infant, and neonatal mortality rates by 30, 20 and 10 per 1,000 live births respectively; reduce stunting, wasting, and underweight in under-5 to 26%, 4.9% and 13%, respectively; and reduce HIV incidence by at least 60% compared with 2010 and achieve zero new infections among children.

Ethiopia has achieved Maternal and Neonatal Tetanus Elimination (MNTE) and becomes the 42nd country validated for MNTE. The joint mission from UNICEF and the WHO Africa Regional Office have made the final validation assessment and notified the remarkable achievement.

PQM contributes to the achievement of the Ethiopian national health targets and goals through ensuring the availability of safe, efficacious, and quality-assured medicines that are intended to address the priority health needs of the people of Ethiopia.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the performance of the medical products registration system of EFMHACA

During the previous quarter (Q2), PQM supported the development of a clinical trial authorization guideline and a biological products registration guideline. PQM also supported development of 6 guidelines, 1 quality manual, 2 strategic documents, and 8 directives. Continually during Q3, the clinical trial authorization guideline was under review by the PQM team and local experts. The development of the guideline involved participation of different stakeholders (importers, wholesalers, manufacturers, implementing partners, regulators, an ethical committee from science and technology, and representatives from universities at a workshop). Furthermore, the guideline is made available on EFMHACA's official website for public comments before finalization. Once finalized, printing of the document will be supported by PQM.

PQM also provided technical assistance in the improvement of the medicine registration information system (MRIS). PQM has also continued its support to improve MRIS through participation in the Technical Working Group (TWG) meetings to discuss new features needed for system upgrade that will improve identified issues, particularly related to the import permit module. The next step after the system upgrade is to train local agents.

Technical leadership was also provided during the concept note development meeting organized by EFMHACA in the city of Adama. The main purpose of the document was to improve the overall registration system toward international standards and to improve the efficiency, transparency, and accountability of the medicine registration system. Twenty-four new tools, including standard operating procedures (SOPs) and manuals, to help standardize processes and address gaps were identified for development.

PQM also provided technical assistance to EFMHACA to streamline the review process of 170 applications pending marketing authorization approvals during this quarter. In this area, PQM supported EFMHACA to solve the pending issues that delayed actual approval of dossiers after the primary review by facilitating and participating in discussions with a group of relevant technical staff. These discussions resulted in the issuance of market authorizations for 170 out of 190 applications (which had been on hold for various reasons). The remaining 20 could not be processed for authorization due to serious deficiencies that need to be fulfilled prior to approval.

Objective 2 – Strengthen the inspection system of EFMHACA and regional/city administration authorities

This quarter, PQM conducted two rounds of trainings on medicine distribution and storage requirements to help EFMHACA operationalize the good distribution and storage practice guideline developed with PQM's support. The main target audiences for this training were staff from the Pharmaceutical Fund and Supply Agency main (national level) and branch hubs (regional), as well as EFMHACA. This training was essential to ensure that the good practices stipulated in the guideline document are actually translated into action as part of the day-to-day duties of the responsible government agencies. A total of 60 experts were trained.

PQM also provided technical assistance to EFMHACA to strengthen its inspection practices through capacity-building and mentorship. This quarter, EFMHACA inspected a total of 76 foreign manufacturers in two rounds (43 and 33, respectively) using a GMP inspection checklist developed with PQM support. Results from the first round of inspections showed that 13 manufacturers fully met the GMP requirements for market authorization, 15 partially met the requirements, and 15 did not meet the requirements and were rejected. The report from the second round of inspections is under development.

Other activities under this objective that PQM supported this quarter include:

- Built the capacity and skills of EFMHACA staff on QMS for ISO 9001:2015 and ISO 17020:2012. A total of 68 staff participated in this training and included FMHACA team leaders, assistant directors, directorate directors, EFMHACA branch office heads, and selected experts. This funding for this training was leveraged: training-related costs were fully financed by EFMHACA, while PQM covered cost of its technical experts.

- Completed preparatory work for training on sterile pharmaceutical GMP inspection to EFMHACA. This includes development of training materials and selection of trainees and venue; the training is scheduled for the third week of August 2017.
- Commenced development of the inspection manual for regional regulatory bodies to institute a consistent, transparent, and accountable inspection system at all regional regulatory bodies and also to ensure that inspection is conducted in a competent and uniform manner. The manual is expected to be completed and ready for use by the end of Q4.
- Supported the training of Ethiopian airline cargo staff on good storage and good distribution practices in collaboration with the Food, Beverage, and Pharmaceutical Industry Development Institute and Ministry of Industry. A total of 10 staff benefitted from the training.
- Developed an assessment plan to evaluate the availability and utilization of three guidelines—GDP, GSP, and pharmaceutical product recall—developed to improve QA practices. The planned assessment will help EFMHACA understand the successes and challenges with effective utilization and implementation of these guidelines and to plan appropriate actions to improve uptake and use of specified approaches in these guidelines. The assessment will be conducted in Q4.
- Continued to provide technical support to EFMHACA in the development of a pharmaceutical products recall directive. The next step for this activity is to conduct a stakeholder discussion and consensus-building workshop by the end of July to enrich the directive. This activity is important for EFMHACA to have a standardized directive for carrying out enforcement of product recalls for poor-quality and falsified medicines detected in local markets.
- Continued provision of technical assistance to the inspection directorate of EFMHACA on document preparation and operationalization, which is required for and will support achievement of EFMHACA's goal of ISO/IEC 17020 accreditation.

Objective 3 – Strengthen product quality testing system of EFMHACA and branch laboratories

In previous quarters, PQM provided support to improve EFMHACA's QA systems through building staff capacity, providing essential materials to the laboratory, and supporting participation in proficiency testing (PT). PT determines the performance of individual laboratories for specific tests or measurements, and it is used to monitor laboratories' ongoing performance. Through continued PQM support this quarter, 4 EFMHACA branch laboratories collected 200 samples for routine PMS, which they also tested using compendial methods. This is evidence that the knowledge and skills transfer by PQM to branch laboratory staff in QC testing was effective. The branch laboratories took full ownership of the process, including procurement of chemicals, while PQM provided reference standards required for the tests. In addition, PQM conducted supportive supervision at all of the four branch laboratories. Although findings reaffirmed actual application of knowledge and skills gained from trainings, a few gaps were also identified, such as inadequate QMS, no electric power generator at the laboratories, and non-regular calibration of laboratory instruments as specified for QMS. The identified gaps provide indications of where PQM's continued support is needed.

Other activities carried out during the quarter included:

- Conducted hands-on training on QMS to staff at the Bahirdar Branch Laboratory of EFMHACA. The main objective of the training was to fill the gaps identified during previous supportive supervision, prepare the laboratory for ISO accreditation, and have a standardized QMS in place. Four staff, including the branch manager, attended the training.
- Provided support to the NMI through the following:
 - Supported one NMI staff to attend a 2-week training on calibration of dimensions in Korea
 - Conducted a 2-week hands-on training on calibration of temperature and pressure measurements to NMI staff members. This training will help NMI improve functions to expand the scope of its calibration (e.g., into temperature, pressure, and dimension), get accredited for the new scopes, and maintain existing accreditation.
 - Procured primary reference standards for calibration of weight for NMI. Shipment is planned for July 2017. The purpose of the support provided to NMI is to build its capacity so that its scope of accreditation will be expanded, capacity of staff will be built, and NMI will ultimately be able to calibrate laboratory equipment/instruments for EFMHACA. This will eventually eliminate the need to hire foreign consultants, result in cost savings in preventive maintenance and calibration, and help

to ensure more sustainable practices for calibration of EFMHACA's laboratory equipment using local resources. When NMI becomes fully capable to support EFMHACA in the intended manner, EFMHACA will see an estimated \$15,000 in annual cost savings, in addition to the long-term sustaining value added through the creation of in-country capacity to ensure availability of on-time and affordable support. This will also help satisfy the existing calibration needs from local pharmaceutical industries.

Objective 4 – Support local medicine manufacturers to improve their GMP compliance

As part of building the capacity of local manufacturers, PQM has provided technical support to nine local manufacturers. In addition, targeted and product-specific support was provided to three manufacturers toward preparation for WHO prequalification. WHO audited one of these manufacturers, Cadila Pharmaceuticals, on May 22–25 to assess its manufacturing practices for ethambutol 400mg. The audit was concluded with no critical observations, and Cadila Pharmaceuticals is working toward the CAPA response from the audit. Attaining WHO PQ will be a great step forward in creating local capacity for producing quality-assured ethambutol 400mg. This product is a first-line anti-TB medicine and will greatly contribute to increasing access to quality-assured medicine in the treatment of TB in Ethiopia and within the region. With the audit, Cadila is optimistic that it will attain prequalification status in the relatively near future. PQM provided technical assistance to build capacity for GMP compliance for this manufacturer and also conducted a mock audit prior to the WHO inspection.

Other activities carried out under this objective this quarter include:

- Participated in a meeting with EFMHACA to discuss and reach consensus on possible use of the Cortellis regulatory intelligence database, which provides the opportunity to monitor regulatory changes and compare requirements and practices across countries regulatory authorities.
- Attended a workshop organized by the Global Fund (GF) in collaboration with the African Manufacturers Association; the purpose of this workshop was to increase the supply of medicines procured by GF from local manufacturers in Africa, where much of the burden of diseases supported by GF exists. Encouraging local manufacturers (without compromising quality) is part of the consideration for ensuring sustainability of current GF support by improving access to priority medicines from local sources.
- Attended a workshop organized by the Ministry of Industry and MOH in collaboration with WHO to provide an update on the status of the national strategy and plan of action for pharmaceutical manufacturing development in Ethiopia. The strategic plan is viewed as a key starting point to promote investment in pharmaceutical manufacturing in Ethiopia. This will help the establishment of current GMP (cGMP) compliant manufacturers, which ultimately contributes to ensuring the supply of quality-assured medicines from local industries. The expansion of the pharmaceutical industry is in line with both local and international sustainability development goals.

Objective 5 – Strengthen the survey of quality of medicines circulating in the national market

This quarter, PQM supported EFMHACA to complete the collection of about 600 antimalarial and MNCH medicines samples for PMS. The testing of these samples will be conducted in the upcoming months, and results will be disseminated to relevant stakeholders and partners. This marks the ninth round of PMS; tremendous experience has been gained and capacity built at the national regulatory authority (EFMHACA) to perform this function. Because of advocacy and support by PQM, EFMHACA has recognized the importance of conducting PMS on a regular basis; as a result, PMS is included as one of the key activities in its annual action plans. PMS is seen by EFMHACA as a routine activity that has been effectively utilized to identify/detect products with quality defects. It has also provided evidence for follow-up regulatory actions that help to protect the safety of the public.

Details of activities performed for PMS during the quarter included:

- Updated the PMS protocol for both antimalarial and MNCH medicines.
- Selected geographical sampling areas, sampling facility list, and sampling outlets in collaboration with key stakeholders in preparation for the PMS exercise.
- Facilitated task force meetings to implement PMS.
- Trained 27 staff on sampling methodologies and deployed them to collect samples from the field. Regular follow-ups were conducted during sample collection. Compiled a detailed list of laboratory supplies for testing PMS samples.

- Began the procurement process of chemicals and reference standards required for testing samples.
- PQM is collaborating with Monash University to conduct PMS of oxytocin. PQM provided technical assistance in the development of the protocol, identification of sampling areas, and determining the sampling size. PQM has agreed to supply reference standards, and testing will be carried out at both EFMHACA and Monash University. The survey is planned to be finalized before end of September 2017, and the final survey report will be published.

Objective 6– Strengthen EFMHACA governance and management system

No updates this quarter.

Objective 7– Provide technical assistance to the School of Pharmacy of the Addis Ababa University in workforce development in regulatory affairs

PQM is providing technical assistance for the development of a modular course curriculum for QMS to be used in post-graduate programs. A module was drafted according to the course syllabus and curriculum of the program. The final draft was sent to the PQM QMS technical team to review and ensure the accuracy of the technical content. The School of Pharmacy plans to use lecturers from the United States to conduct training using this curriculum for the first batch of program enrollees. The purpose of preparing the module is to have standardized training material so that the course may be offered using local staff going forward.

Objective 8 – Support the Regional Bioequivalence Center (RBEC) to be compliant with Good Laboratory Practices (GLP)

PQM participated in a 1-day consortium meeting, jointly organized by WHO and the MOH to discuss building the capacity of RBEC. PQM was selected to be a member of the committee established during the meeting and was assigned to prepare TOR for the committee.

The following activities were supported during the quarter:

- Identified a list of laboratory items required to build the capacity of RBEC and initiated procurement. RBEC has received some of the procured items, while others are en route.
- Identified a training center to provide training and benchmarking for RBEC (planned for July 2017).
- A 5-day training workshop was collaboratively organized and facilitated by WHO and USP/PQM for members of the EAC, which was held in Addis Ababa. Staff from RBEC participated in this workshop, and the training was focused on inspection of CROs and GCP regulations.

Objective 9 – Support the pharmacovigilance activities of EFMHACA

PQM commenced support to EFMHACA for pharmacovigilance (PV)-related activities during Q3. The involvement of PQM in this area is a result of guidance from the local mission to ensure the continuity of support to EFMHACA as part of transitioning activities following the closeout of USAID's Systems for Improved Access to Pharmaceuticals and Services (SIAPS) program. Specific support areas of technical assistance included supporting the data entry and aggregation of adverse drug event (ADE) reports; sharing data with WHO's Uppsala Monitoring Center; strengthening the PV forum/group responsible for reviewing ADE reports with product defect problems and providing evidence needed to take follow-up regulatory measures; and building the capacity of staff at different levels of the regulatory system. In relation to the aforementioned areas, the following activities were performed:

- Entered 20 ADE data into the Uppsala Monitoring Center database for further sharing with WHO.
- Provided feedback in the form of acknowledgment letters to 36 health care providers who have reported an ADE to the center.
- Performed an investigational assessment on the safety of anticancer medicines that are in use at three health facilities. The report was submitted to EFMHACA's General Director.
- Provided PV training at a workshop organized by EFMHACA in Adama (May 25) on antimicrobial resistance containment to regional EFMHACA branches and regulators/stakeholders.

- Supported EFMHACA staff during supportive supervision at 14 health care facilities that are carrying out cohort event monitoring on antiretroviral medicines and are collecting ADE data prospectively.

IV. Lessons Learned

EFMHACA realizes that the existing regulatory guidelines need to be utilized by stakeholders and that some of the guidelines need to be supported by legal authority for enforcement through development and issuance of corresponding regulations in the form of directives that are legally binding. As a result, efforts are underway to create awareness on some of the regulatory tools, such as the GDP and GSP guidelines. PQM has been instrumental in the advocacy of the regulatory tools and has been acknowledged for this support by EFMHACA.

Ghana

I. Quarter 3 Highlights

Ghana's medicine QA/ QC system was strengthened through building the capacity of six GFDA laboratory staff on microbiology, which is a critical quality assessment test conducted for some liquid medicines, such as oxytocin injection. Given the poor results obtained from the last PMS conducted for oxytocin in the country and the risk that this product presents, it is critical to build in-country capacity and skills to perform microbiology tests, specifically sterility tests; this will help ensure at-risk products that need this test (like oxytocin) are not neglected due to insufficient capacity to carry out the test.

Three GFDA QC laboratories (physical chemistry, pharmaceutical microbiology, and medical devices) maintained their ISO 17025 accreditation following a surveillance audit by ANAB. GFDA prepared for the audit visit with minimal support from PQM. This demonstrates GFDA has improved its technical capacity and is nearing complete ownership of its ISO 17025 accreditation maintenance for its laboratories. It also testifies to PQM's success in building the capacity and skills required to carry out this function effectively.

Following the Q2 initiation of PMS for zinc sulfate tablets in the supply chain, GFDA was also able to finalize the report of the surveillance. Data from the surveillance indicated some samples did not meet the expected quality standards, and GFDA has proposed regulatory actions to ensure the quality and safety of products available to its population.

Following a change in PQM program management and a change in leadership at the GFDA, PQM visited GFDA to assure the new leadership of continued support and determine key activities based on the current priorities of GFDA and the USAID mission. Following separate meetings with GFDA and with the USAID/Ghana mission, two activities (the PMS of antimalarial rapid diagnostic test (RDT) kits and a media documentary to highlight GFDA's accomplishments) were canceled, as they do not reflect current priorities. Three additional activities are now added and include support to improve GMP compliance of local manufacturers of priority medicines, support to build GFDA's capacity to conduct its GMP inspection oversight function, and (lastly), agreement to hire a local in-country consultant to enable improved program response to partners and the mission.

II. Country Context

The PQM program was funded by PMI in Ghana in FY 2008 to strengthen the QA of AMLs in the country. PMI Ghana has funded PQM to provide technical assistance and build capacity to improve efforts in ensuring medicines quality in the country. The program in Ghana has focused on support for the FDA by ensuring the QC of medicines prior to registration and on PMS of the quality of AMLs in the marketplace. The antimalarial MQM program in Ghana has led to the identification of several falsified and substandard medicines; this has prompted GFDA to recall several batches of AMLs from the market and to refer the illegal activities to law enforcement agencies. Based on the outcome of the antimalarial MQM over the years, GFDA decided to enhance its PMS activities in 2013 by providing resources for the basic infrastructure to establish two additional sentinel sites, bringing the total to seven. The number of sampling cycles per round of the MQM was also increased to two.

PQM has also received funds from the Maternal and Child Health (MCH) program at USAID/Ghana since 2011 to strengthen the quality control of MCH commodities such as uterotonic medicines in Ghana. The outcome of the FY 2015 MQM report on the quality of uterotonics (oxytocin and ergometrine) indicated that a high percentage of uterotonics available on the Ghanaian market do not meet the required standards of quality, which could have serious

implications with regards to maternal mortality in the country. PQM continues to support MQM activities to monitor the quality of MCH commodities in the Ghanaian market.

III. Quarter 3 Progress by Objective

Objective 1 – Expand MQM to country-owned sustainable post-marketing surveillance

This quarter, PQM provided feedback to GFDA on the first draft of a PMS protocol. The protocol is currently with GFDA, and PQM envisages the protocol will be ready for the next round of PMS activities for antimalarial and uterotonics sampling in Q4.

Expand MQM to include antimalarial RDT

This activity is no longer a priority and is therefore canceled, as it is outside of the scope of current PQM support. Resources previously allocated to this activity will be repurposed to support a new activity to build GFDA capacity for GMP inspections and to provide support for local manufacturers of antimalarial medicines in Ghana to improve GMP compliance.

Objective 2 – Strengthen the capacity of medicine regulatory system to support regulatory actions against poor quality medicines

During a meeting with the USAID mission in May 2017, the mission indicated the need to cancel the media documentary project, as this was a specific request of the previous GFDA leadership. While it is important for GFDA to continue to create awareness within the Ghanaian population about its efforts to combat substandard and falsified medicines, the media documentary is not deemed a priority. Resources previously allocated will be repurposed toward improving the quality of antimalarial medicines manufactured in the country through support to the GFDA inspections division and to activities to improve GMP compliance of local manufacturers of antimalarial medicines in Ghana.

Objective 3 – Strengthen Quality Assurance and Quality Control Systems through building the capacity of Ghana FDA's quality control systems and laboratories toward attaining or maintaining international standards of quality and practices

PQM built the capacity of six GFDA lab staff on microbiology. Assessing sterility is a microbiology test required for some liquid products, such as oxytocin injection used for treatment of post-partum hemorrhage. This training will further strengthen the capacity of GFDA to assess the microbiology-related aspects of medicines quality in Ghana. PQM also provided some needed equipment and supplies, such as an analytical balance and HPLC syringe filters, to ensure the laboratory accreditation is not jeopardized and to ensure staff are trained with the correct and well-functioning equipment. Training for two GFDA staff to strengthen the capacity of the medical lab device laboratory approved in the PQM work plan was put on–hold, as the laboratory priorities had shifted to bednets and outside the scope of PQM support. Upon discussion with GFDA management, it was agreed to defer the training to a later time when GFDA can finance it themselves.

Building on previous PQM technical assistance and capacity improvements, GFDA, with minimal guidance from PQM, was able to take the lead on maintaining the ISO 17025 accreditation for all three labs previously accredited (physical chemistry, pharmaceutical microbiology, and medical devices). The accreditation surveillance conducted by ANAB was responded to by GFDA drawing from previous experience and expertise gained. Building on PQM technical support toward accreditation maintenance, GFDA also took the initiative, leveraging funds from another donor, the United Nations Industrial Development Organization (UNIDO), to expand the scope of accreditation to also include food microbiology. Preliminary reports indicate a favorable maintenance of the accreditation, but the final accreditation outcome is expected in Q4. This activity demonstrates that PQM support to GFDA over the years is yielding positive returns that will help ensure sustained operations and implementation by GFDA.

Guinea

I. Quarter 3 Highlights

This quarter PQM supported the development of various drafts of the new pharmaceutical law. Each draft was shared with different levels of the National Directorate of Pharmacy and Laboratories (DNPL) key stakeholders for their input and with the national commission members charged with finalizing the law document. An assessment of DNPL registration system was also conducted; identified gaps and recommendations were provided by PQM to the country.

II. Country Context

Together with other donors and USAID partners, PQM supports efforts to strengthen the pharmaceutical system as part of the health system. Like other African countries, Guinea is often disproportionately affected by the burden of poor-quality medicines. PQM can play a key role in strengthening the pharmaceutical system and the capacity of the national drug regulatory authority to assure the quality of medicines in the supply chain through registration, inspection, and QC activities. Malaria is the primary cause of consultations, hospitalizations, and deaths in Guinea—it especially affects children under 5 years of age. In 2011, Guinea was included in PMI; USAID and partners in Guinea are not only procuring malaria commodities but are also helping to strengthen health and pharmaceutical systems.

Guinea and other countries in sub-Saharan Africa are often hurt by falsified medicines. One way to combat this public health challenge in Guinea is to ensure that medicines are registered and tested according to international quality standards. Guinea does not have any local pharmaceutical manufacturers and depends on importation for all essential medicines. Proper registration of medicines is a necessary step to ensure that only quality-assured medicines are available in the market and to generate related revenues to sustain NRA activities.

To reduce disease burden, there is an immediate need to ensure reliable access to good-quality, safe, and efficacious essential medicines and to build up the country's QA/QC systems. USAID/Guinea selected PQM to assume this task. To accomplish this, PQM received funds from Maternal and Child Health and Family Planning funding streams to conduct a rapid assessment of Guinea's QA/QC systems and subsequently proposed activities to address the major challenges.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the legal and regulatory framework to enable DNPL to implement a comprehensive QC/QA mandate

As part of strengthening pharmaceutical law, PQM has collaborated with another USAID implementing partner, SIAPS, which also supports DNPL. PQM was directed to lead the development of a new law on health products, while SIAPS focused on revising an existing law on pharmaceutical organizations. After completing the first draft of the new law on health products, PQM submitted the draft to SIAPS for comments and edits.

PQM received feedback from SIAPS and generated a revised draft of the new law on health products, which was subsequently shared with key stakeholders and the national commission (members in charge of reviewing the pharmaceutical law document) for their review and comments. The draft of the new law on health products includes 40 articles, 19 definitions, details regarding various aspects of medicine legislation (e.g., registration, licensing, promotion), standards and norms for PV, homologation of medical devices, introduction to food supplements and cosmetics regulation, falsification of medical products, and introduction of an autonomous national agency for pharmaceutical products. The subsequent draft has been developed and incorporated feedback from DNPL and the commission.

In discussions about whether the aspects of the health products law should be combined with the pharmaceutical organizations law, PQM advised that creating two draft laws would be most effective to facilitate enactment of each law. The basis of this recommendation uses the following:

- Law 1 (health products): the regulation of health products is linked to international evolution of legislation based essentially on WHO technical positions and regional/continental consensus.
- Law 2 (pharmaceutical organizations): the organization of pharmaceutical activities is based on local situations and national consensus.

Going forward PQM will work with DNPL and other partners to finalize the draft laws.

Objective 2 – Continue strengthening DNPL capacity in product registration

In April, PQM conducted an assessment of DNPL's registration department and drafted a report that highlighted the main registration weaknesses and gaps, including the following:

- Lack of legal basis – the legal basis in Guinean Bill 94 is insufficient or non-operational
- Lack of registration guidelines – the registration document must be transformed into an implementing document.
- Lack of internal procedures – procedures must be created for the various steps, starting with the receipt of a market authorization application or its amendment and/or renewal until the final decision is sent to the applicant
- Need for work instruction for registration staff
- Need for the establishment of committees – it is necessary to formalize the evaluation committee by legal disposition
- Lack of qualified staff – DNPL staff is the backbone of the system for evaluating applications for marketing authorization; however there is only one staff out four who is qualified in conducting registration activities, which is not enough to support DNPL's amount of applications for marketing authorization. Therefore, there is a need to dedicate more staff and build their competencies to properly conduct registration activities, which in turn, will reduce the lead time in evaluating marketing authorizations for approval.

As a next step, PQM will work with DNPL in addressing some of the assessment gaps, including the following tasks:

- Review all regulations regarding product registration and revise or draft new regulations reflecting good governance practices, including confidentiality, code of conduct, and conflict of interest.
- Develop registration guidelines according to WHO recommendations.
- Develop registration-related SOPs.
- Have the DNPL decide whether to retain its current registration software (SIAMED version 2) or switch to more user-friendly and easily adaptable software that is affordable and can meet DNPL's needs.
- Have DNPL recruit and hire at least five individuals for registration activities.

Kenya

I. Quarter 3 Highlights

Midway through this quarter, USAID formally directed PQM to suspend activities under the cooperative agreement with USAID that support Kenya's MOH. This suspension meant not only ceasing implementation of joint efforts on PMS strengthening but also activities geared toward helping the NQCL attain ISO 17025 accreditation and building the regulatory capacity of the Pharmacy and Poison Board (PPB) by strengthening its product registration systems and processes.

II. Country Context

USAID/Kenya funding is provided for health systems strengthening interventions, including strengthening of the health workforce; the health information system; and supply chain management for HIV/AIDS, malaria, and family planning materials. In this context, PQM has been engaged to help strengthen the pharmaceutical regulatory system and to improve medicines quality. Kenya and other countries in Africa are disproportionately affected by the burden of poor-quality medicines. The best way to combat this public health challenge—and to increase the impact of other interventions in the malaria, TB, HIV/AIDS, and MNCH programs—is to strengthen the national regulatory authority to ensure that medicines are properly registered and tested, and take corrective regulatory actions related to substandard or falsified products and unlicensed pharmaceutical outlets.

PQM activities are aligned with Kenya's overall strategy of attaining sustainability of established capabilities by strengthening the country's institutions as well as fostering regional cooperation.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen PMS and integrate other essential medicines to existing MQM program at central and county levels

To deliver on an FY 2016 work plan activity that was previously delayed, PQM conducted a workshop to build the capacity of Kenyan health professionals from the National Malaria Control Program (NMCP) and National Microbiology Reference Laboratory (NMRL) to better address the public health challenges presented by malaria. This was done through benchmarking the testing for the quality of RDTs with assistance from two experts from Senegal: the Deputy Coordinator of Senegal's NMCP and an Associate Professor from the Parasitology Department within the University of Cheikh Anta Diop's Faculty of Medicine.

This South-South collaboration between the NMCPs of Kenya and Senegal has been successful; however, PQM's activities in this area are considered concluded, and PQM will no longer support activities for RDTs.

Objective 2 – Build the regulatory capacity of PPB by strengthening product registration

This quarter, PQM revised activities under this objective such that PPB would take full ownership of product registration, including the maintenance of the newly configured registration and inspection system. PQM worked with PPB registration staff to identify critical gaps in the current registration system and helped PPB develop guidelines for reporting poor-quality medicines submitted by sampling teams from the field.

Objective 3 – Strengthen the quality control capacity of NQCL and support maintenance of ISO 17025 accreditation and WHO PQ

Due to the suspension of assistance to Kenya MOH, the South African National Accreditation System (SANAS) accreditation assessment visit planned for June was cancelled. Prior to the suspension, PQM had made preparations for a mock audit providing technical and logistical guidance in anticipation of the accreditation visit. The expectation going forward is that the NQCL will take over this activity and collaborate directly with SANAS to conduct the assessment visit without additional PQM assistance. Under this suspension, other planned activities will be deferred, including the inter-laboratory and proficiency testing, which are two activities important to maintain ISO 17025 accreditation.

Objective 4 – Support the implementation of PQM activities in country and promote regional and international collaboration

Since the onset of PQM activities in Kenya, PMS was conducted in 11 sites and was solely funded through PMI. To expand PMS to 11 additional sites and include other essential medicines, it has been agreed with key partners and stakeholders to join efforts and establish a joint PMS surveillance strategy and step up a national TWG.

During Q3, PQM took the lead in convening a meeting of the TWG. The TWG was established in April 2017 and includes stakeholders such as the USAID Mission, SIAPS, supply entities (e.g., KEMSA & MEDS), laboratories (e.g., NQCL), development partners, county representatives, research organizations (e.g., KEMRI), public and private hospitals, PPB, and MOH. After this initial convening, the TWG will meet periodically to develop an integrated PV/PMS system that broadens the scope of medicines beyond those for HIV, TB, and malaria.

Due to the suspension of activities in Kenya, the TWG will continue working on the planned strategies without the presence of PQM. The immediate tasks to be undertaken by the TWG include identification of funding, establishment of an integrated PMS protocol, and planning training for building human capacity.

Liberia

I. Quarter 3 Highlights

On the night of May 29, 2017, a fire completely destroyed the quality control laboratory (QCL) of the Liberia Medicines and Health Product Regulatory Authority (LMHRA). All equipment and materials were lost, including an HPLC procured by PQM through funding from USAID-PMI.

Other highlights of this quarter include the GMP training provided to LMHRA inspectors. This training will enable LMHRA to use the GMP guidelines to inspect manufacturers that sell their products in Liberia. It is also noteworthy to mention that during this quarter, NMCP was able leverage additional funding to augment PQM's support and increase MQM surveillance sites and conduct monitoring and evaluation (M&E) activities at the surveillance sites. With PQM intervention, the NMCP's M&E strategy will account for the quality of malarial medicines distributed to public health facilities throughout Liberia.

II. Country Context

Malaria is endemic in Liberia and poses a serious public health threat. Malaria accounts for at least 33% of all inpatient deaths, and 41% of deaths occur among children under 5 (NMCP, 2012). In 2012, NMCP reported that hospital records showed malaria as the leading cause of attendance at outpatient facilities. It is also the number one cause of inpatient deaths, making malaria prevention and control a significant concern in Liberia. In collaboration with other international partners, NMCP has made significant efforts to scale up malaria prevention interventions as well as improve public-private partnership in providing access to quality antimalarial medicines.

Since 2011, PQM has provided technical assistance to strengthen PMS in Liberia through MQM for antimalarial medicines and encouraged LMHRA to take appropriate regulatory actions. Through these MQM activities, several antimalarial medicines, including quinine tablets and chloroquine, were removed from circulation. Monotherapies, such as quinine tablets and chloroquine, once widely available but subsequently banned through regulatory action by LMHRA, have become less prevalent. Results from various MQM activities and subsequent regulatory actions have been encouraging; however, the data continues to show that falsified and substandard medicines are still a major concern in Liberia.

In Liberia, PQM is focused on:

- Building LMHRA's QA/QC capacity.
- Reducing the incidence of falsified medications and increasing awareness of quality medicines.

As part of the approved FY 2017 work plan, PQM provides technical assistance to build the QC capacity of the existing LMHRA QCL toward ISO 17025 accreditation, strengthen and expand the monitoring of the quality of AMLs, promote regulatory actions for falsified and substandard medicines, and increase awareness of quality medicines.

III. Quarter 3 Progress by Objective

Objective 1 – Continue building the QA capacities of LMHRA in registration and inspection

In Q3, PQM conducted a 5-day capacity-building training workshop on GMP in Monrovia. Thirteen LMHRA inspectors (nine male, four female) were trained in basic GMP. The training focused on various areas, including QMS, quality risk management, sanitation and hygiene, complaints and recalls, contract production and analysis, self-inspection and quality edits, personnel, and documentation.

Objective 2 – Continue strengthening the quality control of LMHRA QC Lab toward ISO 17025 accreditation

During this quarter the LMHRA QCL was completely destroyed by a fire, including all laboratory equipment and furniture. This fire incident will impact the testing of medicines collected for MQM, as well as medicines to be registered for marketing authorization. To minimize this impact, LMHRA is considering alternative means, including third-party testing of medicines at an accredited laboratory and the use of a transitional laboratory facility. To support LMHRA's effort to build a transitional laboratory, PQM provided guidance regarding model laboratories that can be built in 6 months. Currently, LMHRA is in discussion with GF to finance this model laboratory. PQM is also in discussions with USP to potentially provide some testing support for the QC laboratory samples.

Objective 3 – Build the capacity of LMHRA on the Post Marketing Surveillance Program for the monitoring of the quality of antimalarial medicines

To ensure PMS sustainability in Liberia, PQM promoted the integration of the PMS program—specifically for antimalarials—into the NMCP M&E plan. In early March, PQM staff traveled to Liberia and proposed the idea to NMCP of incorporating quality into the national malaria M&E strategy. The idea was accepted in April 2017 by LMHRA and NMCP and was included in the 2016–2020 M&E plan. For the first time, NMCP's M&E strategy will account for the quality of malarial medicines distributed to public health facilities throughout Liberia. Under the new arrangement, LMHRA will be charged with the responsibility of performing PMS activities in accordance with

established protocol developed in collaboration with PQM. PQM will continue to support the strengthening of LMHRA's PMS capacity. For the first time, future PMS activities will be conducted at NMCP's five surveillance sites. As part of overall health systems strengthening, LMHRA is planning to have one of its inspectors relocate to one of the sites to ensure that LMHRA inspections are conducted properly and to enforce any regulatory actions at the surveillance site. This activity will be conducted jointly with the National Drug Service, NMCP, and LMHRA.

Although not recommended for malaria treatment, antimalarial monotherapies are still circulating widely throughout counties in rural Liberia (e.g., Nimba, Bong, Lofa, Bomi, Grand Geddeh, River Gee) virtually all of which are illegally imported from Guinea. In March, PQM staff travelled to Liberia to support the drafting of an action plan by LMHRA, which included the development of a resolution calling for the complete removal of antimalarial monotherapies from circulation in Liberia. The resolution has since been forwarded to NMCP, the Pharmacy Division, and the Pharmacy Board for review this quarter. The resolution is expected to be signed by all parties shortly, and is then submitted to the Minister of Health. This will pave the way for the removal of the monotherapies and make the importation and selling of antimalarial monotherapies illegal. Liberia joins Senegal in combatting the sale of monotherapies, with both countries working towards eradicating illicit markets for the products at regional sites.

The action plan of the resolution also called for raising public awareness about the resistance issues surrounding the use of monotherapies. However, implementation of the action plan has been postponed until Q4 due to the fire incident at the laboratory.



Incineration of non-registered and poor quality medicines found during previous PMS activities in Liberia

Objective 4 – Promote regulatory actions and raising awareness about poor quality medicine in country and at regional levels:

PQM engaged in two main activities under this objective in Q3:

- PQM participated in this year's World Malaria Day held in Bong County. Joined by LMHRA and NMCP, PQM highlighted the importance of quality by displaying samples of failed antimalarial medicines and explained to event attendees (including students, dignitaries, and pregnant women) how to detect substandard and falsified medicines by simple visual inspection. Samples of antimalarial monotherapy were also displayed, and the team used that opportunity to raise awareness about why monotherapies are not effective. Additionally, PQM encouraged civil society to support LMHRA in the fight against substandard and falsified medicines and explained to them their roles and responsibilities toward this goal. For instance, PQM provided guidance on reporting any suspicious products to LMHRA and how to advocate on the use of ACTs from the public sector and avoid the use monotherapies for malaria treatment.

- PQM participated in a 1-day implementing partners (IPs) conference in Monrovia focusing on the Liberia Strategic Analysis role in M&E. The conference was well-attended by several USAID IPs. The gathering provided an opportunity for IPs to learn about Performance Indicator Database System (PIDS) use requirements, performance indicator data collection and reporting, environmental compliance, and the Liberia Development Conference to Country Development Cooperation Strategy. The Liberia Strategic Analysis provides IPs with analytical and advisory services in support of strategic planning, project and activity design, and performance M&E. This interactive conference provided a unique opportunity to share information with other IPs on PQM's role in the fight against poor-quality medicines in Liberia.

IV. Key Challenges

Despite the total loss of the laboratory facility and equipment due to the fire incident, LMHRA is attempting to make rapid adjustments that will enable it to use Minilab™ where possible as a screening tool to resume testing of samples from importers of pharmaceutical and health products. Minilab™ is not a sufficient tool to fully assess the quality of medicines. LMHRA will need to identify a third-party laboratory to support routine QC testing.

V. Lessons Learned

The fire at LMHRA that led to the destruction of laboratory building and critical equipment, as well as the loss of quality data, have underscored the importance of ensuring that laboratories have safety measures in place that prevent such unexpected situations.

Mali

I. Quarter 3 Highlights

In Q3, PQM facilitated development of the National Laboratory of Health (Laboratoire National de la Santé; LNS) strategic plan outline. This was achieved during a 3-day meeting with the LNS Technical Deputy Director and managers of different services. The draft was adopted at a workshop with local partners.

To continue developing the LNS QMS, PQM facilitated the drafting of 34 SOPs; these are currently under review.

PQM facilitated the collection of 568 samples from the District of Bamako and the Regions of Koulikoro, Mopti, Sikasso, and Segou. Screening of select samples using Minilab™ is underway at LNS.

PQM conducted a full assessment of the Directorate of Pharmacy and Medicine (Direction de la Pharmacie et du Médicament; DPM). Identified gaps and recommendations were provided to the DPM. To complement the information collected during the assessment, PQM reviewed laws and regulations relating to the pharmaceutical sector and identified opportunities for change and improvement.

II. Country Context

Malaria is the primary cause of morbidity and mortality in Mali. The goal of PMI in Mali is to reduce malaria deaths and substantially decrease malaria morbidity, toward the long-term goal of elimination. Through USP-PQM, USAID has been assisting Mali's MOH in strengthening the medicines QA systems since 2008. The activities have focused on strengthening the capacity of DPM and LNS in PV, drug registration, MQC, and PMS.

The objectives of PQM interventions in Mali are in line with PMI's strategic approach in the area of building capacity and health systems, as described in the PMI 2015–2020 strategic plan. PQM proposed activities in Mali fall under PMI's core operating principles that "ensure that all commodities provided to countries are of high quality and that systems are in place to continually improve the quality of services delivered."

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the Capacity of the National Quality Control Laboratory in Mali

Implementation of the LNS strategic plan

In Q3, PQM organized a 3-day meeting with the LNS Technical Deputy Director and managers of services to draft the LNS strategic plan. The draft defined LNS' vision and mission and outlined strategic directions. It also defined the logical performance framework for a 5-year period, which includes the following six targeted outcomes:

1. LNS has an effective role in medicines' and medical devices registration in Mali.
2. LNS is fully capable of controlling the quality of all registered health products in Mali.
3. LNS has a clear legal mandate organizing its QC role in Mali according to international standards.
4. LNS has an effective information, education, and communication unit promoting its role and activities.
5. LNS has functioning QMS in compliance with WHO and ISO 17025.
6. Policies and tools in line with LNS values are in place and functional.

The participants in the meeting provided recommendations to LNS management. The recommendations focused on the need for LNS to implement Sahel Women's Empowerment and Demographics Dividends, finalizing the vision and the mission of the laboratory, revising the organizational flowchart, upgrading premises, and hiring new staff.

The draft strategic plan outline has been adopted at a workshop on strategic action plan for collaboration between the LNS, the Directorate of Pharmacy and Medicine, and the Inspectorate of Health. This workshop was sponsored by WHO. Drafting of the narrative of the plan is underway. A next step is for LNS to submit the final plan to the Ministry of Health and Public Hygiene upon completion.

Develop Quality Management System documents

To help LNS develop its QMS documentation, PQM assisted the laboratory in drafting and reviewing 34 new SOPs. During this process, LNS rewrote six SOPs developed earlier in this quarter. The SOPs cover different aspects of the laboratory's activities. LNS developed several SOPs as follow-up to training that PQM provided to laboratory staff, such as GDP, HPLC, dissolution, and calibration of laboratory equipment.

Objective 2 – Strengthen Post Marketing Surveillance of Antimalarial medicines in Mali

Facilitate one round of sampling and testing of antimalarial medicines

PQM facilitated one round of sampling of antimalarial medicines at the sentinel sites of Koulikoro, Mopti, Segou, Sikasso, and the District of Bamako. A total of 568 samples of antimalarial medicines were collected. Except for samples from Mopti, the samples were verified and visual inspections conducted, and a set of samples was selected for further screening using Minilab™. Test results led to suspicion of falsified quinine products; they were flagged to LNS to prioritize the testing of these samples and to inform the Directorate of Pharmacy and Medicine, as well as the Inspectorate of Health, for immediate action if confirmed. The suspected falsified products were collected from public and private sectors and a denominational hospital.

Objective 3 – Facilitate studies on the efficacy and resistance of antimalarial medicines

Facilitate study of ACT efficacy and the combination sulphadoxine-pyrimethamine (SP) and amodiaquine resistance through a sub-award with USTTB

In collaboration with the Laboratory of Applied Molecular Biology, PQM developed fixed-amount award packets to conduct studies of ACT efficacy and the combination of sulfadoxine-pyrimethamine, as well as amodiaquine resistance at two locations. PQM's support will focus on the quality assurance of the products. This packet was submitted for review and approval to USAID/Washington. The activities are expected to start by the end of July.

Objective 4 – Strengthen the capacity of the Directorate of Pharmacy and Medicine (DPM)

Advocate for full restructuring of the DPM

PQM carried out a full assessment of DPM using the WHO assessment tool. At the end of the assessment, PQM debriefed DPM management on the findings.

Highlights of the findings included:

- DPM does not have full authority to regulate the pharmaceutical system.
- DPM lacks financial autonomy, has no policy regarding good governance (code of conduct, confidentiality, and management of conflict of interest), and the QMS needs improvements.
- Equipment, premises (limited space), and management of information (making information available to the public) are insufficient.
- Human resources are limited and personnel training is insufficient to build the capacity for its functions.
- There are no legal provisions for GDP.
- DPM has no authority to withdraw or suspend licenses for pharmaceutical outlets.

PQM also conducted a review of pharmaceutical regulations of Mali. The review showed inadequacies in several regulations relating to regulatory functions; many are outdated and need to be revised. As a next step, PQM will submit a report to DPM with recommendations on priority actions that the Directorate needs to take to address main gaps and start discussions on steps to revise regulatory provisions.

IV. Key Challenges

The process of review and approval of the fixed amount award (FAA) continues to be a challenge. Direct implementation of PMS activities is being facilitated by PQM local consultants.

Mozambique

I. Quarter 3 Highlights

The National Quality Control Laboratory (LNCQM) continued to improve its QC capacity through PQM support toward procurement of essential laboratory equipment and supplies and maintenance of its key functional setup. One significant achievement by LNCQM this quarter is its enrollment in the USP Complimentary Standards program, which makes LNCQM eligible to receive USP reference standards free of charge for QC testing of medicines.

Following the recent changes in PQM program management for Mozambique, PQM visited the country to conduct a review of ongoing approved PQM work plan activities and reprioritize according to country needs. During this visit, PQM met with directors of the Pharmaceutical Department (PD) and LNCQM, Deputy Director of the Department of Public Health, Deputy Minister of Health, WHO, Global Fund, and partners to discuss country gaps and priorities. As a result, PQM reached an agreement with USAID/Mozambique to delay one planned activity and cancel another (establishment of collaboration with academia and ISO 17025 pre-assessment, respectively), modify current work plan activities based on identified priorities, and add one new activity (lab expansion justification and support with national medicine policy) to this year's work plan. These changes were necessary to support LNCQM and the PD with priority and time-sensitive activities.

II. Country Context

USAID and USP have been providing technical assistance to Mozambique through PQM since 2010. Activities have focused on strengthening the QA/QC capabilities of Mozambique's MRA, the PD.

PQM conducted a rapid assessment of the PD's QA/QC capabilities in December 2010, which revealed that LNCQM's infrastructure, equipment, and staff were inadequate to provide QC services. The assessment also identified a lack of PMS of medicines quality. In 2011, PQM and PD partnered to establish an MQM program that included training on screening medicine quality.

In 2012, PQM facilitated significant investments in a variety of laboratory equipment, supplies, and reagents necessary for a QC laboratory to adequately test medicines. These investments also included training in equipment operation and in testing procedures required to analyze malaria and HIV medicines.

Throughout 2013 and 2014, PQM developed and trained LNCQM technical staff and provided them with day-to-day laboratory consumables, equipment, supplies, and reagents to run the QC lab. To date, LNCQM has improved its

technical capacity in analytical testing, proficiency, and use of key QC lab equipment. Through this PQM training, LNCQM is better able to collaborate with other Portuguese-speaking countries.

III. Quarter 3 Progress by Objective

Objective 1 – Continue to strengthen the capacity of Mozambique National Laboratory, LNCQM

To strengthen LNCQM's capacity to carry out its functions, this quarter PQM provided laboratory equipment and supplies to ensure it has the functional setup necessary for a QC laboratory to test medicines. In order for LNCQM to continue to function effectively, PQM supported fixing a broken hydro pump that left the laboratory without water. Although this could have been fixed with laboratory budget, the lengthy process to get government approval for release of funds would have left LNCQM without any water source for weeks.

PQM supported the overhaul of LNCQM's WiFi system to make sure the laboratory has working Internet to update essential software for the laboratory equipment and to facilitate ease of communication with clients, stakeholders, and partners. To ensure the laboratory can continue to sustain maintenance of the Internet system, PQM obtained MOH commitment to continue to pay for the cost of regular Internet consumption and maintenance. Also, PQM supported the LNCQM with installation of a new computer and software program for the HPLC and carried out performance verification to ensure correct operation of the equipment. HPLC vials and 17 British Pharmacopeia reference standards were also supplied to the laboratory for quality testing of essential medicines, including maternal and child health, family planning, and malaria products.

With PQM's support, 12 essential SOPs were also developed by LNCQM to strengthen its QMS.

During the visit to Mozambique this quarter, in agreement with USAID, PQM committed to help LNCQM develop critical documents required to justify the \$1 million grant request from the Global Fund to expand the LNCQM physical space. The Global Fund grant-making meeting where this discussion will be held is planned for August 2017. The first step of this support was to identify key activities needed for the justification. LNCQM has submitted a request to MOH to obtain formal approval to use government land for the space expansion. PQM has engaged an architect to come up with the blueprint, construction cost, and budgets. However, PQM needs information on the square footage of approved government land before this work can commence. PQM work plan activities were also prioritized based on PD and LNCQM immediate priorities. PQM agreed with USAID to delay/cancel two work plan activities—ISO 17025 pre-assessment and establishment of collaboration with academia—in order to accommodate country priority activities (lab expansion justification and support with national medicine policy). PQM will continue to implement these priority activities in Q4.

Objective 2 – Support and strengthen post-marketing surveillance

No updates this quarter.

Objective 3 – Provide technical assistance to the Pharmaceutical Department (PD)

During the visit this quarter, PQM had a half-day work session with PD's management team. Participation included the Heads of PD's Registration, PV, Inspection, and Legal Departments to discuss technical assistance needs. It was agreed that the most urgent support PD required was for development and finalization of priority medicine regulations, which have to be submitted for approval within 6 months after the final signing and release of the new pharmaceutical law. Support was also requested to strengthen the medicine registration, inspections, and PV systems. Another area highlighted was to review and provide technical assistance for the national medicines policy of the country. PQM already started providing technical assistance in this area to support establishment of TOR for the committee that will spearhead national medicine policy development process.

Objective 4 – South-South collaboration with SADC countries and PALOP countries

No updates this quarter.

Nigeria

I. Quarter 3 Highlights

PQM continues to provide technical assistance to strengthen regulatory system functions in the country. Integral components of PQM technical support include strengthening NAFDAC's NQCL to raise laboratory standards; strengthening local manufacturers' capacity to attain stringent international GMP standards necessary for the supply of quality medicines; and strengthening the PMS function of the agency to remove substandard and falsified products from the market.

Highlights during this quarter included:

- Achievement of 100% test score result in one proficiency test evaluation for Agulu laboratory. This is a strong prerequisite for the laboratory as it prepares for an ISO reaccreditation surveillance audit next quarter.
- Official notification of ISO/IEC 17025:2005 accreditation for seven scopes for NAFDAC Kaduna regional laboratory.
- Completion of an extensive gap assessment at the National Institute of Pharmaceutical Research and Development (NIPRD). Findings suggested the laboratory requires technical support to strengthen its practices.
- One round of PMS of antimalarial medicines in the six geopolitical zones. Minilab™ testing of 864 sampled antimalarial products was conducted by 5 regional laboratories; results showed 1.6% failure (14 samples failed).
- Completion of the 6 months accelerated stability study with favorable outcome for magnesium sulfate, a product used to treat eclampsia and pre-eclampsia in pregnant women. This breakthrough will create a pathway for quality-assured magnesium sulfate in the local market.
- Commencement of oxytocin injection stability studies with anticipated successful completion in June 2018. When achieved, Nigeria will have its first local source of quality-assured oxytocin injection. Advantages of this include reduced lead time from the manufacturing site to the patient and possibly reduced risk of product degradation due to distribution and storage concerns (2–8 degrees Celsius), as smaller quantities and more frequent supply from the local manufacturer can reduce the total time products are exposed to potentially poor storage conditions before use.
- Facilitation of dissemination meeting by NAFDAC to discuss results of oxytocin injection study, which showed that 74% of sampled products (159 total samples collected) failed QC testing. Key actions were taken as a result of this meeting, including removal of failed products from the market and reinforcement of the requirements for storage conditions. NAFDAC also requested the market authorization holders to provide a list of their distributors to NAFDAC for collaboration in addressing the challenges of storage conditions.

II. Country Context

Within the Nigerian context, through PMI funding, USAID/Nigeria is focused on strengthening NAFDAC's regulatory capacity and increasing the availability of locally manufactured, quality-assured AMLs to support PMI's overarching goal to reduce malaria-associated mortality by 50% in Nigeria.

USAID/Nigeria is also working to increase the availability of MNCH medicines in support of the UN Commission on Life-Saving Commodities for Women and Children. The commission was established in April 2012 to improve affordable access to medicines and supplies essential to the health and welfare of women, newborns, and children under the age of 5—populations who most often die of preventable causes. The UN Commission on Life-Saving Commodities for Women and Children has recommended 13 essential health commodities for women and children that it considers will have the greatest impact on achieving health-related UN Millennium Development Goals.

PQM's overall goal in Nigeria is strengthening NAFDAC's regulatory capacity and increasing the supply of locally manufactured quality-assured priority medicines. To accomplish this goal, PQM will continue to provide technical assistance to NAFDAC, the Federal Ministry of Health, the Pharmacists Council of Nigeria, NIPRD, and the National Malaria Elimination Program. In addition, there are pharmaceutical and nutraceutical manufacturers and other stakeholders whose activities directly impact the system strengthening of NAFDAC and PQM-supported local manufacturers.

III. Quarter 3 Progress by Objective

Objective 1 – Continue to provide technical assistance to selected manufacturers with strong interest and commitment to locally producing products of interest (zinc/ORS, CHX, amoxicillin DT, artemether/lumefantrine, oxytocin injection, magnesium sulfate injection, and ready to use therapeutic foods [RUTF]) in compliance with international quality standards

PQM delivers broad technical assistance to local manufacturers to address GMP and other quality-related concerns. By doing so, PQM increases access to a steady supply of essential medicines of assured quality, safety, and efficacy, including antimalarial and critical medicines for mothers and their children, thereby contributing to the wellbeing of the population. Technical assistance is provided to local manufacturers throughout the process to become approved by an SRA, or local national regulatory authority, from early initiatives to the final submission of the application or dossier.

Breakthrough with Magnesium Sulfate

This quarter marked significant progress as PQM's continuous technical assistance has yielded the successful completion of 6 months' accelerated stability study for magnesium sulfate, an anticonvulsant recommended for pregnant women with severe pre-eclampsia and eclampsia. The result showed that all parameters correspond to specification as stated in the official compendium. Next steps for Juhel Pharmaceuticals include commencement of dossier compilation that meet SRA standards or demonstrate compliance with donor agencies' procurement requirements, as this will expand the procurement reach of this product beyond Nigeria.

Juhel Pharmaceuticals, a PQM-supported local manufacturer, records successful development of first batch of oxytocin injection in Nigeria

In FY 2016, PQM supported the development of a roadmap for the production of oxytocin in Nigeria. The team continuously provided technical assistance to Juhel Pharmaceuticals to resolve the identified corrective and preventive actions (CAPAs) and develop QMS documents for the product. This quarter, the product has been successfully developed and is undergoing stability studies. With the anticipated successful completion of stability studies in 2018, Nigeria will have their first local source of quality-assured oxytocin injection, with the advantage of a reduced lead time from the manufacturing site to the patient and possibly reduced risk of product degradation due to distribution and storage concerns (2-8 degrees Celsius); as smaller quantities and more frequent supply from local manufacturer can reduce total time products are exposed to potentially poor storage conditions before use. Overall, local manufacturing of this product will contribute to decreased maternal mortality attributable to post-partum hemorrhage. Next steps include continued monitoring of product stability studies; preparing the protocol for manufacturing process validation; beginning dossier compilation; and providing continuous support to the laboratory on good practices for pharmaceutical quality control.

Objective 2 – Strengthen regulatory quality assurance and quality control systems through building the capacity of NAFDAC's quality control laboratories to attain international standards of quality and practices

PQM builds the capacity of NQCLs to improve laboratory standards through hands-on training and technical assistance. Internationally recognized standards, such as ISO accreditation and/or WHO PQ, are just one possible result of this increased capacity. ISO accreditation signifies that a laboratory is technically proficient to produce consistently valid results; regulatory agencies and medicines manufacturers typically accept test results only from accredited labs. WHO PQ aims to increase the supply of quality priority medicines by applying unified standards of acceptable quality, safety, risk, and efficacy to guide procurement decisions of United Nations agencies and other entities involved in procuring bulk medicines.

NAFDAC Agulu regional laboratory prepares for surveillance audit

This quarter Agulu regional laboratory passed one proficiency test as a result of technical assistance from PQM. This is a critical requirement as the laboratory prepares for an ISO reaccreditation surveillance audit. The proficiency test results were in seven scopes, which include HPLC, ultra-violet visible spectroscopy, pH measurement, Dissolution, loss on drying, Karl Fischer water content determination, uniformity of dosage form (weight variation and content uniformity). Next steps include the review of the QMS documents of NAFDAC's Agulu regional laboratory toward the ANAB surveillance visit.

NAFDAC Kaduna regional laboratory receives official notification for ISO/IEC17025:2005 accreditation

Last quarter, ANAB audited the Kaduna regional laboratory, and only four minor observations were observed. This quarter, PQM provided technical assistance to the regional laboratory in resolving CAPAs identified during the ANAB official audit. NAFDAC's Kaduna regional laboratory has received official notification for ISO/IEC 17025:2005 accreditation in seven scopes (HPLC, ultra-violet visible spectroscopy, pH measurement, Dissolution, loss on drying,

Karl Fischer water content determination, uniformity of dosage form). This will be first of its kind in the northern region of the country. With this, 100% of medicine quality tests are conducted in ISO-accredited laboratories in Nigeria.



USP CEO, Ron Piervincenzi (left), NAFDAC's Acting Director-General, Yetunde Oni (center), and USP-Nigeria Chief of Party, Chimezie Anyakora attending the NAFDAC Kaduna regional laboratory accreditation ceremony

NIPRD prepares for accreditation

An advocacy meeting was held this quarter with NIPRD management. The focus of the meeting was to develop a roadmap for accreditation as PQM continues technical support to NIPRD. During the meeting, a new roadmap was developed with timelines after a status assessment was conducted in the laboratory. Observed findings during the status assessment indicated that NIPRD, although a prominent research laboratory, urgently needs technical assistance and consumables to enable the laboratory prepare for and attain ISO 17025 accreditation. As a result, procurement for consumables for the laboratory commenced this quarter. Based on the new roadmap, NIPRD has also commenced the process of equipment procurement, and PQM has begun technical support to key personnel in the laboratory. Next steps include commencement of the implementation plan for accreditation for NIPRD and QMS and laboratory hands-on techniques training scheduled for next quarter.

Objective 3 – Strengthen NAFDAC's registration unit (R&R) capacity to manage registration information

Assessment of NAFDAC Registration Directorate completed

PQM collaborated with NAFDAC's Registration and Regulation Directorate to ascertain the needs for development of a medicines registration information management system that creates the necessary procedures for improved efficiency in product registration processes. This quarter, PQM shared the completed assessment report of existing capabilities of the registration unit's information system and its impact to other directorates, which should ultimately help improve the product registration process with the agency.

Next steps are to commence the implementation of recommendations, including the review of SOPs. The recommendations will form the foundation to strengthen and improve the product registration and monitoring system and will help reduce lead time (average time span between application submission and the date of issuance of the registration certificate) for registering pharmaceutical products, including antimalarials and MNCH products.

Objective 4 – Strengthen NAFDAC Drug Evaluation and Research Directorate capacity for inspections and Dossier Evaluation

The Drug Evaluation and Research Directorate is committed to the development and continued improvement of its QMS to ensure a robust and effective inspectorate that will guarantee safe, effective, and quality medicines. The unit has used an inspection guideline that was last reviewed in 2009. PQM is providing technical support to the unit to review this guideline to ensure it is harmonized with regional and international standards. Next steps after the guideline revision will include implementation and operationalization of the guideline, which includes the NAFDAC inspection directorate conducting at least one round of inspection each to three different local manufacturers.

Objective 5 – Strengthen NAFDAC’s PMS directorate capabilities

PQM Nigeria focuses on building NAFDAC’s capacity to perform PMS as a regulatory function, which is aimed at assessing product quality in the market. This includes monitoring the quality of marketed products throughout the levels of the supply chain. A dissemination meeting with stakeholders was held this quarter to discuss the outcome of the analysis of antimalarial and MNCH products sampled to evaluate product quality in the six geopolitical regions. In attendance were representatives from the NAFDAC Acting Director General, Directors of the various directorates, the PQM team, Directors of State Pharmaceutical Services (Kaduna and Ogun states), Chairman and Executive Secretary of the Pharmaceutical Manufacturers Group of Manufacturers Association of Nigeria, President of the Pharmaceutical Society of Nigeria, and Director of the PV/PMS Directorate, as the anchor for the meeting.

Key outcomes of the meeting included to:

- Strengthen NAFDAC PV/PMS to conduct surveillance.
- Conduct an assessment of storage conditions, which is a critical risk factor affecting quality of products (nationwide for cold-chain products such as oxytocin and insulin injection).
- Address and improve the integrity of the supply chain for medical products. Improve collaborative efforts with all stakeholders, especially in hard-to-reach areas. Request Marketing Authorization Holders to provide a list of their distributors to NAFDAC for collaboration in addressing the challenges of storage conditions.
- Develop a roadmap with stakeholders to address challenges highlighted with medicines storage.
- Revisit the national drug distribution guideline and its implementation in the country.

A next step after the dissemination meeting was the commencement of poor-quality medicine batch collection from all affected health facilities and markets to ensure the ineffective products cannot be accessed and used on pregnant women. So far, 258 ampoules of poor-quality oxytocin were collected from various locations in three states of the Federation. The recall exercise will be continuous, and a subsequent report is expected from NAFDAC before the end of Q4.

The FY 2017 round of PMS of antimalarial drugs in Nigeria was carried out successfully by NAFDAC with technical assistance from PQM in the six geopolitical zones this quarter. Five regional laboratories carried out Minilab™ tests of 878 sampled antimalarial products, and data analysis of the results showed 1.6% failure; 14 samples failed quality testing, while 864 samples passed. A comprehensive report is expected next quarter.

Objective 6 – Strengthen human capacity and program effectiveness of key regulatory agencies, local manufacturers and local PQM staff

PQM serves as a global technical leader in medicines quality assurance and an advocate for medicines quality in collaboration with a number of partners. Technical leadership support from PQM entails contributing to an expanding body of knowledge on pharmaceutical quality-related health systems research, as well as developing and disseminating innovative, efficient, and risk-based quality testing techniques and approaches. Advocacy efforts involve the promotion of quality medicines and eradication of falsified and substandard products, forged through collaboration with diverse partners at local, national, and international levels, as well as visibility in external information outlets.

This quarter PQM held a meeting with Federal Ministry of Health to discuss the use of monotherapy in Nigeria for the treatment of malaria. The meeting was intended to ensure that chloroquine and monotherapies are banned from the Nigerian market.

World Malaria Day spotlights the global effort to control malaria. Each year on April 25, organizations around the world unite to celebrate success and highlight the need for continued investment and sustained political commitment for malaria prevention and control. On this occasion, PQM had an exhibition booth provided by USAID/Nigeria at the United States Embassy Abuja for this year's celebration. The exhibition showcased tools such as Minilab™ test kit, Truscan devices, and results generated using these tools during PMS. This opportunity was also used to raise awareness of the public about the importance of monitoring products to identify and remove substandard and falsified medicines circulating in local markets.

Capacity and skills in GMP were built and strengthened by the PQM GMP team through onsite training for 58 staff (20 females, 38 males) of two local manufacturers (Juhel and Pharmatex Pharmaceuticals). Topics covered include good documentation practices, good practices in production and quality control, sanitation and hygiene, pharmaceutical quality system, GMP requirements for personnel and premises, internal self-inspection/audit, HVAC system (modules 1-4), and managing non-conformance. Capacity and skills were also built in the area of QA/QC by PQM. Thirty-five staff (14 females, 21 males) of NAFDAC Agulu regional laboratory were trained on QMS. Topics covered include writing an effective SOP, good documentation practices, good practices for pharmaceutical quality control laboratories (GPPQCL), conducting internal audits, proficiency testing/inter-laboratory testing, management review meeting, and measurement uncertainty. Pre- and post-knowledge checks were administered to verify the levels of understanding; virtually everyone scored above 70% in the post-test, which was a great improvement from the initial average score of 20%.

PQM also participated in the quarterly National Procurement and Supply Chain Management–Technical Working Group meeting. In this meeting, PQM played a role of advocating for quality-assured medicines in supply chain system.

Senegal

I. Quarter 3 Highlights

PQM continues to work on the preparation of the FAA documents for the national quality control laboratory, Laboratoire National de Contrôle des Médicaments (LNCM) and DPM. The FAA will enable these two entities to establish a well-structured financial system within their entities and will ensure that activities are implemented according to the project description and reported against each milestone as requested by USAID.

The next step is to submit the whole FAA documents for PQM internal review, followed by final review by USAID Mission, and USAID Washington final approval. After this step, PQM will oversee the implementation of the FAA activities and submit reports on the achievements to USAID and key stakeholders.

II. Country Context

Since the beginning of its involvement in Senegal in 1979, USAID has supported development of the health system in order to help the country improve maternal and child health, fight infectious diseases, and make health services accessible to the Senegalese population at large. Malaria, in particular, remains a major cause of morbidity and mortality and is a high priority for government programming. Malaria is endemic throughout Senegal, and the entire population is at risk. The country has made significant progress against malaria and remains a leader in piloting and scaling up new recommendations and innovative strategies. In this context, USAID is expanding integrated health services countrywide through PMI.

In collaboration with the regulatory authority (DPM) in August 2015, PQM organized an Inter-Ministerial Workshop on Reinforcing Regulatory Actions Against Counterfeit and Substandard Medicines that included illicit markets. The main objective of the workshop was to develop a road map with an enforceable action plan detailing how to join efforts among DPM and enforcing entities. One of the recommendations included the organization of an operation called "Coup de Point" to eradicate at least one illicit market in Senegal in addition to the one in Dakar that had been removed in 2012. As of April 2016, PQM has done strategic planning on how to execute this activity jointly with inter-ministerial committee members. Delays in receiving PMI funds pushed PQM to execute this activity in late 2016.

As part of strengthening LNCM QC capacities, in 2014 PQM performed an audit of the laboratory that revealed the following problems: inadequate QMS; inability of skilled laboratory staff to maintain their roles and responsibilities in the laboratory due to university work commitments; lack of motivation, which led to staff members not fulfilling their assigned duties; insufficient technical capacity of the laboratory staff to conduct QC testing of medicines according to

compendial methods, a part of ISO 17025 and WHO PQ requirements; delays in procuring laboratory equipment; lack of equipment maintenance and services leading to non-calibrated analytical balances and improper use of verification and calibration tools; lack of regular employees, as opposed to contractual staff, which led to high turnover; periodic turnover or restructuring, which has hindered progress toward ISO 17025; and the need for five additional full-time, trained, qualified staff in the physical chemistry group.

Under the new LNCM leadership, some of the deficiencies listed above have already been addressed. The LNCM director restructured the organization and defined new roles and responsibilities for the staff. Following the interventions of the PMI advisor, the LNCM Director, and the MOH Director of Health, the status of two laboratory staff members was changed from contractual to full-time employees.

Presently, laboratory management seeks to pursue compliance with international standards and attain WHO PQ or ISO 17025:2005 accreditation.

West Bank and Gaza

I. Quarter 3 Highlights

Upon request, PQM submitted a work plan to address identified priority areas for the country to strengthen its QA system for medicines. The mission provided comments on the work plan, and PQM is revising the work plan accordingly. As requested by the mission, PQM also submitted a report describing activities, accomplishments, and remaining gaps in the QA system for medicines. This report was to close out the previous activities implemented by the PQM program.

Asia



Bangladesh

I. Quarter 3 Highlights

PQM's activities during the Q3 of FY 2017 were focused on the implementation and support of Objectives 2, 3, and 4 in the approved work plan. This quarter's highlights include the following:

- PQM actively contributed to the finalization of the Directorate General of Drug Administration's (DGDA) 5-Year Strategic Plan and FY17 Action Plan. The dissemination meeting for the Strategic Plan and the FY17 Action Plan was held on June 8 at the DGDA conference hall. The development of this action plan will serve to guide the agency on the key activities and milestones in progressing to a regulatory agency of international standard.
- PQM delivered two capacity-building trainings for staff at the National Control Laboratory (NCL) in Dhaka and the Drug Testing Laboratory (DTL) in Chittagong. Technical staff from USP Rockville facilitated these two trainings: (1) laboratory equipment calibration/performance, and (2) verification and preventive maintenance of HPLC, pH meter, and timers. These trainings were held during the period of May 21 and June 1 at NCL in Dhaka and are an important step in developing an internal calibration program for the laboratories.
- PQM supported an introductory workshop with the top 15 manufacturers at the DGDA conference hall on May 22 to introduce PQM GMP technical support and explain how WHO PQ for essential medicines is attained. The workshop was followed by visits to two manufacturers (Square Pharmaceuticals and Eskayef Pharmaceuticals Ltd.) on May 23–25. This will support the identification of manufacturers interested in working with the PQM technical team to produce priority MNCH and family planning products in Bangladesh and thereby contribute to increasing the cost-effective supply of essential medicines.
- PQM assisted DGDA and completed work on WHO's nine functions for self-assessment in June. Among the nine functions, PQM local staff led four functions of the assessment: laboratory access and testing, NRA lot release, clinical trial's oversight, and regulatory inspection system. PQM Bangladesh is now preparing the relevant technical and guidance documents, as well as drafting the legal provisions for inclusion in the Bangladesh Drug Act. This WHO self-assessment is a complementary step in moving DGDA to a regulatory agency of international standard.
- PQM worked closely with DGDA and stakeholders to finalize the DGDA organogram, which in June was submitted to the Secretary of the Ministry of Health and Family Welfare for approval.

PQM also attended the USAID Implementing Partners meeting on June 8 and presented PQM program updates and progress to the meeting participants.

II. Country Context

PQM's goal in Bangladesh is to strengthen the institutional capacity for sustainable regulatory and QA/QC systems that meet international standards. To achieve this goal, PQM has developed strategic objectives based on a PQM gap analysis conducted in April–May 2016 and discussions and consultations with the USAID country mission, DGDA, SIAPS, and other relevant partners/stakeholders.

PQM is partnering with SIAPS and WHO to strengthen selected DGDA regulatory functions in line with extensive discussions and consultations between the two programs teams and in alignment with guidance from the Agreement Officer's Representative and the USAID Country Mission. For those areas in Objectives 3 and (especially) 4 where SIAPS has been working, including product registration (dossier format and registration software), GMP training, and PMS, PQM will provide technical support to SIAPS, which takes a leading role in providing technical assistance to DGDA. In consultation with USAID, PQM and SIAPS will continue to work on transitioning these areas of work to PQM before the closeout of the SIAPS program in March 2018. For those areas where SIAPS does not provide assistance, PQM will provide direct technical assistance in collaboration with relevant partner(s) to DGDA and other relevant clients.

III. Quarter 3 Progress by Objective

Objective 1 – Conduct a well-designed gap analysis on regulatory related to the quality assurance and quality control systems, develop FY17 work plan, and take part in the peer review work plan meeting

Work toward this objective was completed in FY 2016 Q4.

Objective 2 – PQM to provide direct support to DGDA National Control Lab (NCL) in Dhaka and Drug Testing Lab (DTC) in Chittagong toward achieving international ISO/IEC 17025:2005 accreditation or WHO PQ

In terms of laboratory capacity-building, PQM has been providing technical guidance to NCL in the following areas to strengthen its QMS and move the laboratory toward ISO 17025 accreditation:

- PQM worked alongside NCL management and technical staff to follow up on its progress in terms of the CAPA against the findings from the gap analysis and recommendations provided by PQM.
 - A recent inspection by the Bangladesh Accreditation Board identified 39 CAPA items with a defined completion timeline. Those items that did not require procurement or external partner support were to be completed by May 2017. Evidence of progress or completion was confirmed for 28 CAPAs.
 - The Bangladesh Accreditation Board (BAB) CAPA progress and completion reports were submitted in May 2017 by NCL management. PQM support enabled the CAPAs to be completed during April and May 2017, which helped NCL with timely submission of responses to BAB.
- PQM worked closely with NCL to develop and review critical SOPs to improve the traceability of work processes, QC, and instrument life cycle. The 15 completed SOPs address the following areas: management review, qualification, calibration and preventive maintenance of laboratory equipment, control of documented procedure, reagent and consumable materials (including inventory list), non-conformance of analytical data, disposition/obsolete of quality of document, SOP for SOP, logbook management, vendor qualification, reference standard management, archive management, training, internal audit, and CAPA management.
- In addition to SOPs, QMS documents were also prepared in June to support improved operations of the laboratory, including procurement of 100 laboratory notebooks, training needs assessment, deviation report form, change control report form, logbook front page label format, template for internal audit report, internal audit register, internal audit schedule template, management review report format, distribution record form, vendor qualification questionnaire, 12 job descriptions of NCL personnel, preparation of laboratory equipment master data for NCL, and Health and Safety Executive gaps document.
- GLP follow-up actions in this quarter included labeling of laboratory equipment, solutions, reagents, and apparatus, personal protective equipment (PPE) use, and glassware cleaning. In addition, for safety practices, a meeting was held with the NCL engineer and four vendors to assess the laboratory requirement for a fire extinguisher and smoke detectors. Lastly, an initial assessment was carried out in June, and cleaning services will commence in the next quarter. All of this work in document preparation and GLP serves to position the laboratory for ISO 17025 accreditation.
- As noted in the highlights above, PQM provided two trainings on laboratory equipment for both NCL and DTL staff (20 participants in total). These trainings will improve internal calibration and maintenance capacity, ensuring that equipment is properly calibrated to test products and with less reliance on external service providers for this essential lab function, leading to a cost-savings estimated as high as \$17,000 annually.
- In May, a list of equipment/instruments needed by NCL was finalized. This will serve as the list to explore potential complimentary sources of funding to support procurement. Currently this lack of equipment/instruments is a bottleneck in ensuring the proper testing of medicines in the laboratory.



Hands-on training on calibration of equipment with the NCL/DTL team by PQM staff, Shawn Hernandez

Objective 3 – PQM collaborates with SIAPS to improve the GMP compliance of local pharmaceutical manufacturers toward WHO Pre-qualification Program for priority MCH/FP products

In order to increase access to MNCH commodities, PQM, in partnership with DGDA and the Bangladesh Association of Pharmaceutical Industry, conducted a WHO PQ workshop for 15 manufacturers in May to assess the manufacturers' interest in the WHO PQ/U.S. FDA/EU quality assurance and approval pathways. This initiative is to build capacity in the local manufacturers to manufacture quality-assured, low-cost MNCH products (like oxytocin) to increase supply of essential medicines. Following this assessment, PQM identified two pharmaceutical manufacturers—Square Pharmaceuticals and Eskayef Pharmaceuticals—with a strong interest in participating in WHO PQ and exporting their products to an SRA market. As a result, these two manufacturers have agreed to work with PQM to strengthen their current GMP and improve the overall quality of their products to be manufactured and distributed in Bangladesh.

Objective 4 – PQM to provide technical support to SIAPS in strengthening the DGDA's regulatory functions

There were several activities implemented in order to address DGDA regulatory capacity, including strategic planning, human resources, international standards, and improved PMS.

- As mentioned in the highlight section, PQM was instrumental in working with stakeholders to develop and finalize DGDA's 5-Year Strategic Plan (2017–2021) and FY17 Action Plan. PQM met with SIAPS and other stakeholders on June 8 as the means to obtain final inputs on the two plans. These plans will dictate DGDA's primary activities and support its development in terms of ensuring quality-assured medicines in the market.
- PQM helped lead the review and provide pragmatic inputs on the redesign of DGDA's organogram to reflect its mission and strategic vision, as well as to gradually align it with the international standard of a fully functional regulatory agency. In addition, PQM completed the expertise and skills mapping of key NCL staff positions and reviewed job descriptions to ensure quality human resources at the laboratory. The organogram has been submitted to the Secretary of the Ministry of Health and Family Welfare for approval and is central in building the human resource needs of the agency in key functional areas.



DGDA and PQM observe the organogram being finalized

- PQM worked with WHO to prepare DGDA's self-assessment; the PQM field team was assigned to lead the four functional areas among the nine WHO recommended functions: (1) laboratory access and testing, (2) NRA lot release, (3) clinical trial oversight, and (4) regulatory inspection system. This self-assessment will lend to the action needed to move the agency to the WHO international standard.
- One of the bottlenecks that NCL is facing is the lack of some critical laboratory equipment, including (but not limited to) an HPLC system with auto-sampler, dissolution tester, Karl Fischer, friability tester, disintegration tester, analytical microbalance, ultraviolet-visible (UV-Vis) spectrophotometer, vacuum oven, reference weight, and mechanical calibration kit. In light of these deficiencies, PQM worked with DGDA and NCL management to develop a priority list of equipment/instruments that need to be acquired. PQM is exploring possible sources of funds for their purchase, installation, and operationalization in the laboratory. By acquiring these equipment/instruments, NCL will improve its testing capability and thus ensure products meet QA standards.

Objective 5 – Increase visibility and relevance of QA/QC in support to National Health Programs

PQM staff have met and initiated discussions to implement one activity in Q4 under Objective 5. The PQM Technical Manager will first work with DGDA and stakeholders to develop an overarching policy and then have DGDA conduct a workshop with the national priority health programs to explain the purpose for the policy, as well as to obtain their inputs. A sound national QA/QC policy will assure that medicines obtained through the priority health programs meet with DGDA's standards for product distribution among the general public.

Training	Date	Lab Designation	Gender	Total Trained
QMS; Good Pharmaceutical Practices; Hygiene, Protection and Safety; Good Document Practices	Feb 28 – Mar 12	18 NCL 2 DTL Chittagong	16 Male 4 Female	20
Pharmaceutical Analytical Techniques	Mar 10 – Mar 20	24 NCL 3 DTL Chittagong	17 Male 10 Female	27
Calibration of Essential Equipment	May 21 – May 31	17 NCL 3 DTL Chittagong	15 Male 5 Female	20
Total to Date			48 Male 19 Female	67

IV. Additional Program and Operational Activities

PQM is actively establishing program operations locally in Bangladesh. This includes the following activities:

- Dr. Syed Umar Khyam joined the field office team on May 28 as the Chief of Party to manage the PQM Bangladesh project with the support of the country team and guidance and oversight from USP Rockville. In addition, the QA/QC Specialist and the QMS Specialist were on-boarded in the month of April.
- PQM Bangladesh met with the USAID Mission on June 1 to provide a program update and to discuss work plan implementation.
- Recruitment is proceeding for the following positions: Regulatory Affairs Specialist, Senior Finance Office, and Procurement and Logistics Officer.
- Local legal counsel has been engaged to support the USP-PQM registration process. Registration documents were prepared and submitted to the NGO Affairs Bureau.
- A professional employment organization has been hired to provide national staffing and administer payroll, benefits, lease of office space, and monthly payments services.
- Temporary office spaces that can accommodate five PQM local team members were secured at DGDA and NCL, and their fittings/configurations were completed. In addition, the main office space has been leased at Gulshan-2 in Dhaka City, and procurement of furniture and minor renovation work is ongoing.
- The Chief of Party and the Senior Operation Manager visited the Rockville office to gain guidance and support, as well as to strengthen the interaction and build a strong relationship between the Rockville and Bangladesh offices.

PQM also updated the Performance Monitoring Plan for Bangladesh, with compilation of the FY 2016 baseline data in May 2017. PQM will monitor its progress against the targets by collecting data throughout program implementation to demonstrate both progress and impact.

V. Key Challenges

- The recruitment of four approved positions has been a challenging endeavor, given the difficulty in finding suitable candidates who meet the program expectations. The recruitment process of the new staff will continue in Q4.
- The program has had difficulty with customs clearance and duties in Bangladesh; it has been very challenging to ship supplies (essential analytical reference standards, chemicals, training supplies, and reference materials) to Bangladesh due to complicated processes and procedures in customs clearance, as well as the costs incurred in shipping them from overseas.
- Coaching and mentoring local technical staff/consultants to be trainers/technical providers poses some challenges. PQM has implemented a plan to ensure that the national technical staff develop good working relations with the project partners and thereby deliver the technical assistance successfully.
- The tax exemption from the Bangladesh National Board of Revenue for reference substances, Minilab™ kits and other supplies to support the program requires a long procedural time.
- Field office registration has been progressing, but the process is time consuming and complicated; legal counsel has been working to facilitate the process.
- Safety and security remain concerns for PQM technical staff while providing technical assistance in Bangladesh. The USP Global Security Director is closely monitoring the security situation.

Burma

I. Quarter 3 Highlights

The goal of the PQM program in Burma is to provide technical assistance to the Department of Food and Drug Administration (DFDA) in strengthening its overall QA systems. More specifically, the goal is to build DFDA's capacity to ensure the quality of antimalarials available in the country, which will, in turn, contribute to Burma's efforts to eliminate malaria by 2030. This quarter, PQM focused on two priority activities:

- PQM provided technical assistance to the DFDA on a design of new laboratory construction project to cope for the rising need of analytical testing capacity to detect substandard and falsified medicines on the market. PQM recommended the incorporation of a well-designed analytical work flow and proper systems (ventilation, waste management, and gas and water purification systems) in order to comply with the international requirements for analytical testing laboratories.
- PQM worked with the DFDA laboratory (Nay Pyi Taw) to prepare for an ISO 17025 reaccreditation assessment by ANAB.

II. Country Context

Malaria has been one of the key public health burdens in Burma, and the spread of drug-resistant malaria poses a major challenge to the country, especially in the border areas. The combined effort of international donors and the country has led to significant reduction in malaria morbidity and mortality in Burma. However, the incidence of poor-quality medicines in the country imposes a substantial risk to efforts to contain resistant malaria. Furthermore, poor-quality medicines not only contribute to treatment failure but also waste scarce resources to fight the disease.

DFDA is responsible for tackling poor-quality medicines in Burma. As DFDA is undergoing rapid expansion with field offices and laboratories being opened in every state/division and region of Burma, PQM's capacity-building technical assistance to DFDA is highly useful to the country. DFDA is planning to open four new laboratories in four states and regions to cope with the increasing demand for analytical QC testing. PQM's technical assistance to the Nay Pyi Taw laboratory toward ISO 17025 accreditation is gaining momentum. Once accredited, this laboratory will serve as the reference laboratory in Burma and will be the key technical resource to build the capacity of other regional laboratories using its scientists and the knowledge gained from PQM.

In order to modernize DFDA and develop strong QA systems for Burma, alongside with developing laboratory capacity, other key functions—such as product evaluation and registration, licensing, supply chain inspection, and PMS systems—need to be strengthened. Pharmaceutical legislation, such as the National Drug Policy and National Drug Law, needs to be reviewed and revised. In order to use the available resources efficiently, PQM is working closely with DFDA to identify gaps in the current regulatory framework and system and tailor technical assistance to specific areas of need. PQM's technical assistance to build DFDA's capacity will result in increased availability of quality medicines in the country. This is expected to contribute toward achieving the National Malaria Control Program objectives to eliminate malaria by 2030.

II. Quarter 3 Progress by Objective

Objective 1 – Strengthen the capacity of DFDA laboratories in Nay Pyi Taw and Mandalay, in preparation for ISO 17025 accreditation

DFDA Burma is building two new laboratories in Nay Pyi Taw and Mandalay. PQM is providing assistance in the technical configuration and layout of the new laboratories. PQM, working with ARC2LAB, (an architectural firm specialized in laboratory design and planning based in Munich, Germany) developed technical and structure design specifications based on requirements of ISO 17025:2005 accreditation of testing laboratories. PQM's recommendations for the new laboratories considered three important principles of efficient laboratory system development, outlined below:

- **Sustainability:** Sustainable design strategies, including the use of daylighting, energy-efficient building systems, and sustainable materials, will assist in reducing environmental impact while producing a building that functions longer than its normal life expectancy.
- **Open environment:** There are many advantages to an open environment, where contiguous modules form a generic zone. Open spaces and projects are less costly to construct due to fewer walls and material interfaces. They are inherently safer, providing occupants with a higher level of visual and audible knowledge of a potential threat or incident. Open projects are more easily assigned and reconfigured for people and processes, leading to shared opportunities for a variety of functions. More important is the potential for collaboration and interdisciplinary activities that occur in the open environment.
- **Modular design:** The first and most fundamental concept of planning is the application of modular design. This approach maintains the highest level of flexibility by allowing the functional requirements of the space to influence the form - to design from the inside out. The modular approach provides interchangeability of spaces, as well as opportunities for increased efficiency.

DFDA reviewed the concept design and made some adaptations to the current floor plans. The construction process is ongoing, with a target date for completion at the end of August 2017. Drawing on lessons learned from Cambodia, PQM proposed to DFDA to establish a construction oversight committee to ensure that the laboratory construction proceeds in accordance with PQM's guidance on technical requirements.

PQM continues to provide technical assistance on QMS-related activities to DFDA Nay Pyi Taw laboratory. DFDA Nay Pyi Taw laboratory is due for annual reassessment of its ISO 17025 accreditation by ANAB in December 2017. PQM's commitment to strengthen QMS in Burma continues with the revisions and updates to the laboratories' operational guidelines, quality manual, and support of DFDA's internal audits ongoing through July to prepare the laboratory for a management review.

Cambodia

I. Quarter 3 Highlights

PQM assisted the Global Fund and the National Health Products Quality Control Center (NHQC) in Q3 to review the TOR for a service provider to calibrate critical equipment at NHQC.

Following this review and recommendations, the Global Fund and NHQC selected Teang Sina Import-Export Co. Ltd. (TSC) to provide preventive maintenance of key equipment in the laboratory. The Calibration Laboratory Technical Center of Standards Metrology and Quality from Vietnam was selected to provide the calibration services to NHQC; the calibration process will take place the first week of July in accordance with the TOR schedule.

The PQM program in Cambodia is at its final stage of closing. All FY 2017 activities, supported by the existing pipeline funds from FY 2016, have been implemented. The ongoing closeout process is targeted to be completed at the end of next quarter, with the final program closeout report to be submitted to USAID/Cambodia, including a transition plan that will be co-developed and handed over to the Cambodia stakeholders, such as the Department for Drug and Food, NHQC, and other appropriate partners.

Indonesia

I. Quarter 3 Highlights

PQM Indonesia's highlights for Q3 include the following:

- A high-level National Agency for Drug and Food Control (BPOM) delegation visit to USP Rockville, led by Dr. Ir. Penny Kusumastuti Lukito, Head of BPOM, provided a unique opportunity to increase cooperation between USP and BPOM.
- The Technical Arrangement between USAID and BPOM was signed, creating a legal framework within which PQM can operate under the overall Individual Arrangement umbrella agreement between USAID, the MOH, and the Ministry of Finance. The ratified Technical Arrangement will serve to facilitate PQM's work in Indonesia through the end of the project.
- An internal audit and data integrity training was conducted at the national QC laboratory (PTBB) of BPOM in preparation for submission of the laboratory information file (LIF) to WHO, as part of preparation toward prequalification.
- A stakeholders' planning workshop was convened in preparation for the upcoming 11-province Joint Sampling and Testing exercise between MOH and BPOM to initiate implementation of the MOH regulation Permenkes 75/2016, a new framework that allows for interagency information sharing.
- A local medicines manufacturer, Sanbe Farma/Caprifarmindo, obtained WHO inspections conclusions that both penicillin plant and the sterile preparations plant are considered to be operating at an acceptable level of compliance with WHO GMP for amoxicillin 250mg dispersible tablet and oxytocin injection, respectively. The two facilities received WHO Public Inspection Reports (WHO PIRs) during Q3. Sanbe Farma oxytocin injection for injection 10IU/mL was prequalified and listed on the WHO PQ website on June 30, 2017.

II. Country Context

PQM receives field support funding through TB and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) funding streams from the USAID Indonesia Mission Office of Health.

Since 2011, PQM has conducted activities to strengthen the QA/QC systems of medicines to treat TB and HIV/AIDS in Indonesia (with PEPFAR/HIV funding starting in FY 2014). PQM focused first on supporting selected local TB medicines manufacturers to strengthen their QA/QC systems and GMP toward achieving WHO PQ status. Beginning in 2013, PQM expanded its activities to build the capacity of BPOM, additional private manufacturers of TB and HIV medicines, and select local CRO for BE studies to improve their QA/QC systems.

PQM's overall vision and strategic engagement with Indonesia is to support all aspects of medicines QA from the point of manufacture or import, through the supply chain, down to the service delivery point. To this end, PQM has designed a comprehensive approach for engaging directly with manufacturers, regulators, government disease programs, supply chain specialists and warehouses, CROs, and official medicines QC laboratories across the country. This holistic approach ensures that all aspects of medicines quality is addressed, with the long-term aim of systematically developing robust and reliable QA/QC systems, based on international standards, for medicines in Indonesia.

III. Quarter 3 Progress by Objective

Objective 1 – To strengthen Indonesia's medicines quality assurance system by supporting the MOH and BPOM regulatory, inspection, post-marketing surveillance, falsification investigations, and quality control (of national and provincial laboratories) functions with a focus on TB and essential medicines to achieve international standards of practice

Collaboration with Global Funds for AIDS, TB, and Malaria

PQM Indonesia continued to support procurement activities of \$2 million USD (through a direct Global Fund contract) in equipment for 11 provincial BPOM QC laboratories. The \$2 million direct funds from GF further attest to the continuing work of PQM in Indonesia to build capacity and increase awareness on issues of QC of medicines. Through this grant, PQM is further supporting the capacity-building of 11 provincial BPOM institutions to work together to monitor the quality of medicines, focusing on TB and HIV, in the government medicines supply chain.

PQM convened a GF-funded planning workshop with the National TB Program and 11 provincial health offices and laboratories on the "Joint Sampling and Testing of TB and HIV Medicines" as part of the GF contract. This activity involved identifying the medicines to be sampled and tested, as well as the provincial and district warehouses from which samples would be taken. This is a joint activity between MOH and BPOM to encourage rapid implementation of the Permenkes 75/2016 regulation on ensuring MQC activities in government-sector programs. With USAID support, PQM will provide oversight, planning and logistics, technical assistance on sampling and testing, and needed reference standards for testing. Reagents, consumables, HPLC columns, and other equipment are provided by GF, as well as the funding for the sampling activity. Sampling will take place during Q4 FY 2017 at the provincial sites for Joint Sampling and Testing collaborative exercise between BPOM, Balai Besar POM (BBPOM), and MOH (provincial and district).

The provincial sites for the Joint Sampling and Testing collaborative exercise between BPOM, BBPOM, and MOH (provincial and district) are North Sumatra, Daerah Khusus Ibukota (DKI) Jakarta, West Java, East Java, Bali, East Nusa Tenggara, North Maluku, North Sulawesi, South Kalimantan, Papua, and West Papua. During Q4, following procurements and further planning exercises, partners will finalize the sampling, testing, and data dissemination planning.

A key outcome of these activities for joint sampling is to successfully implement the Permenkes 75/2016 regulation on QC of medicines in the government sector, including dissemination of quality testing data to relevant MOH partners in a timely manner. This is a crucial step toward a robust QC system in Indonesia.

PQM also oversaw the installation and operation qualification of the Dionex ion chromatography instruments at the National Reference Standards Laboratory and Jayapura. These instruments were procured as part of the GF grant to equip provincial QC laboratories with state-of-the-art instruments for analysis and detection of falsified second-line anti-TB medicines. As part of the installation and qualification, PQM conducted a week-long training workshop in both laboratories on the proper use of the ion chromatography instrument to test kanamycin, streptomycin, and amikacin according to international best practices. This activity was part of a collaborative exercise between the National TB Program (MOH), Global Fund, USAID, PQM, and BPOM.

With Global Fund financial support, PQM is procuring roughly \$200,000 USD worth of laboratory software for the PTBB lab equipment. This software upgrade will enhance the overall quality of testing services while maintaining the data integrity requirement to protect the confidentiality of patients' information.

Supporting WHO Prequalification

PQM continues to support PTBB to develop and review LIF documentation in preparation for WHO PQ of the national QC laboratory. In this effort, PQM had worked with laboratory management and staff to address critical areas of document control, SOPs, process mapping, and good document practices to complete an LIF. It is anticipated that the laboratory will be able to submit the LIF to WHO by the end of the third quarter to allow for inspection and accreditation of the laboratory by WHO.

As part of WHO PQ, the laboratory has received a reaccreditation by the local accreditation body, the Indonesian National Accreditation Committee (KAN), for its ISO 17025 accreditation status. The KAN certificate is a required supporting document for LIF submission to WHO. The current KAN accreditation was product-based, which limited the laboratory's capacity to conduct quality testing of products that were not accredited. It is in this light that PQM is working with the laboratory to change from product-based accreditation to method-based accreditation, administered by WHO, which allows for all products to be analyzed using similar methods/techniques.

Support to Provincial Laboratories

In line with the goal of WHO PQ for PTBB and to build the capacity of priority provincial laboratories, PQM conducted training on internal auditing and data integrity for PTBB Division, National Reference Standards Laboratory, and provincial BBPOM Jakarta DKI staff. The training provided participants with an opportunity to improve their understanding of data integrity and internal auditing in both theory and application. The training enhanced the laboratory's capacity to identify data integrity issues and perform self-assessment of its quality and technical operations. An understanding of how to develop an internal audit program, perform internal auditing, gather objective evidence during audits, write non-conformance work, and report on internal audit activities was developed.

Similarly, PQM continues to support four provincial BBPOM laboratories: Papua, West Papua, Bali, and Jakarta DKI, to build stronger sustainable capacity in QA of medicines. Although PQM is still active in all provincial BPOM labs, in a subtle way through its support to the national laboratory and collaborative efforts with MOH, the program will actively support these four key provincial laboratories to focus on building essential capacity for ongoing testing of TB and HIV medicines. PQM provides training, equipment, calibration services, QMS capacity-building (e.g., audits, implementation of corrective actions), and other activities to these laboratories.

To effectively monitor the progress of support to these laboratories, an implementation plan was signed between PQM and the four provincial laboratories with the aim of attaining WHO PQ by the end of 2018. Attaining WHO PQ will enable these labs to serve as an important regional reference hub for QC testing and also act as regional collaboration centers with neighboring countries (Timor-Leste and potentially Papua New Guinea).

Lastly, PQM facilitated a session on utilizing rapid screening technologies, such as the Minilab™, as part of a robust national PMS system at a national conference on "Scientific Seminar and Dissemination of Research Result by Research Center for Drug and Food of Badan POM." This also set the stage for planning on upcoming pilot projects on training and implementing of Minilabs™ to support QC testing and PMS in Jakarta DKI and Papua provinces planned for Q4.

Upcoming activities planned for Q4 include the following:

- Training of trainers and national technical training for provincial QC laboratories at the PTBB division for the entire BPOM system (national).
- Follow-up planning meeting for GF-sponsored 11 province joint sampling and testing exercise for MOH and BPOM.
- Planning on antiretroviral sampling and testing in five provincial sites.
- Internal auditing and data integrity and follow-up visit toward WHO PQ for BBPOM Bali/Denpasar and Papua/Jayapura.
- Continued technical assistance for LIF submission to WHO for PQ of the BPOM PTBB laboratory (submission during Q4).
- Joint Sampling and Testing MOH & BPOM in 11 provinces.
- Training on gas chromatography (GC) and infrared (IR) for West Papua and Bali.
- Minilab™ pilot program training for Jakarta DKI and Papua.

Objective 2 – To increase the local supply of quality-assured TB medicines in Indonesia by providing technical assistance to the BPOM Inspectorate, selected local pharmaceutical manufacturers and contract research organizations to achieve international standards, including GMP and WHO prequalification

In partnership with local manufacturers, PQM continued to make significant progress toward submitting two levofloxacin 500 mg tablet product dossiers to WHO for PQ by the end of 2017. PQM has intensified its GMP support to four local manufacturers with a focus on TB medicines: Sanbe Farma/ Caprifarmindo (privately owned), Kalbe Farma (privately owned), Phapros Tbk (parastatal/public), and Kimia Farma (parastatal/public).

Sanbe Farma/Caprifarmindo has completed most activities in preparation for its product dossier submission to WHO for PQ. These activities include CAPA closure, formulation optimization, comparative dissolution, receipt of the drug master file and letter of access from Zhejiang Langhua Pharmaceutical Co Ltd. for API, validation cleaning, and method validation. There were significant delays in the verification of residual solvents due to both technical and analyst issues with the GC method. PQM spent considerable time assisting in the training and troubleshooting of these issues, and anticipates they will be resolved.

During Q4, Caprifarmindo will continue residual solvent testing, stability studies. It will also continue to produce a pilot scale batch and all associated activities with the intention of submitting the product dossier to PQM for review in August. The current aim is for Caprifarmindo to submit its product dossier for levofloxacin to WHO by December 2017.

Sanbe Farma/Caprifarmindo achieved WHO prequalification for oxytocin injection and ERP approval for amoxicillin 250mg dispersible tablets, to be procured by UNICEF. PQM was essential in assisting to building the overall QC systems for Sanbe Farma/Caprifarmindo, as well as providing GMP support, which helped allow the company to reach WHO PQ and ERP approval for the products, respectively. These two priority products will lead to an increased supply of quality-assured products for maternal and child health on the global market.

Kalbe Farma also made considerable progress toward finalizing its product dossier for levofloxacin 500 mg tablets and is currently in the process of conducting stability studies (real time and accelerated) for its laboratory scale product. In Q3, the PQM GMP team conducted an onsite evaluation product dossier review and assessment to assist in the final compilation of the product dossier prior to submission to WHO by the end of August. Kalbe Farma had demonstrated problems in the assay analysis for its product and was previously unable to identify a root cause. After a considerable amount of time, it chose to reformulate, following the comparator's formulation instead, with the same results of an unacceptable assay result. PQM provided hands-on, step-by-step guidance, and Kalbe Farma was then able to meet the required specification for the levofloxacin monograph for the assay for content. Kalbe Farma also went through a process of deciding to do in-house GC testing instead of contracting to a third party, thus also resulting in some delays.

PQM trained 46 analysts from Kimia Pharma and Phapros Pharmaceutical on GDP as the two manufacturing companies prepare for WHO PQ of TB medicines.

Phapros is working with the National TB Program (NTP) to change its current formulation in response to new treatment guidelines issues by NTP, from daily dosing of two fixed-dose combination (FDC) isoniazid/rifampicin to intermittent dosing. The training provided by PQM prepared the privately owned manufacturing company to comply with the stringent requirement of WHO PQ. It is anticipated that, with the training received by the company, the staff will be able to prepare essential documents to achieve WHO certification.

Objective 3 – To enhance the technical capacity of the government of Indonesia to develop and implement inter-agency (MOH, BPOM, donors, professional associations, other stakeholders) policies and procedures for medicines quality assurance (coordination, advocacy, and developing appropriate public awareness tools), and to support the National TB Program and FARMALKES to ensure quality and production is in line with procurement policy/new treatment guidelines

The most significant programmatic achievement in Q3 was the official signing of the technical agreement between USAID and BPOM, which formalizes the relationship between the United States and the government of Indonesia for PQM to continue providing technical support to MOH and other government agencies. This agreement will positively affect the way PQM works in the country to support the ongoing challenge of legal compliance with the government of Indonesia.

During Q3, PQM was active in developing the QA/QC aspects of the NTP and National AIDS Program (NAP) funding request to the GF for the 2018–2020 funding cycle. PQM was involved with the country coordinating mechanism and TWGs, contributing to, for example, activities, narrative, and budgets. As a result, QC activities are included as part of

the next GF grant, and PQM will help to provide needed technical assistance to the government as requested. The GF grants are an important component of the overall strategy in building the QA/QC system using multiple donors and resources, including USAID (via PQM), GF, and the government of Indonesia's annual budgets. Additionally, the strategic action plans of the government, as well as the newly minted Permenkes 75/2016, ensures that medicines quality receives priority, including issues such as availability and supply chain management.

Through years of advocacy, PQM has helped the government to better design and implement medicines quality policy, as well as ensure an adequate budget to meet the needs of both the MOH programs and BPOM. During the next 3 years, there will be ample opportunity to refine and contribute to implementing medicines quality assurance, through support for scaling up sampling and testing of program medicines during PMS, as well as working with MOH and manufacturers on the availability of appropriate formulations and regimens for their treatment programs. In the context of Universal Health Care (JKN), PQM will play an important role as the government increases its procurement of essential medicines to support the roll-out and scale-up of its disease control programs under the JKN by 2019.

Sampling and Testing

A planning workshop was held with interested stakeholders to design sampling and testing in 11 provinces using a GF grant through the NTP. PQM initiated this activity, including procuring \$2 million USD of equipment and reagents for the 11 BBPOM laboratories where sampling and testing will take place. PQM convened the planning meeting in order to address potential delays in obtaining government approvals and/or logistics involved in reaching the 11 provincial laboratories. PQM was also involved in several planning meetings to coordinate with key stakeholders for upcoming activities, including the Stakeholders Forum to discuss revisions of the national treatment guidelines for TB. These stakeholders are MOH (including disease control programs and the Farmalkes procurement directorate), local manufacturers and importers, BPOM (multiple directorates), representatives from the Ministry of Finance, state-owned enterprises, WHO, and multilateral donors. This important forum will help the government ensure adequate lead time on new medicines to be registered/imported, as well as changes in the formulation for existing medicines to meet the needs of the changing AIDS Health Care Policy (P2PML) policies.

PQM has also been working on coordinating official government requests between MOH and BPOM on testing ARV medicines. PQM will help facilitate sampling activities in five provinces with antiretroviral (ARV) samples to be tested by the PTBB laboratory of BPOM in Jakarta. As part of this arrangement, GF will pay in advance for testing, PQM will provide reference standards and technical assistance, and data will be shared between partners to ensure adequate follow-up or regulatory enforcement as needed.

In addition, in Q3 PQM also worked with BPOM and NTP on facilitating registration issues for delaminid and bedaquiline as part of ongoing pilot projects for NTP. These products were initially slated for "fast track" registration through BPOM as per request from the NTP program (for new medicines, registration within 100 days after the program requests it). However, registration has been delayed for a number of years, and WHO had previously sent inquiries to BPOM without response. PQM worked hand-in-hand with BPOM and NTP to respond to WHO's questionnaires and queries to update them on the registration status. BPOM then requested further clinical evidence in support of the registration, including requesting Phase III and Phase IV clinical data from WHO for further consideration. At present, this issue is still pending.

Upcoming activities in Q4 include:

- Multi-Stakeholder Forum to Ensure Availability of Quality-Assured TB Medicines.
- Joint Sampling and Testing of TB and HIV medicines in 11 Provinces (GF, MOH, BPOM, PQM).
- Sampling and testing of ARVs from five provinces under special request by NAP.
- Support to Indonesian Pharmacists' Association (IAI) for development of SOPs on implementation of good pharmacy practices at 34 hospitals in West Java.
- IAI Annual Scientific Symposium.

Objective 4 – To support the overall management and functions of the PQM Indonesia field office, including reporting, monitoring and evaluation, logistics, and staff development

In an effort to strengthen overall PQM program management and operations on the ground, the following key actions were taken:

- The new USP Indonesia office fit-out was well underway in Q3, with some unanticipated delays. All procurements were underway, contracts signed, construction in process, information technology equipment being installed, and furniture being delivered. PQM anticipates a July 25 move-in date for the new office.

- During Q3, the Communications Specialist resigned to pursue graduate studies, significantly affecting office operations. Recruitment is in process for a Project Coordinator, M&E Specialist, and a QMS Specialist.
- In view of better planning and developing the FY 2018 work plan with buy-in from the national partners, PQM convened a stakeholders' workshop in preparation of FY 2018 work plan development, including representatives from the NTP, NAP, Farmalkes, BPOM, National Medicines Quality Control Laboratories of BPOM (PPOMN), IAI, CROs, and manufacturers. This effective and collaborative workshop helped to lay important groundwork for proposed activities under FY 2018.
- PQM hired the former Head of BPOM, Dra. Kustantinah, as a Senior Technical Advisor Consultant to help with several ongoing activities and to lead high-level advocacy within MOH and BPOM.
- Following the signing of the technical agreement between USAID and BPOM, PQM can now proceed to implement the VAT refund strategy as guided by USAID. In addition, the Chief of Party has successfully received both residency permit (KITAS) and work permit (IMTA).

IV. Key Challenges

- The late signing of the USAID-BPOM technical agreement had delayed the implementation of some activities under the approved PQM work plan, thereby impacting the timeline for deliverables. PQM is intensifying its effort to alleviate the impact on the timeline during Q4.
- Significant additional work burdens (in addition to routine work) were placed on the operations team since moving to a new office requires much procurement, planning, designing, and logistics support. During Q3, the PQM Indonesia office still faced considerable challenges in identifying viable and technically competent candidates to fill open positions, some of which have been open for a year and a half already with no suitable candidates. The current staff remains overstretched with FY 2016 and FY 2017 activities, Global Fund procurement, and ongoing and increasing reporting requirements by the government of Indonesia, donors, and others.
- Technically, there have been some analytical method issues at both Kalbe and Sanbe manufacturers that have delayed the dossier submission timelines. In addition, delays in the awarding of the certificate of reaccreditation for ISO 17025 for the PTBB laboratory by KAN resulted in delayed submission of the LIF to WHO for PQ.

Pakistan

I. Quarter 3 Highlights

PQM has been providing technical support to four local manufacturers to improve and attain compliance with current GMP for chlorhexidine (CHX) 7.1% gel products. As a result of this support, two CHX 7.1% gel products were approved for registration by the Drug Registration Board during the second quarter, and with PQM's continued support, two additional CHX 7.1% gel products were registered in the third quarter. An important step of the recommendation for price fixation was completed with the Drug Pricing Committee's recommended pricing of CHX 7.1% gel to the Federal Government. Once the CHX 7.1% gel products are made available in the marketplace by the four local manufacturers (M/s Atco Laboratories, M/s Aspin Pharmaceuticals, M/s Akhai Pharmaceutical, and Zafa Laboratories), they will not only improve access to this critical medicine for the people of Pakistan, but also lead to an expected reduction in neonatal mortality due to sepsis. These manufacturers may also be able to export the CHX 7.1% gel product to neighboring countries in the region. This in turn may contribute to global reduction in neonatal mortality due to umbilical cord infections.

PQM expanded its technical support to the pharmaceutical industry in Pakistan with the addition of two anti-TB manufacturers (M/s Schazoo Zaka and M/s Pacific Pharma). Current GMP assessment visits to these two manufacturers were conducted this quarter to review compliance with WHO cGMP requirements. PQM's technical support includes the development of a CAPA implementation plan, road mapping the prequalification process, and providing support to address identified non-compliances.

PQM continues to support the Drug Regulatory Authority of Pakistan's (DRAP's) efforts to move toward international standards of regulations. This quarter, after completing the assessment of the regulatory registration process, and DRAP's decision to adopt the Common Technical Document (CTD) as the registration application submission format, PQM supported the Division of Pharmaceutical Evaluation & Registration (PE&R) by conducting a series of trainings

for the CTD assessment for assessors and submission process for manufacturers. In April training, was conducted in Islamabad for DRAP officials on assessment of CTD format dossier from the regulatory evaluation perspective. The objective of the training was to train the newly inducted Assistant Directors and senior staff on assessment of a dossier. PQM conducted three back-to-back trainings for the pharmaceutical industry on preparation and submission of CTDs in Lahore, Karachi, and Rawalpindi utilizing PQM's consultant with global expertise and a senior cGMP expert from USP Rockville.

As part of PQM's continuing support to QC laboratories in Pakistan to achieve ISO 17025 accreditation and beyond with WHO PQ, the following activities were conducted:

- Evaluation of CAPA implementation by the Pakistan Drugs Testing and Research Center (PDTRC)–Lahore against the initial gap assessment.
- Visit to Drug Testing Laboratory (DTL) in Lahore and observations from a 1-day laboratory visit.

II. Country Context

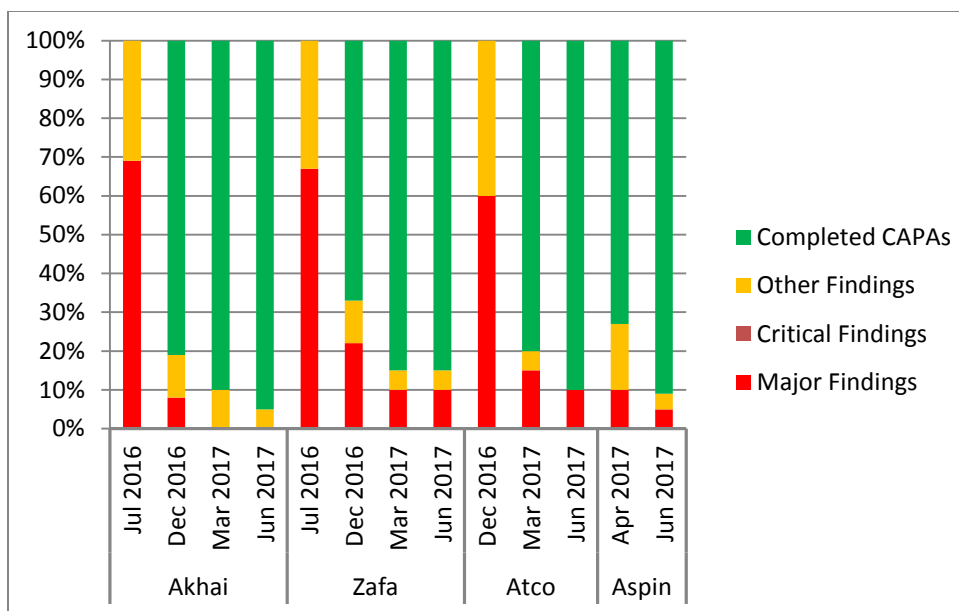
The U.N. Commission on Life-Saving Commodities for Women and Children recently added chlorhexidine as a priority medicine on the essential list. PQM is called to work with other implementing partners to support USAID's goal of introducing quality-assured CHX in Pakistan. The collective effort would contribute to the Pakistani government's effort to reduce the mortality (currently at 200,000 deaths/year, or about 22 cases per hour) of newborns caused by cord infections, mainly due to the lack of quality-assured CHX gels.

PQM is tasked with providing technical assistance to potential manufacturers of CHX gel in improving their manufacturing practice standards. In addition, PQM will help strengthen DRAP's capacity, improving medicines registration processes, PMS, and other key functions, including capacitating the QC laboratories toward international standards of practices. To effectively safeguard the quality of essential medicines, including CHX, a systems approach to pharmaceutical regulation and management must be implemented throughout the country. PQM's response to combating poor-quality medicines covers all key components of the medicines QA framework. Its efforts rely on further collaboration and firm support via adequate legislation and regulations. In addition, the implementation of and correlation among these components needs to be regularly monitored, evaluated, and documented to track and measure improvement.

III. Quarter 3 Progress by Objective

Objective 1 – Continue to provide technical assistance to selected manufacturers with strong interest and commitments to producing CHX products (7.1% chlorhexidine digluconate gel, delivering 4% chlorhexidine) to successfully register their products at DRAP

PQM conducted follow-up visits to four manufacturers – Zafa Pharmaceuticals, Akhai Pharmaceuticals, Atco Laboratories, and Aspin Pharmaceuticals – to assess the implementation of recommended CAPAs and to identify areas where they need PQM support to address the remaining corrective actions. The manufacturers are progressing well in addressing their respective CAPAs, as noted in the figure below.



Objective 2 – Strengthen Regulatory, Quality Assurance and Quality Control Systems through building the capacity of DRAP’s quality control systems and laboratories toward attaining international standards of quality and practices

PDTRC Lahore

PQM continues to support PDTRC, following up on the comprehensive assessment of PDTRC’s QMS that was performed in Q1 of FY 2017. Based on the assessment results, a CAPA implementation plan was developed, and PQM is assisting PDTRC to address the non-compliances. A follow-up visit was also conducted in April 2017. The agenda of this visit included:

- Evaluation of CAPA implementation by PDTRC–Lahore against observations from the October 2016 initial gap assessment.
- Discussion of the importance of data integrity and administration of related trainings.
- Discussion of plans for follow-up activities.

During the visit, a comprehensive review of the CAPA implementation plan was performed along with a complete reassessment of all activities. Based on this reassessment, training on data integrity, good documentation practices, good weighing practices, good practices with washing laboratory glassware, and the basic aspects of dissolution testing were conducted.

In continuation of the institutional capacity for regulatory workforce sustainability improvement, training was conducted for both PDTRC staff and the newly inducted DTL Lahore staff on UV spectrophotometry, dissolution apparatus, and Fourier transform infrared spectroscopy. This training was held April 24–May 5. For this training, the Government of Punjab called new staff from other Punjab Government DTLs to attend; in all, 63 analysts (35 males and 28 females) participated in the training.

Drug Testing Laboratory (DTL) Peshawar

PQM conducted a comprehensive assessment of DTL Peshawar on June 21–23. This baseline audit identified gaps, including deficiency in staffing, absence of QMS, lack of training of existing staff, and a shortage of equipment. DTL Peshawar is situated in a building that is not suitable to house a QC laboratory. The laboratory lacks reference standards and is using reference standards provided by the manufacturers. It does not have a generator installed. This laboratory needs a lot of input from PQM, and a comprehensive plan needs to be presented and discussed with the Government of the Province of Khyber Pakhtunkhwa to bring the laboratory at least on par with the other national QC laboratories in the country before it can vie for ISO 17025 or WHO PQ.

Objective 3 – Capacity building of DRAP Pharmaceutical Evaluations and Registration Division (PE&R) to improve its registration system to effectively evaluate all essential medicine products quality

Based on advice from PQM, PE&R decided to replace the existing template of Form “5” and Form “5” (A, D, & E) with the CTD for medicines registration applications. The legal process for the adoption of the CTD template is being fulfilled by DRAP. The biggest challenge in this process was that the industry, in general, was not ready for this change due, to limited understanding of the benefits they would gain from this investment. To inform and explain the CTD, PQM proposed to deliver training on CTD use, adoption, and requirements to regulators and industry by utilizing available resources, under USAID’s approval. The training was conducted in close collaboration with DRAP for its regulatory staff for evaluation/assessment and for industry in Lahore, Karachi, and Islamabad and included the development and submission of dossiers. The first training for regulators was conducted in April 2017 in Islamabad. In total, 32 officers (10 males and 22 females) from DRAP participated in the training. The training was supported and delivered by PQM’s technical staff.

The first training for the industry was delivered in Lahore April 2–4 for pharmaceutical industry and government officers, with 145 participants in total (96 males and 49 females). The second training session was conducted in Karachi for manufacturers situated in Karachi and surrounding areas. The training continued on May 17–19 and was attended by 165 participants (107 males and 58 females). The third training session was conducted in Rawalpindi for the manufacturers situated in Rawalpindi/Islamabad and Khyber Pakhtunkhwa (KPK Province). The training continued on May 23–25 and was attended by 155 participants (120 males and 35 females). Altogether 497 technical staff from industry (333 males and 164 females) were trained in the CTD registration application submission format, building awareness both within DRAP and the industry on the use of this format to enhance efficiencies in product registrations in the country.



CTD training in Rawalpindi, Pakistan attended by 155 participants

PQM also made progress in supporting the automation and establishment of DRAP’s Integrated Regulatory Information Management Systems (IRIMS). The initial system assessment was performed, and an action plan is being drafted to transfer and organize all paper-based information and data to an electronic data base. In May, PQM visited DRAP to help develop the action plan with the DRAP team.

Objective 4 – Capacity Building of Inspectorates at Federal & Provincial levels to perform their role effectively in pharmaceutical establishments licensing, and post-marketing surveillance

The Provincial Inspectorate is a very important part of the MQC system in Pakistan, especially in PMS. In pursuance of this objective, PQM delivered a PMS and good sampling practices training for inspectors of the Province of Baluchistan. The training was held in Quetta on April 14–15; overall, 22 provincial inspectors (19 males and 3 female) attended this training. The Director General of Health and Secretary of the Provincial Ministry of Health attended the

inaugural session. The closing session was attended by the Secretary of Health and Vice Chancellor of Baluchistan University. The Department of Health's Secretary appreciates PQM's efforts and USAID's support and thanked both organizations on behalf of Government of Baluchistan.

IV. Key Challenges

The key challenge that remains is the registration of the field office in Islamabad. The registration progress has been very slow. During the first month of this quarter, key queries raised by the Ministry of Interior (MOI) and other departments were addressed. The contacts in recent weeks with MOI officials confirmed that so far they do not have new observations. Reports suggest that MOI is keen to complete the process, but so far only 62 registrations have been granted by MOI, which includes INGOs already working on the ground before the new regulations came into place.

Programmatic Challenges

The non-accessibility to multiple entry visas remains a major programmatic challenge. PQM has been introducing an innovative approach in its technical assistance by planning for and combining multiple activities in one trip by multiple travelers, as well as hiring ad hoc local consultants to help implement the program on the ground. The situation is likely to further improve after the office registration is granted by the government, as the policy allows 1-year multiple entry visas for the INGO officials traveling for programmatic work.

Operational Challenges

The biggest operational challenge is the lack of availability of funds at the local level and lengthy procedures for transferring funds. Delays in program activity implementation are considerable, thus increasing the risk of not being able to complete time-sensitive activities on time. Another operational challenge is the unavailability of office space in the country. Establishing a temporary siting place may help improve program operation.

V. Lessons Learned

PQM has been working in close collaboration with all the key stakeholders in Pakistan involved in regulatory system strengthening and strives to maintain open communication with these stakeholders at both the federal/central and provincial levels.

At the federal level, the Appellate Laboratory, which is pivotal in the QC system of Pakistan, is also facing challenges. Despite repeatedly highlighting the requirements proposed by PQM, it appears that no concrete action has been taken by the Ministry of National Health Services, Regulations and Coordination to address the issues faced by the Laboratory. These issues include equipment and staff as first priority before any further development can be undertaken by the lab management. PQM is trying to get the support of Global Fund Health System Strengthen Grant.

PQM has been proposing to DRAP and the Ministry of National Health Services, Regulations, and Coordination to consider transferring the laboratory equipment that is available but not being used at the Federal Drug Surveillance Laboratory (FDSL) in Islamabad to Central Drug Testing Laboratory in Karachi in order to address the equipment limitations. The FDSL facility is based at the Medical College and is under the same Ministry.

PQM works closely with DRAP to strengthen its regulatory capacity; however, the review of provincial health authorities has also established that there is need to extend even more technical assistance support to the provincial authorities, especially the smaller provinces, to promote standardization of processes and actions countrywide to improve the quality of medicines and protect public health.

Philippines

I. Quarter 3 Highlights

PQM completed a workshop on improving the quality of essential medicines through good storage and distribution practices inspection for 24 Philippines FDA inspectors (7 males and 17 females). The number of collected samples for this quarter increased with a greater range of sites visited, including sample collection and inspection of directly observed treatment, short-course (DOTS) facilities.

As part of the program closing activities, PQM worked on complete the outstanding activities and centralizing the project's historical data and documentation in preparation for drafting the closeout report. The closeout report will include a transition plan to help in country partners continue to address the outstanding quality assurance issues.

II. Country/Health Element Context

The Philippines has an estimated 417 per 100,000 prevalence rate of TB, with an estimated 11,100 multidrug-resistant tuberculosis (MDR-TB) cases in 2015, according to the WHO. The Department of Health (DOH) NTP recognizes the important challenges to improve the TB drug supply and management in the country. Based on the 2015 Joint Program Review, the challenges include the complete absence of a logistics management information system for first-line drugs, poor storage conditions and practices, inadequate drug QA systems, and low-quality pediatric drugs. This is exacerbated by limited consideration for QA in the procurement, dispensing, and storage practices for medicine at health facilities. The Philippines FDA and DOH continue to work and seek support to address the challenges to assuring the quality of medicines and their supply at the regional level.

In collaboration with the Philippines FDA and DOH NTP, PQM strengthens medicines QA/QC in the supply chain through monitoring the quality of anti-TB medicines as part of PMS in the country. In addition, PQM provides FDA with technical and professional assistance to enhance its regulatory capacity to evaluate and register pharmaceutical products through the introduction and build-up of internationally accepted quality standards, processes, and procedures, including building the capacity of FDA satellite laboratories toward achieving ISO/IEC 17025 accreditation.

PQM also helps NTP to disseminate up-to-date information about medicines quality and raise awareness among the general public about medicine quality issues to mobilize policymakers, regulators, and health professionals.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the regulatory system of the Philippines Food and Drug Administration

The training workshop on improving the quality of essential medicines through good storage and distribution practices (GSDP) inspection for the Philippines Regulatory Authority was conducted June 26–30 at the Philippines FDA facility. The 5-day training workshop consisted mainly of inspectors from the regional offices that are involved in the inspection of drug distributors (wholesalers, importers, exporters) and drug retail outlets. GSDP is as an important and integral part component for ensuring quality and protecting the supply chain integrity. As part of GMP, GSDP inspection is critical for the quality of medicines. It is important for the regulatory authority to have the capacity to conduct appropriate inspection of storage and distribution facilities in line with international standards.

PQM designed and developed the GSDP training program based on WHO international standards and delivered it successfully to 24 Philippines FDA inspectors. The program content consists of nine modules, two case studies (group exercises), and two mock audits of traders/importers and distributors. The mock inspection was performed through actual group activities observed by the technical expert. Reports are prepared by inspectors after receiving input from the instructor. Inspection report writing was also a part of this activity. The reports were presented and discussed through group discussions.

Pre-tests and post-tests were given to participants to determine the impact of the training program. Results demonstrate a significant positive impact, and several inspectors were identified to become potential in-house trainers on GSDP.

Objective 2 – Strengthening the capacity of FDA Common Services Laboratories (Alabang, Cebu, and Davao Testing and QA Laboratory)

Via sample collection and quality testing of TB drugs, evidence-based data on the medicines available in the market were obtained. The FDA relies, in part, on the information obtained with PQM support to identify and take action against poor-quality TB medicines, which also benefits the NTP. From April through June, 233 TB samples were collected, excluding those not yet submitted/reported by Region 7. Currently, the samples are being tested for quality using the Minilab™.

Medicine Quality Monitoring for TB Drugs FY17 (Collected and Tested Samples Using Minilab™)				
Sentinel Site	Q1 (Oct–Dec 2016)	Q2 (Jan–Mar 2017)	Q3 (Apr–Jun 2017)	Q4 (Jul–Sep 2017)
Bicol	49	0	20	
Calabarzon	13	61	48	
Cebu	21	10	0	
Davao	23	6	3	
Iloilo	13	27	0	
La Union	0	17	53	
Pampanga	0	0	79	
Zamboanga	8	22	30	
Total (collected):	127	143	233	
Passed (tested)	127	134	To be determined	
Failed (tested)	0	9	To be determined	
Number of samples submitted to FDA Laboratories for confirmatory analysis/quality testing				
Passed	9	12	To be determined	
Failed	0	0	To be determined	

PMS from April to June revealed several suspicious medicines. Some of these medicines have the same batch/lot number as the reported failed samples in the Q2 report. FDA still has an ongoing investigation for those TB medicines, and PQM is in close communication with the agency’s Legal Services Support Center and Product and Research Standards Development Division.

From May to June, the PQM team visited DOTS facilities in Regions 1, 3, 4A, and 5 and came across a major finding during facility inspection. A DOTS facilities currently undergoing building improvement did not take into account the conditions of the temporary storage area of TB medicines. The inspection also showed that most DOTS facilities do not have a room thermometer to monitor the storage temperature. During the inspection process, the PQM team discussed and educated the staff on the proper handling of medicines and its importance in the treatment of patients. PQM provided recommendations for the improvement of their practice and facility.

The PQM team also supported PMS in private pharmacies in Regions 1, 3, 4A, and 5 using the “mystery buyer” technique. It was observed that many private pharmacies still sell TB medicines without prescription. Meanwhile, PQM has started the collection of first-line TB medicines in randomly selected DOTS facility in Region 4A. The TB medicines will undergo a tiered approach of testing, comprising three levels of testing for the collected samples. The data from these PMS activities provide information on the quality of first-line TB medicines currently being used by NTP.

RDMA

I. Quarter 3 Highlights

USAID Regional Development Mission for Asia (RDMA) and PQM management held a conference call to review the scope and timeline for activities and funding left to be completed this fiscal year. The Mission provided PQM with guidance on its priorities and recommended the following work plan changes for technical assistance to Laos Food and Drug Quality Control Center (FDQCC):

- Provide the Mission with a status report on Laos FDQCC ISO 17025 accreditation loss, providing the challenges faced by both PQM and FDQCC in advocating for sustainability and lessons learned, as well as how PQM can help countries prevent this from happening to other laboratories.

- RDMA closing report to include successes, lessons learned, and recommendations for sustainability.

As part of the program closing activities, PQM worked on preparing the closeout report and also on centralizing the project's historical data and documentation. Through the closeout report and associated materials, PQM will submit the following documentation to USAID:

- Medicines quality monitoring historical data
- Trip reports
- Assessment reports
- Financial reports

A program closeout planning meeting was held to go over the checklist of items to be completed, set timelines for completion, and gather all elements necessary for close-out.

Eastern Europe & Central Asia



Kazakhstan

I. Quarter 3 Highlights

During Q3, PQM made major progress in implementation of the FY 2017 work plan activities, including the following:

- Based on PQM's recommendations, three MQC laboratories supported by PQM completed cross-audits of their QMS by dedicated laboratory staff from Kostanay, Karaganda, Astana, and Almaty (headquarters of the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM)) laboratories in April.
- As part of the preparation to apply for WHO PQ, PQM assessed three MQC laboratories in Kostanay, Astana, and Karaganda for their compliance with ISO 17025 and WHO GPPQCL standards in June.
- PQM provided a hands-on training on essential testing methods (HPLC and dissolution) for the staff of Kazakh MQC laboratories, in particular the staff of Kostanay, Karaganda, and Astana laboratories. This training aimed to improve staff skills to appropriately use the equipment to achieve accurate and reliable results about the quality of TB medicines and other pharmaceuticals in the country.
- PQM met with the NCEM Director and Deputy Director to discuss next steps and plan for activities in preparation for WHO PQ of the labs.
- PQM continued to provide technical assistance in GMP to Nobel Pharmaceutical factory in order to enhance its capacity to manufacture quality-assured anti-TB medicines. This effort will increase critical supply of second-line anti-TB medicines at a reasonable cost to combat the spread of MDR-TB.

II. Country Context

The Republic of Kazakhstan is situated in Central Asia and Europe. It is the ninth-largest country in the world, covering an area of 2,727,300 km². The country has a population of 17.29 million.

According to WHO, estimated TB incidence in Kazakhstan is 99 per 100,000 people (Global TB Report, 2015). Kazakhstan is also a high MDR-TB burden country; MDR-TB reached 26% among new cases and 58% among previously treated cases.

In response to these challenges, Kazakhstan adopted a "Complex Plan for Tuberculosis Control in Kazakhstan: 2014–2020." One of the challenges stated in the plan is that the TB medicines procured locally are not WHO prequalified. One of the ways to address this problem is to increase GMP standards of local manufacturers to apply for WHO PQ.

Kazakhstan has a well-established national medicines regulatory authority: the Kazakhstan FDA. Medicines regulation in Kazakhstan is based on numerous legislative and regulatory documents. However, medicines quality still remains a problem in Kazakhstan. Over a period of 10 years (2004–2014), in 40 cases about 40,000 units of falsified medicines were withdrawn from the market by the Kazakhstan FDA.

In 2009, WHO conducted a survey on the quality of anti-TB medicines in six former Soviet Union countries, including Kazakhstan. The results of the survey were published in a 2011 report. Kazakhstan had the highest overall proportion of substandard samples (23.3%). Though the WHO survey has limitations, including a low number of samples collected and tested and limited scope of medicines targeted, these results indicate that there are quality issues related to noncompliance with GMP, as well as issues with QC of medicines and regulatory enforcement.

PQM began receiving funding from USAID/Kazakhstan in FY 2013, with the goal of improving the quality of anti-TB medicines produced by the major medicines manufacturers in the country and enhancing the capacity of these manufacturers to comply with international GMPs. According to Order No. 9 of the Ministry of Health of the Republic of Kazakhstan dated January 14, 2015, Kazakh manufacturers must have a GMP certificate for state registration of their medicines starting from January 2018; thus, the technical assistance provided by PQM is of high importance.

From FY 2013 to FY 2015, PQM worked with two manufacturers of anti-TB medicines in Kazakhstan—Pavlodar Pharmaceutical Factory (Romat Pharmaceutical Company) and Nobel Almaty Pharmaceutical Factory—on the implementation and improvement of their GMP to further participate in the WHO PQ program. Romat Pharmaceutical Company has not invested in the infrastructure of its facility, as it promised to do in the beginning of the project. However, Nobel Almaty Pharmaceutical Factory is committed to continuing cooperation with PQM and improving its GMP standards. Although Nobel already has a national GMP certificate, certain areas require improvements to reach compliance with international GMP requirements.

The Ministry of Health and Social Development of Kazakhstan entrusted the Kazakhstan FDA with a task to strengthen the capacity of the NQCLs in the context of entering of Kazakhstan in the Eurasian Economic Union and the necessity of mutual recognition of test results by its member countries. The Kazakhstan FDA decided that three NQCLs in its national lab network should reach WHO PQ, and it addressed the USAID country mission with a request to provide assistance for WHO PQ through the PQM program, so it could effectively control the quality of medicines in Kazakhstan, including the quality of anti-TB medicines.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the medicines quality control system through technical assistance to regional quality control laboratories of the Kazakhstan FDA to achieve WHO prequalification

In Kazakhstan, PQM Collaborative Learning Model, allows three of the country's laboratories to learn from each other's experience and facilitate consistent progress across the sites. In April, in accordance with PQM's recommendations, Kostanay, Astana, and Karaganda MQC laboratories completed cross-audits of their QMS by dedicated laboratory staff from Kostanay, Karaganda, Astana, and Almaty laboratories. Based on the audit results, the laboratories made revisions in their QMS documents to prepare for PQM's follow-up assessment.

In June, PQM conducted a follow-up assessment of three MQC laboratories in Kostanay, Astana, and Karaganda. PQM reviewed the laboratories' QMS documents, observed demonstration of methods, and provided corresponding recommendations. The PQM team was accompanied by a representative from Almaty headquarters responsible for the QA of Kazakhstan MQC laboratories and representatives of other NCEM laboratories. This allowed the PQM team and the laboratories participating in the PQM program to share their experiences, ensuring the sustainability of PQM assistance to Kazakhstan laboratories.

The PQM team is developing confidential assessment reports for each of the laboratories, and they will develop CAPA plans to address the identified deficiencies. Per results of the assessment, it was observed that the Karaganda laboratory had made the most significant progress, and it was recommended to be the leading laboratory among the three in Kazakhstan planning to apply to the WHO PQ program. PQM will continue remote assistance to improve QMS documents and develop the LIF. PQM also will support in translation of LIF and other relevant documents into English. It was agreed that the Karaganda laboratory would share its documents with the two other laboratories (Kostanay and Astana). To facilitate this process, PQM recommended establishing a Quality Group by the representatives of the three laboratories participating in PQM program; the laboratory representatives will discuss their QMS documents and develop uniform QMS in all three laboratories.

After completion of the assessment, the PQM team met with the Director and Deputy Director of NCEM, who highlighted the importance of WHO PQ of the three laboratories for the Kazakh government. The Director emphasized that the government requests to get three laboratories prequalified in 2017. PQM emphasized that the laboratories still have work to do, and that it would require acceleration of efforts from the NCEM and the laboratories to prepare for application for WHO PQ. It was agreed that the newly established Quality Group would revise all relevant QMS documents and develop a LIF template in July 2017; PQM will subsequently review them and provide comments. As soon as the documents are ready, PQM will send them for translation into English (in the summer of 2017). This may allow the Karaganda laboratory, as well as the Astana and Kostanay laboratories, to apply for WHO PQ in 2017.

In addition to the follow-up assessment of the laboratories, PQM provided a 5-day hands-on training on essential testing methods—HPLC and dissolution—in Almaty headquarters of NCEM. PQM trained 17 analysts from Kostanay, Astana, Karaganda, and Almaty laboratories as well as from some other laboratories of NCEM's network in analytical techniques on correct procedures to use HPLC and dissolution equipment. The trained staff improved their skills and were provided recommendations on how to appropriately demonstrate methods for equipment during WHO PQ inspections.

Objective 2 – Help increase the supply of quality-assured TB medicines in Kazakhstan through technical assistance to manufacturers of second-line anti-TB-medicines in reaching compliance with international GMP requirements and WHO prequalification

In Q3, PQM continued remote assistance to Nobel Almaty Pharmaceutical Factory in improving its QMS and GMP compliance. This is very important, as the company is in the process of preparing a new facility for production of medicines, including levofloxacin and moxifloxacin, two anti-TB medicines supported by PQM for potential WHO PQ. PQM reviewed a number of documents on qualification of equipment and provided comments to Nobel with recommendations for improvement.

In June, PQM met with the representative from Nobel Almaty Pharmaceutical Factory and discussed next steps for support. PQM will continue remote assistance to Nobel by reviewing documents on qualification of engineering systems and preparing some sections of the validation master plan. The new site at Nobel, where the production of anti-TB medicines (levofloxacin and moxifloxacin) will be transferred, plans to commence operations in August 2017. After that, PQM will discuss with Nobel potential dates for a GMP assessment visit to the new site.

Uzbekistan

I. Quarter 3 Highlights

Implementation of PQM program in Uzbekistan was delayed for several months, as the program was not approved by the Government of Uzbekistan. As a result of the great support from the USAID Mission in Uzbekistan and coordinated work with country stakeholders, the PQM program in Uzbekistan was approved by the Government in February 2017. Furthermore, a Memorandum of Understanding between USAID/Central Asia and Uzpharmsanoat was signed in June 2017 on implementation of the PQM program in Uzbekistan. This allowed PQM to start implementation of work plan activities in Q3.

In Q3, PQM conducted a 4-day GMP training for the staff of Nobel Pharmsanoat, manufacturer of second-line anti-TB medicines.

PQM also conducted a 6-day GMP training for the GMP Inspectorate of the Head Department of Drug and Medical Equipment Quality Control of the Ministry of Health of the Republic of Uzbekistan.

PQM had several meetings with the main Uzbek counterparts, Uzpharmsanoat and Head Department of Drug and Medical Equipment Quality Control, to discuss further collaboration and upcoming activities.



Dr. Jatinder Cheema, USAID/Central Asia Regional Mission Director (left), and Dr. Mirzanazim Dusmuratov, Chairman of the Board of the Uzbek State Joint Stock Pharmaceutical Company, Uzpharmsanoat, participated in a signing ceremony that formalized collaboration between Uzpharmsanoat and USAID

II. Country Context

Uzbekistan is situated in Central Asia. It covers an area of 448,978 km² with a population of 31,576,400. According to the WHO, the estimated TB incidence in Uzbekistan is 82 per 100,000 individuals (Global TB Report, 2015).

Uzbekistan is classified as a high MDR-TB burden country; MDR-TB reaches 23% among new cases and 62% among previously treated cases.

To respond to these challenges, Uzbekistan adopted a “Consolidated National Strategic Plan for TB in Uzbekistan 2016–2020.” The plan underlines the importance of the availability of quality-assured TB medicines for patients and supports interventions ensuring the availability of quality-assured medicines supplied through the GDF mechanism as well as those produced and procured locally.

Uzbekistan has an established National Medicines Regulatory Authority: the Directorate of Medicines and Medical Equipment Quality Control (Uzbekistan FDA). Medicines regulation in Uzbekistan is based on numerous legislative and regulatory documents. There is a network of QC laboratories in the country. The central laboratory (State Center of Expert Examination and Standardization of Drugs) is ISO/IEC 17025 certified and seeking WHO PQ. However regional laboratories are neither ISO 17025 accredited nor WHO prequalified.

Quality of medicines still remains a problem in Uzbekistan. In 2009, WHO conducted a survey on the quality of anti-TB medicines in six former Soviet Union countries, including Uzbekistan. The results of the survey were published in a 2011 report. The study found that in Uzbekistan 3 out of 7 samples of rifampicin capsules and 3 out of 11 samples of isoniazid tablets failed quality tests. Though the WHO survey has limitations, including the low number of samples collected and tested and the limited scope of medicines targeted, these results indicate that there are quality issues related to noncompliance with GMP, as well as issues with QC of medicines and regulatory enforcement.

The type of GMP technical assistance that PQM provides is highly needed in the country. Uzbekistan graduated from Global Fund support for procurement of first line anti-TB medicines to procurement with the domestic funds. The government’s strategy is to develop local manufacturing capacity for anti-TB medicines and ensure that locally produced quality-assured anti-TB medicines are available on the local market. For this purpose, PQM’s technical assistance to manufacturers of anti-TB medicines to improve their GMP compliance standards and to the medicines regulatory authority to improve their capacity in terms of ensuring quality of medicines on the local market is very important.

III. Quarter 3 Progress by Objective

Objective 1 – Increase availability of locally manufactured quality-assured anti-TB medicines

In May–June, PQM conducted a 4-day practical training on GMP for 31 representatives of Nobel Pharmsanoat, manufacturer of second-line anti-TB medicines. The training consisted of three courses: deviations and nonconformities; corrective and preventive actions; and change control and quality risk management. The training will help the company to improve its practices and GMP compliance in the listed areas.

The PQM team also visited the Nobel Pharmsanoat facility and conducted a walk-through tour of the new site. PQM and Nobel Pharmsanoat discussed further collaboration. It was agreed that PQM will conduct a gap analysis of the new site after the new site has been commissioned and operations started. The exact time will be discussed at a later date, as soon as Nobel Pharmsanoat finalizes the schedule of activities with its parent company.

Objective 2 – Strengthen the medicines quality assurance system by building the human capacity of the national stakeholders

In June, PQM conducted a 6-day GMP training for 20 GMP inspectors of the Head Department of Drug and Medical Equipment Quality Control of the Ministry of Health of the Republic of Uzbekistan. The comprehensive training course focused on GMP inspection and the Pharmaceutical Inspection Co-operation Scheme (PIC/S). In addition to the theoretical sessions, the training included daily group discussion sessions where participants discussed real-life situations from GMP inspections. PQM received very positive feedback from the participants about the usefulness of the training and how it will help improve their daily functions. The training will help GMP inspectors enhance their capabilities to ensure that the pharmaceutical manufacturers (including the manufacturers of anti-TB medicines) comply with GMP standards.

The Uzbekistan GMP Inspectorate expressed great interest in receiving further technical assistance from PQM to support the country toward achieving PIC/S membership. PQM and the Head Department of Drug and Medical Equipment Quality Control identified PQM’s assistance in strengthening Uzbekistan’s GMP inspection system to meet PIC/S membership requirements as the main area of potential collaboration.

IV. Key Challenges

According to the approved PQM program in Uzbekistan, PQM should support Uzpharmsanoat—State Joint Stock Concern of Pharmaceutical Industry—in developing QMS for the MQC laboratory it is going to establish. This

includes procurement and provision of certain equipment, subject to a needs assessment. Although Uzpharmsanoat indicated that it identified a building where the laboratory will be established and is in the process of developing its design, the laboratory still does not exist. Thus, PQM is not able to progress on this activity.

Core Portfolio



Cross Bureau

I. Quarter 3 Highlights

During Q3, the following activities were the main highlights from the Cross Bureau project:

- PQM presented at the 2017 Consortium of Universities for Public Health Conference to increase the global awareness of the importance of medicines quality.
- PQM participated and contributed to the East African Community–Medicines Registration Harmonization (EAC–MRH) Joint Dossier Assessment meeting and the Expert Working Group on Good Manufacturing Practices.
- PQM's completed the risk-based PMS implementation guidelines after external review.

II. Cross Bureau Context

PQM's approach to Cross Bureau priorities focuses assistance on MRAs and advocating for medicines quality. Being a core program, implementing activities at the global and regional levels is a priority. This includes developing tools and approaches for sustainable regulatory functions in various settings and promoting regional harmonization. The approach also includes advocacy for medicines QA systems by raising awareness among key stakeholders about the quality of medicines—specifically for medicines that address the key health goals of Ending Preventable Child and Maternal Deaths (EPCMD), AIDS-free Generation, and Protecting Communities against Infectious Diseases.

PQM is increasingly recognized for its international role in the medicines QA arena and is viewed by national institutions, international organizations, and regulatory authorities as a leader in promoting medicines quality. Cross Bureau funds allow PQM to explore new opportunities, develop innovative solutions, and overcome challenges to promoting medicines quality in USAID priority countries around the world.

EPCMD is one of the three shared goals of the U.S. Government in global health. To address this goal, PQM is focusing resources on developing tools and approaches that could be piloted or adopted in the 24 priority countries. The USAID Office of Health Systems (OHS) embraces implementation of USAID's strategy to promote effective, sustainable, country-owned health systems. The priority areas for the OHS within the EPCMD priority countries are the focus for all programming priorities, including pharmaceutical systems strengthening and improving quality of essential services.

PQM's overall technical assistance contributes to USAID Core Global Health Priorities—Saving Mothers, Child Survival, Fostering an AIDS-free Generation, Fighting Infectious Diseases, Family Planning and Reproductive Health, and Health Systems Strengthening. PQM support for Cross Bureau has been primarily focused on raising awareness of the importance of medicines quality, supporting regional networks, and helping to develop new approaches to strengthen medicine regulatory functions.

Technical assistance provided by PQM will continue to focus on improving MRA capacity, promoting the use of quality-assured and effective pharmaceutical products, and supporting development of new QC testing tools for medicines. PQM will execute on these priorities in close collaboration with partner organizations with the common goal of strengthening medicines QA systems and tools.

III. Quarter 3 Progress by Objective

Objective 1 – Increase awareness of the importance of medicines quality

PQM presented at the 2017 Consortium of Universities for Global Public Health Conference. This is one of the leading academic global health conferences, which began in 2008 and attracts more than 1,800 delegates, including committed leaders, professionals, educators, students, and global health partners. PQM's presentation focused on multi-country experience supporting MRAs in low- and middle-income countries to keep falsified medicines—including antimalarials, maternal and child health products, and family planning products—from circulating in their markets. The presentation was part of a session entitled "Fake Medicines: an Unseen Threat to Global Health." Speakers from the U.S. FDA, the U.S. National Institutes of Health, Fogarty International Center, University of California San Diego, PSI, and Pfizer presented at this session, which was attended by over 100 participants.

Also this quarter, the MQDB Alert (database) was updated to include information on poor-quality medicines identified through PMS activities from the Philippines and Peru MRAs.

Objective 2 – Provide technical leadership to regional networks of medicines quality assurance professionals

PQM participated in the EAC–MRH Joint Dossier Assessment meeting held in Entebbe, Uganda. PQM provided technical leadership during the review of dossiers for the registration of health products, including MNCH commodities. A meeting of the Expert Working Group on GMP was also held to review the GMP status of manufacturers that had applied for registration of their products utilizing the EAC–MRH joint assessment mechanism. This mechanism supports the registration of USAID priority commodities, including MNCH priority products. The joint assessment and registration of products through harmonized procedures enhances the regulatory system and reduces the backlog in registering products among participating regulatory agencies.

Objective 3 – Risk-based quality assurance systems—Models for self-sufficiency and sustainability

In Q3, PQM finalized the risk-based QA framework document after internal review. The Framework was also circulated to WHO and few other external reviewers for comments. The final draft will be submitted to USAID in Q4.

The risk-based PMS implementation guideline was also completed, including external review. External reviewers included experts from the London School of Tropical Medicines and Hygiene and Johns Hopkins Bloomberg School of Public Health. PQM developed a tool to operationalize the implementation of the guideline. The current version of the tool is being converted into a web version that will be user-friendly and easily accessible by countries. The final draft of the risk-based PMS implementation guidelines will be submitted to USAID in Q4.

To map PMS in select EPCMD countries, indicators have been selected and will be used in Q4.

Objective 4 – Revision of USAID's Health Systems Assessment Approach (HSAA)

The tool has been finalized in previous quarters of FY 2017. This activity is complete.

Objective 5 – Development of e-Learning course on medicines quality assurance

No updates this quarter. The outline for the course was proposed to USAID in Q2.

Objective 6 – Establish regulatory system country profiles

An information-gathering tool has been initiated. It will be used to collect information on medicine regulatory systems in select countries in Q4.

Objective 7 – Provide guidance on the importance of medicines quality in Universal Health Coverage (UHC) schemes

No updates this quarter.

Objective 8 – Promote regional framework for compliance with international GMP standards by local pharmaceutical manufacturers in Africa

No updates this quarter.

Core TB

I. Quarter 3 Highlights

NCPC Pharma received full WHO prequalification for streptomycin FPP with the assistance of PQM. Also with PQM support, Celltrion Pharmaceutical Company achieved an important milestone—it has submitted an Abbreviated New Drug Application (ANDA) for linezolid to the U.S. FDA. Celltrion Pharmaceutical Company's FPP dossier for linezolid was also accepted for review by WHO PQ.

PQM progressed in terms of providing technical assistance to the manufacturers in Pakistan, which is transitioning from Global Fund-supported procurement of anti-TB medicines to domestic procurement of anti-TB medicines. In Q3, PQM conducted a GMP assessment of two manufacturers of fixed-dose combination first-line anti-TB medicines in Pakistan. Based on the assessment, a CAPA plan will be developed. Also, with PQM's technical assistance, Pakistani manufacturer Pacific Pharmaceuticals Limited received a Certificate of GMP Compliance from the Medicines and Healthcare Products Regulatory Agency (MHRA). The company produces ethambutol—a single dose first-line anti-TB medicine.

II. Health Element Context

The mobilization of the global efforts for intensifying the fight against TB and achieving an end to the global epidemic is demonstrated by the adoption of the WHO's End TB Strategy by the World Health Assembly in 2014, its endorsement in several WHO Regional Committee meetings during 2015, and the inclusion of "ending the TB epidemic" as a target within the health-related Sustainable Development Goal 3 by the United Nations General Assembly in September 2015.

Moreover, the United States Government published its strategy for the global fight against TB, included in the following documents: "Reach, Cure, Prevent - United States Government Global Tuberculosis Strategy (2015-2019)" and the "National Action Plan for Combating Multidrug-resistant Tuberculosis". Both documents are consistent with the WHO End TB Strategy and outline the US Government's support to ensuring availability of affordable quality-assured TB medicines.

Consistent themes within these publications are safeguarding treatment for all people with TB including, drug-resistant TB, preventive treatment for persons at high risk, regulatory frameworks for quality, and the rational use of medicines. Whereby making the uninterrupted availability of affordable quality-assured anti-TB medicines crucial to achieving the desired treatment outcomes for people with TB, as well as for the prevention of drug-resistant TB.

III. Quarter 3 Progress by Objective

Objective 1 – Increase the supply of quality-assured TB medicines and medical products

NCPC Pharma received full WHO prequalification for streptomycin FPP with the assistance of PQM. Celltrion Pharmaceutical Company's FPP dossier for linezolid was accepted for full review by WHO PQ in June. Celltrion also submitted its linezolid FPP dossier to the U.S. FDA at the end of June. Linezolid is one of the core medicines for treatment of MDR-TB. With the potential approval of Celltrion's linezolid FPP by U.S. FDA and WHO PQ, one more source of quality-assured linezolid will be added to the two manufacturers that are currently prequalified by WHO. This would increase access to quality-assured linezolid at an affordable price on the global market. Potentially, it will be supplied through the GDF mechanism.

During Q3, PQM provided technical assistance to the manufacturers of the following TB medicines:

- **Clofazimine API and FPP:** PQM conducted a mock audit of the contract manufacturing organization (CMO) for FPP manufacturing in May 2017. The manufacturer is currently completing all of the corrective actions; PQM has also been working closely to plan the new cross-over BE study design.
- **Gatifloxacin API:** An API manufacturer engaged a third-party firm to prepare the API master file for submission to WHO.
- **Kanamycin API:** The manufacturer initiated a study to reduce the impurity in the final API by using a starting material from a different source.
- **Kanamycin FPP:** PQM provided technical assistance in dossier follow-up.
- **Linezolid FPP:** Celltrion Pharmaceutical Company achieved an important milestone by submitting an Abbreviated New Drug Application for linezolid FPP to the U.S. FDA and having its dossier accepted for review by WHO PQ.
- **PAS sodium API:** PQM worked with a manufacturer to implement CAPAs from the mock audit in preparation for a WHO inspection.
- **Streptomycin FPP:** NCPC Pharma received full WHO prequalification with the assistance of PQM.

- **Rifampicin/isoniazid/ethambutol/pyrazinamide (4FDC):** GMP assessments were conducted in May 2017 for two companies in Pakistan. Both manufacturers are undergoing CAPAs.
 - One company is in the process of constructing a new manufacturing facility dedicated to TB medicines. This manufacturer also received MHRA approval for ethambutol 400 mg tablets with PQM's assistance. 25% of the CAPAs are completed from the May GMP assessment.
 - The second manufacturer has initiated dossier compilation for the 4FDC, as well as cycloserine. 40% of the CAPAs are completed from the May GMP assessment.

The request for applications (RFA) for selection of manufacturers of rifampin (rifampicin) for U.S. FDA submission has been drafted, reviewed, and submitted to PQM's editorial team for final review prior to publication. The RFA will be advertised for one month and selection of the manufacturer will be made Q4. The intent of the RFA is to identify a manufacturer of rifampin (rifampicin) which will be supported by PQM for approval by U.S. FDA. This would ensure that an additional source of rifampin (rifampicin) is available on the U.S. market, reducing a risk of any potential interruption in supply. Also, after U.S. FDA approval, this product will become eligible for supply through GDF to countries which benefit from the GDF mechanism.

In Q4, PQM will continue to provide technical assistance to the manufacturers of priority anti-TB products. Also, based on the RFA, PQM will select a manufacturer of rifampin (rifampicin) for support toward U.S. FDA approval.

Objective 2 – Provide technical leadership in support of availability of quality-assured TB medicines

In April, PQM staff attended the annual GDF manufacturers' meeting in Luang Prabang, Laos. During the meeting, PQM presented on PQM's approaches to strengthening the QMS and GMP compliance of manufacturers of anti-TB medicines, as well as PQM's planned activities and potential engagement of manufacturers. Participation in the workshop was very beneficial in terms of receiving updates from partners, such as GDF and the WHO PQ team, and coordinating collaboration with them.

In Q3, PQM worked on preparation of the workshop, "Ensuring the Quality of Medicines on the Public Health Market" for manufacturers of TB and NTD medicines and MRAs. The objective of the workshop is to raise awareness about pharmaceutical quality and to provide information to MRAs and manufacturers of anti-TB and NTD medicines about opportunities for using PQM technical assistance to strengthen quality systems. The workshop will discuss PQM technical assistance, the WHO PQ process, current GMPs, dossier requirements, and risk assessment for cleaning validation, among other topics. Participants of the workshop will also learn about quality standard requirements and procurement processes through global mechanisms, as well as WHO's Collaborative Registration Procedure and the opportunities for using this mechanism to improve access to TB and NTD medicines in the countries. The workshop will also facilitate dialogue among MRAs and pharmaceutical manufacturers. Thus far, representatives from more than 30 manufacturing companies and 5 national TB programs and MRA members are registered to attend. The workshop will be held in Q4.

Core NTD

I. Quarter 3 Highlights

In Q3, PQM continued implementation of FY 2017 work plan activities, including the following:

- PQM continued provision of technical assistance to manufacturers of priority NTD medicines: praziquantel, albendazole, and mebendazole, which are in different stages of preparation for WHO PQ.
- The questionnaire for the NTD situation analysis on supply and production of NTD medicines in five priority countries was developed. Collection of information for the situation analysis has been initiated.
- The expression of interest (EOI) for assistance in the praziquantel BE study has been closed. PQM received five applications in total. The applications will be evaluated, and manufacturers to receive PQM's assistance will be identified in July. Final scoring and results will be available in early July.

II. Health Element Context

NTDs have been a global concern for decades and a major cause of morbidity and mortality worldwide. More than a billion people—one-sixth of the world's population—suffer from one or more NTDs. These diseases affect the world's most vulnerable populations, almost exclusively impoverished populations living in rural areas and urban slums of low-income countries. The impact of NTDs on individuals and communities is devastating. Many of them cause severe disfigurement and disabilities.

A major constraint to the effective scale-up of NTD control and elimination programs is the scarcity of quality-assured medicines suppliers and limited number of products. WHO has invited manufacturers to submit EOI for NTD product evaluation in an effort to support national and global efforts to increase access to and affordability of treatments. The most recent invitation from WHO focuses on five single-ingredient medicines (albendazole, diethylcarbamazine, ivermectin, mebendazole and praziquantel) used in the treatment of lymphatic filariasis, soil-transmitted helminthiasis, onchocerciasis, and schistosomiasis. Of the five treatments listed in the WHO EOI, albendazole, mebendazole, and praziquantel have become the priority products for WHO and USAID NTD teams.

As PQM continues support for manufacturers to achieve prequalification of NTD medicines, some constraints for manufacturers have become evident, including a scarcity of API suppliers that can fulfill the WHO requirements of FPP manufacturers to participate in the PQ of their products. One mechanism available to manufacturers that the WHO NTD team has begun rigorously implementing is the ERP process. This process allows manufacturers to partake in a rapid quality risk assessment of their product dossier and the level of GMP compliance at their manufacturing sites.

Additional constraints toward the submission of an application for WHO PQ include the lack of capital investment for promising FPP manufacturers that would allow them to improve their infrastructure and equipment capabilities to meet the GMP requirements, as well as a lack of funding for conducting BE studies in a CRO that is compliant with good clinical practices. One significant advantage for manufacturers of NTD products requiring BE studies is that the ERP process allows an FPP manufacturer to go through this rapid assessment prior to investing in costly BE studies. With only acceptable comparative dissolution studies, a manufacturer may submit an application for the ERP process with a commitment to complete BE studies at a future date.

To overcome these challenges, it is necessary to provide technical assistance to API and FPP manufacturers in order to increase the pool of GMP-compliant suppliers.

III. Quarter 3 Progress by Objective

Objective 1 – Increase availability to quality-assured NTD medicines

During Q3, PQM provided technical assistance in to the manufacturers of the following NTD medicines:

- **Praziquantel API:** PQM continued to provide technical assistance to one manufacturer in implementation of a CAPA plan, developed as result of PQM's audit. In May, PQM conducted an onsite walk-through of a second manufacturer. This company received notification of WHO PQ inspection for September 2017. It is agreed with the company that PQM will provide a follow-up visit and further technical assistance after the WHO inspection in September.
- **Praziquantel FPP:** PQM continued to provide remote technical assistance to three manufacturers on the different product development quarries.
- **Albendazole API:** PQM continued to provide remote technical assistance to one manufacturer in implementation of CAPA.
- **Albendazole FPP:** PQM is providing technical assistance to two manufacturers. One manufacturer conducted a risk assessment for potential cross-contamination in May 2017. The conclusion indicated that the risk was too high, and the manufacturer was recommended to produce the product on separate equipment. PQM also provided review of qualification protocols and will continue to help develop its validation master plan in the next quarter. The second manufacturer is in product development stage. PQM provided remote technical assistance to support the process.

In Q4, PQM will continue to provide technical assistance to manufacturers to ensure that they are making progress toward WHO PQ.

PQM also continued to work on the situation analysis on the availability of quality-assured priority NTD medicines in five high-NTD burden countries (Nigeria, Ethiopia, Tanzania, India, and Indonesia). The study questionnaire for the different stakeholders has been developed. A list of persons representing different stakeholders that should be interviewed in each country was defined, and collection of the information for the analysis has started. As a result of the analysis, PQM will identify and engage local manufacturers of NTD medicines for technical assistance to improve their GMP compliance and potentially prepare for WHO PQ. This would ensure sustainable supply of quality-assured NTD medicines in the high NTD incidence countries. The study will be completed during Q4.

Objective 2 – Technical support for bioequivalence study

In order to fill a gap in the supply of praziquantel and increase the number of quality-assured sources of this product, PQM is identifying manufacturers for support in conducting BE studies, which is an important milestone in the process of WHO PQ. In Q3, PQM developed and published an EOI for assistance in a praziquantel BE study. PQM received five applications in total. The applications will be evaluated, and manufacturers for PQM's assistance will be identified in July. The selected manufacturers will be provided with technical and financial assistance by PQM to ensure that the BE study is successfully conducted. A successful completion of a BE study will help manufacturers to get their praziquantel prequalified by WHO. Thus, additional quality-assured sources of praziquantel will become available on the market, which would help in closing a current gap in supply of this product.

Results of the EOI scores will be available in early July 2017. Then the manufacturers will be notified, and contracts will be initiated.

Objective 3 – Provide technical leadership in support of availability of quality-assured NTD medicines

In Q3, PQM worked to prepare the workshop, "Ensuring the Quality of Medicines on the Public Health Market" for manufacturers of TB and NTD medicines and MRAs. The objective of the workshop is to raise awareness about pharmaceutical quality and to provide information to MRAs and manufacturers of anti-TB and NTD medicines about opportunities for using PQM technical assistance to strengthen quality systems. The workshop will discuss PQM technical assistance, the WHO PQ process, current GMPs, dossier requirements, and risk assessment for cleaning validation, among other topics. Participants of the workshop will also learn about quality standard requirements and procurement processes through global mechanisms, as well as WHO's Collaborative Registration Procedure and the opportunities for using this mechanism to improve access to TB and NTD medicines in the countries. The workshop will also facilitate dialogue among MRAs and pharmaceutical manufacturers. Thus far, representatives from more than 30 manufacturing companies and national TB program and MRA members are registered to attend. The workshop will be held in Q4.

Core MNCH

I. Quarter 3 Highlights

In Q3, PQM continued to provide technical assistance to manufacturers of essential MNCH medicines. One manufacturer for chlorhexidine solution was able to complete its qualification for the packing equipment, as well as three commercial scale process validation batches with assistance from PQM. The company also completed its CAPAs. Thus the manufacturer was prepared for the audit from Save the Children, which potentially can procure the product for its programs.

II. Health Element Context

In 2015 the Sustainable Development Goals were adopted by world leaders to build on the success of the Millennium Development Goals. Goal 3, "Ensure healthy lives and promote well-being for all at all ages," encompasses similar targets with USAID's "Ending Preventable Child and Maternal Deaths (EPCMD)" initiative. The EPCMD initiative focuses resources on 24 priority countries and toward life-saving interventions that have the greatest impact on mortality. These 24 countries, primarily in sub-Saharan Africa and South Asia, account for 70% of child and maternal deaths.

In the 24 priority countries, 4.6 million children and 200,000 mothers have been saved through interventions supported by USAID. Although much success has been accomplished, a greater collaborative effort is needed to achieve the EPCMD goal of saving the lives of 15 million children and nearly 600,000 women by 2020.

Other recent USAID initiatives such as, “USAID’s Vision for Health Systems Strengthening (2015-2019),” also contribute to the EPCMD goals of saving the lives of women and children. Within the vision, a health system consists of six core functions, one of which is medical products, vaccines, and technologies. This function not only includes ensuring an uninterrupted supply of quality-assured medicines, but also strengthening medicines regulatory capacities to protect against poor-quality medicines, which is the essence of PQM’s technical expertise.

III. Quarter 3 Progress by Objective

Objective 1 – Help increase the availability of quality-assured MNCH medicines

During Q3, PQM provided technical assistance in to the manufacturers of the following MCH medicines:

- **Chlorhexidine solution FPP:** PQM visited the manufacturer in May. With PQM’s support, the manufacturer completed the equipment qualification and conducted the process validation of chlorhexidine solution for three commercial size batches. The manufacturer also completed the CAPAs based on the earlier audit from Save the Children. Once the manufacturer receives assurance of GMP compliance, Save the Children will purchase 500,000 vials from the manufacturer. The company is currently selling 3 million vials in Myanmar and Bangladesh, so quality of those products also will be assured.
 - **Magnesium sulfate FPP:** PQM is providing remote technical assistance to three manufacturers. Responses and recommendations to the different inquires by the manufacturers were provided.
 - **Amoxicillin FPP:** PQM provided remote CAPA technical assistance to one manufacturer.
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Objective 2 – Provide technical leadership on MNCH medicine quality assurance

The Institute of Pharmaceutical Sciences at Monash University has an oxytocin team that is engaged in an ongoing program investigating the quality of oxytocin injection ampoules supplied to resource-poor settings. This program includes collaboration with the United Nations Population Fund (UNFPA) to understand the robustness of oxytocin supplies after repeat exposure to elevated temperatures and audits of oxytocin quality in the Democratic Republic of Congo (ongoing) and Ethiopia (proposed). As PQM collaborates with Monash University on this project, it was requested to provide assistance to understand the compliance of collected samples with the USP monograph methods for assay and related substances. PQM received the samples (ampoules) of oxytocin collected by the Monash team in the DRC for testing. The main aim of the testing was to identify whether an unknown impurity detected in all DRC ampoules tested by Monash using an alternate non-USP method is also detectable using the methods detailed in the USP monograph for oxytocin injection. Based on the testing, it was concluded that samples did not comply with the USP monograph. PQM will continue collaboration with Monash University to answer the original question about identifying whether the impurity detected in ampoules tested by Monash using an alternate non-USP method is also detectable using the methods detailed in the USP monograph for oxytocin injection.

In Q4, PQM staff members are planning to attend the joint UNICEF–UNFPA–WHO Manufacturers’ Meeting in Copenhagen in September 2017.

Core Malaria

I. Quarter 3 Highlights

During this quarter, the development of profiles for selected PMI funded countries was initiated. The profiles will include information on medicines’ regulatory QA systems and data on the antimalarials utilized in the country. A tool to gather key indicators and information from the countries was finalized, data were collected from Ethiopia and Nigeria, and a country profile for Ethiopia was completed and submitted to USAID. The tool and profiles finalized during this quarter will help streamline the development of additional profiles during Q4.

II. Health Element Context

Although tremendous progress has been made in the fight against malaria, the disease continues to affect the health and economy of endemic countries globally. Current treatments may be rendered ineffective if proper measures are not taken to ward off the threat of resistance. The mainstay for malaria control recommended by WHO is ACTs, which

have demonstrated good efficacy against the malaria parasite. However, resistance of the malaria parasite to ACTs has been reported in Southeast Asia, raising concerns about the possibility of the spread of the drug-resistant parasite to Africa. Certain practices favor the development of resistance, including unregistered medicines of unknown quality and efficacy, as well as diversion of donated medicines to the private sector where those medicines may be used irrationally and without proper prescription.

III. Quarter 3 Progress by Objective

Objective 1 – Provide technical leadership & global advocacy to raise awareness about the potential dangers of using substandard or counterfeit antimalarial medicines

This quarter, PQM developed malaria country profiles for Ethiopia and Nigeria. Country profiles included information on the status of medicines regulatory QA systems in general and specifically on antimalarial medicines utilized in the country. Profiles also included information on the technical assistance provided by PQM to strengthen QA systems, the outcomes of the assistance, and existing gaps and planned activities to address gaps. To achieve this, PQM developed a tool to gather information on key indicators of QA systems; profiles were developed based on PQM records, and data were gathered with the tool and information from the country's medicines regulatory authority website.

Ethiopia's country malaria profile was finalized and submitted to USAID for review and approval. A draft profile for Nigeria is available. Next steps for this activity include finalizing and submitting the Nigeria profile to USAID, updating and refining the data collection tool developed based on the two country experiences, and collecting information from at least two additional countries that will be determined with the PMI adviser.

Also during Q3, a Nigeria diversion study report was delivered to PMI, which this completes the submissions for the three diversion studies performed in 2016.

Management Overview

PQM continued to focus on working with the USAID Mission and Core Health Element team to secure approval for FY 2017 work plans during Q3. By the end of June, 24 of 26 work plans (92%) had been fully or partially approved, with only 2 work plans still awaiting USAID approval.

In Q3, PQM began the process of developing annual work plans for FY 2018, which will be submitted to USAID by the end of August. In order to ensure quality work plans are submitted and that lessons learned are continuously brought into the fold of subsequent planning, PQM uses a cyclical work planning approach. During Q3, the process was kicked off by:

- Reflection – reviewing of the past year’s implementation and lessons learned.
- Getting Priorities Right – identifying priorities and opportunities at the program and project level.
- Pre-planning – holding Problem Analysis workshops and Work Plan Development weeks.

This year, PQM introduced facilitated Problem Analysis workshops to the work plan development process. Problem Analysis is a systematic process used to determine causes and effects of a problem and to link their relationships. The workshops allowed PQM staff to identify and analyze problems with their root causes and effects, then subsequently prioritize interventions that work to provide solutions for the identified problems. Coupled with top-down priorities set by PQM leadership, the Problem Analysis workshops laid the foundation for strong work plan development.

Following the Problem Analysis workshops, PQM held two Work Plan Development weeks where staff from headquarters and field offices had the opportunity to critically examine their proposed work plan activities with the PQM technical and functional support teams. Staff also had the opportunity to collaborate across projects to encourage peer-to-peer knowledge sharing.

PQM Director Jude Nwokike attended two key meetings during Q3. The first was participation in the World Health Assembly on May 22–26, where he spoke at two sessions: “Against All Odds: Strengthening Health Systems to Better Serve Vulnerable Women and Children” and “Antimicrobial Resistance: How is Medicine Quality Important?” Director Nwokike also participated in the WHO Coalition of Interested Partners Task Force Meeting on June 29–30. Both meetings took place in Geneva, Switzerland, and provided opportunities for PQM to engage with key stakeholders and partners for our work.

USP was also pleased to hold a commemorative event in June: “Celebrating 25 years of Collaboration: USAID and USP.” During the event, individuals from USAID, the USP Board of Trustees, and the USP Executive Team provided remarks, and our constituents relayed what the work has meant to them. The story of how our collaboration began and evolved over time was discussed by USP’s CEO, Ron Piervincenzi, and former USAID Project Manager for PQM and its predecessor projects, Anthony Boni. The event not only helped to catalog the USP and USAID past and present, but also to outline areas for potential collaboration in the future.



USP CEO, Ron Piervincenzi (left) and Former USAID Project Manager, Anthony Boni



Attendees at the *Celebrating 25 years of Collaboration: USAID and USP* event