PROMOTING THE QUALITY OF MEDICINES

Promoting the Quality of Medicines (PQM)

FY 2016 Second Quarter Report
January 1 - March 31, 2016

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The Promoting the Quality of Medicines (PQM) program combats the proliferation of falsified and substandard medicines. Funded by the U.S. Agency for International Development (USAID), PQM is the successor to the Drug Quality and Information (DQI) program, implemented by the United States Pharmacopeial Convention (USP).

By providing technical assistance to developing countries, PQM achieves three main goals:

1. builds local capacity in medical quality-assurance systems;
2. increases the supply of medicines to USAID health programs;
3. ensures the quality and safety of medicines globally.

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About the Promoting the Quality of Medicines Program (PQM)

USAID Funding Sources	Global Health Bureau; Office of Health Systems; Office of Health, Infectious Diseases and Nutrition; USAID Country Missions
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Executive Summary

The Promoting the Quality of Medicines (PQM) program is implemented by the U.S. Pharmacopeial Convention (USP) and funded through the generous support of the United States Agency for International Development (USAID). PQM provides technical assistance to build capacity of medicines regulatory authorities and quality assurance systems in countries with emergent health systems. The following report captures progress made towards PQM's four intermediate result areas during the second quarter of FY16, from January 1st to March 31st, 2016.

An aggregate view of program achievements according to four intermediate result areas are reported, followed by detailed portfolio level summaries of progress made towards work plan objectives.

The first result area encompasses program progress towards expanding the capacity of national medicine regulatory agencies. Accomplishments during the quarter included the strengthening of regulations, as in Indonesia where the Ministry of Health Regulation Number 02/2016 entitled "Guidelines for Sampling and Testing Medicines from Government/Public Facilities" is an important step forward in facilitating cooperation between the Ministry of Health and the national medicines regulatory agency (BPOM) towards ensuring that public program medicines are routinely sampled and tested per government policy. Previously, no such formal guide for cooperation existed and the national post-marketing surveillance system of BPOM only covered private sector markets, and thus could not access tuberculosis (TB), HIV, malaria, and other priority disease medicines for quality control purposes. PQM also provided support for the development of good practices guidance documents for international standard accreditation and trainings to strengthen regulatory workforce.

The availability of quality medicines, the second result area, outlines PQM's broad technical assistance with select manufacturers to address quality-related issues. PQM supports manufacturers to establish good manufacturing practices and develop quality-related documents necessary to achieve compliance with internationally accepted practices and prequalification programs. Such measures ensure increased production of locally sourced and quality-assured medicines.

PQM's work to combat falsified and substandard medicines comprises the third result area. Technical assistance towards this aim is conducted by assessing existing quality assurance and quality control systems, and then providing necessary support in collaboration with a country's medicine regulatory agency and national health programs. Assistance in this context includes training field staff in: sampling, testing with Minilab™ methods, data reporting, and training national laboratory staff in advanced testing methods.

PQM serves as a global technical leader in medicines quality assurance and an advocate for medicines quality in collaboration with a multitude of partners. The fourth result area, 'Global Advocacy on Medicines Quality Enhanced through Technical Leadership,' highlights PQM's technical contribution to the expanding knowledge in pharmaceutical quality-related health systems research, as well as developing innovative and efficient 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.

Acronyms

API	Active Pharmaceutical Ingredient
BPOM	Indonesian National Agency of Drug and Food Control
CAPA	Corrective and Preventive Action
CHX	Chlorhexidine
DDF	Department of Drugs and Food (Cambodia)
DFDA	Department of Food and Drug Administration
DNPL	National Medicines Regulatory Authority (Guinea)
DPM	Directorate of Pharmacy and Medicine
DRAP	Drug Regulatory Authority (Pakistan)
EFMHACA	Ethiopian Food, Medicine and HealthCare Administration and Control Authority
ERP	Expert Review Panel
FDA	Food and Drug Administration or Authority
FDQCC	Food and Drug Quality Control Center (Laos)
GMP	Good Manufacturing Practices
HPLC	High Performance Liquid Chromatography
ISO	International Organization for Standardization
LMHRA	Liberian Medicines and Health Products Regulatory Authority
MOH	Ministry of Health
MQM	Medicines Quality Monitoring
NHQC	National Health Products Quality Control Centre (Cambodia)
NTD	Neglected Tropical Disease
PMS	Post-Marketing Surveillance
PQM	Promoting the Quality of Medicines
QA/QC	Quality Assurance and Quality Control
QMS	Quality Management System
SOP	Standard Operating Procedures
TA	Technical Assistance
TB	Tuberculosis
UNICEF	The United Nations Children's Fund
USAID	United States Agency for International Development
USP	United States Pharmacopeial Convention
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification Program

Program Background and Framework

Since 1992, the U.S. Pharmacopeial Convention (USP) has worked cooperatively with the United States Agency for International Development (USAID) to help developing countries address critical issues related to poor quality medicines and their appropriate use. PQM's mission is to help ensure the quality, safety, and efficacy of medicines essential to USAID priority diseases, particularly malaria, HIV/AIDS, tuberculosis, and maternal and child health. The PQM program is USAID's response to the growing development challenge posed worldwide by falsified and substandard medicines. There is increasing recognition of the burden of these poor quality medicines and their threat to public health, especially in low- and middle-income countries. Falsified and substandard medicines can cause treatment failure and adverse reactions, increasing morbidity and mortality, and they may contribute to antimicrobial resistance. They represent not only a waste of scarce resources but also a substantial risk to public health. They further risk undermining decades of health investments, including those made by USAID.

Figure 1: PQM Program Reach Worldwide

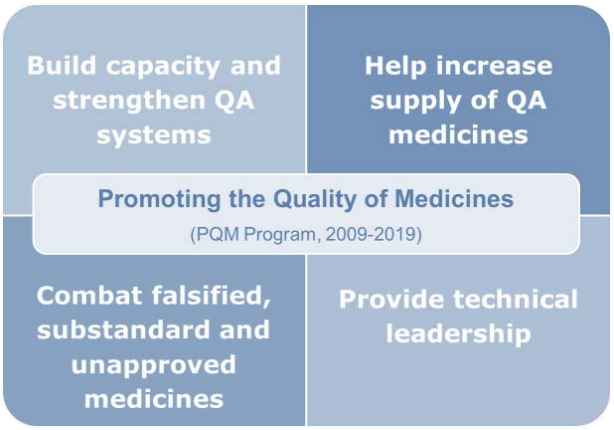
Global Overview of Progress

The PQM program has presence in four countries (Ethiopia, Indonesia, Nigeria, and Philippines) and programs in 34 non-presence countries. Using a systems-based approach, PQM offers technical assistance (TA) in several areas to achieve the above stated strategic objectives. Many of these approaches are replicated globally but tailored to fit the needs of individual countries or regions. These approaches include building the capacity of medicine regulatory authorities to review and approve quality essential medicines and strengthen their ability to protect their own population from poor quality medicines. PQM works with national and regional regulatory authorities to build sustained capacity for medicines evaluation, manufacturing inspection, and surveillance. PQM supports national quality control laboratories (NQCLs) through hands-on training and technical assistance to improve laboratory standards, with one goal being to assist those labs to attain internationally recognized certifications, such as International Standardization Organization (ISO) accreditation and/or World Health Organization (WHO) prequalification (PQ).

PQM also helps NQCLs implement or improve post-marketing surveillance (PMS) programs. One aspect of PMS is field-based medicines quality monitoring (MQM), which involves laboratory staff collecting medicine samples at sentinel sites. These samples are screened in the field using GPHF-Minilab™ and subsequently undergo confirmatory testing in the laboratory.

PQM's system-based approach also extends to medicines manufacturers. PQM experts in good manufacturing practices (GMP) travel to manufacturing sites to help companies improve their GMP compliance and develop dossiers to submit to the WHO Prequalification program.

PQM's work is based on four **Strategic Objectives** and four **Intermediate Results**:



IR 1	**National regulatory systems strengthened**
IR 2	**Availability of quality medicines increased**
IR 3	**Incidence of falsified, substandard, and unapproved medical products reduced**
IR 4	**Actions taken to support quality medicines at regional and global level increased**

IR 1: National Regulatory Systems Strengthened

Medicines quality assurance worldwide depends to a large extent on the capacity of national medicine regulatory authorities – a capable authority is a prerequisite to safeguarding the quality, safety, and efficacy of medicines in the market. Strengthening the national regulatory system, the first PQM intermediate result, encompass a diverse array of activities, from advancing national health policy to lending technical support to laboratories to providing trainings and essential equipment.

Pharmaceutical Policy

PQM advanced medicines quality assurance related policies, legislation, regulations, guidelines, and standard operating procedures (SOPs).

Nigeria PQM provided technical assistance and advocacy for the adoption of the national Quality Assurance Policy (QAP) developed with PQM support and recently adopted by Nigeria's National Council of Health at their annual meeting. The Council recommended sensitization to state governments on the policy. As part of the sensitization efforts, PQM was tasked with strategizing and developing a plan for the QAP guideline and SOPs. PQM will take the lead in dissemination which will be completed by the next quarter. During the second quarter, PQM initiated the development of the guidelines and SOPs to facilitate implementation of the QAP in six states. This will be concluded by next quarter. **Ethiopia** PQM continued to participate in a technical committee to review of the Ethiopian Food, Medicine and HealthCare Administration and Control Authority (EFMHACA) Proclamation 661, which defines the regulation of the food and medicines trade, as well as health care services in the country. PQM's recommendations have been incorporated into the proclamation which is currently under review for approval. **Indonesia** Following a year and a half process from development to approval, the Minister of Health signed Regulation Number 02/2016 entitled "Guidelines for Sampling and Testing Medicines from Government/Public Facilities." PQM assisted to develop the guidelines and supported the approval process.

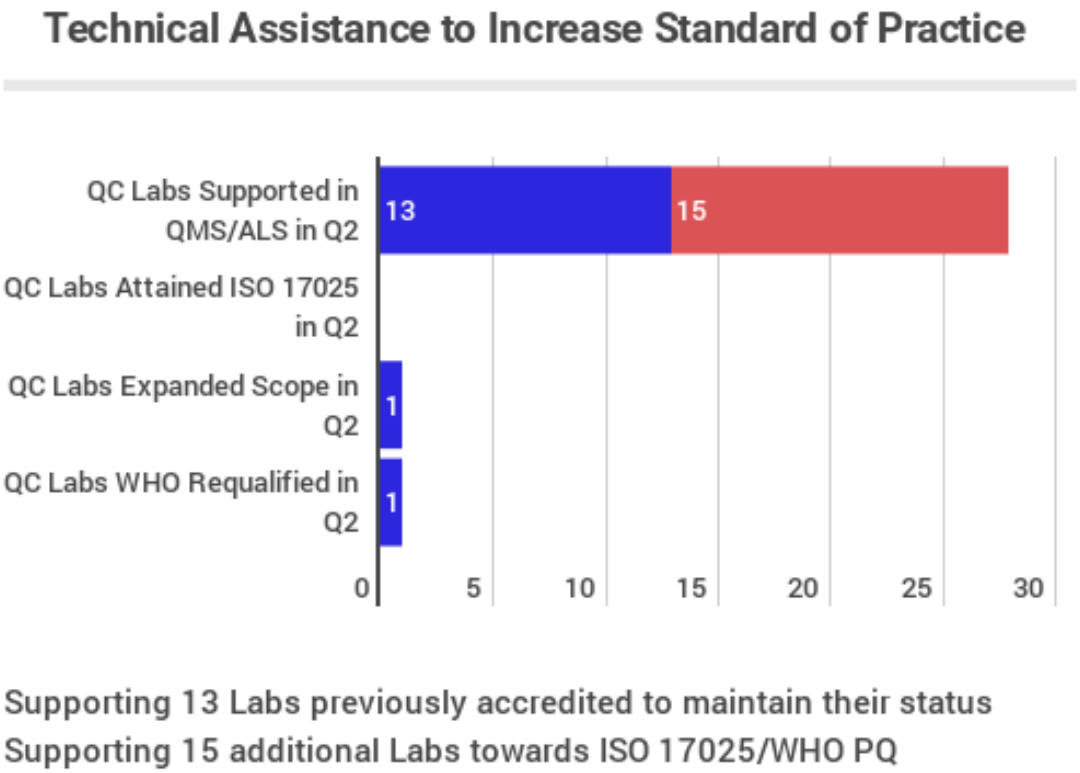
Medicines Registration

PQM supported medicine registration system strengthening, an essential regulatory function of a strong medicine quality assurance system.

Ethiopia PQM supported the Ethiopian Regulatory Authority (EFMHACA) to strengthen the medicines registration system and medical product registration. Trainings provided to EFMHACA staff on dossier assessment enabled the authority to conduct an initiative to assess medicine dossiers. In the second quarter, more than 300 dossier assessments were conducted with the assistance of staff from multiple directorates who have benefitted from basic dossier assessment trainings provided by PQM. The availability of trained staff within different directorates has allowed EFMHACA human resource flexibility to satisfy regional operational need. In addition, EFMHACA provided a five-day training to external dossier assessors from Addis Ababa University, Jima University, and the Ethiopian Pharmacy Association. This initiative furthers EFMHACA's strategy to increase the number of dossiers reviewed. The PQM program also supported the development of registration related documentation (revised clinical trial approval guidelines, draft guidelines for registration of biological products, etc.) to the Ethiopian authority's medical product registration system, thereby extending the reach of medical products for public health. **Guinea** PQM assisted the Guinean Regulatory Authority (DNPL) to develop a more robust registration system to ensure that all medicines entering the country are registered. PQM evaluated the existing registration system and enhanced its capacities for information management related to the registration processes and the development of secured medicines marketing authorization and secured certificate of analysis.

Technical Assistance to Increase Standards of Practice

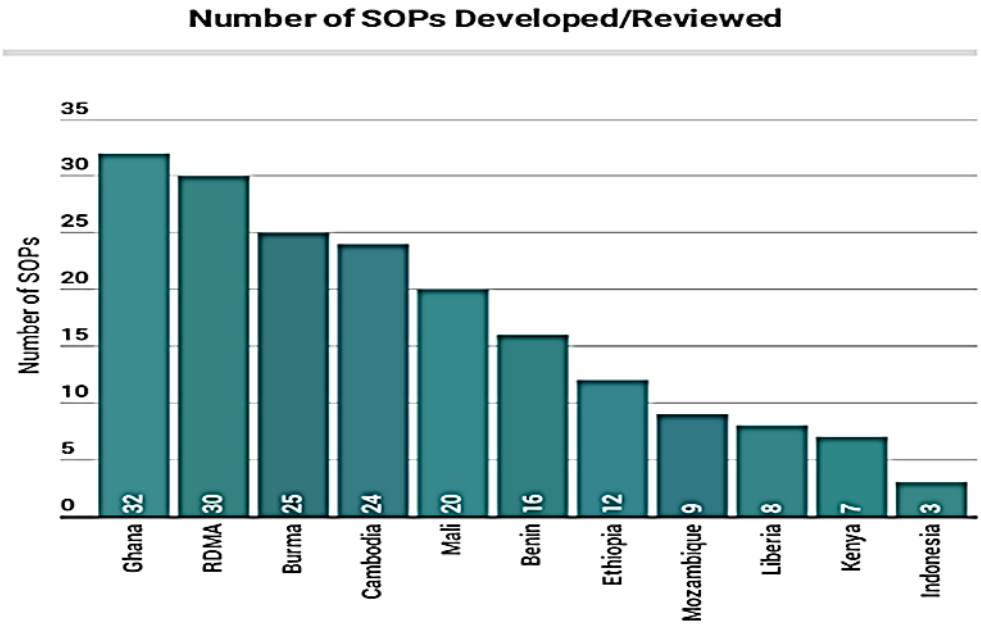
As part of accreditation, a laboratory's quality management system is thoroughly evaluated on a regular basis to ensure continued technical competence and compliance with ISO or WHO standards. PQM is supporting quality control laboratories to achieve accreditation with these international standards in order to make them technically competent and able to produce precise and accurate test and/or calibration data. This ensures these laboratories operate in line with quality standards.



Ethiopia In preparation for ISO 17020 certification, PQM conducted a rapid gap assessment of the EFMHACA inspection system and provided staff training. A concept note and terms of reference were developed in relation to the certification process and on-the-job ISO 17020 training was delivered to EFMHACA inspection directorate staff. The gap assessment lays the foundation for the development of tools based on the findings and ensures the inspection system's preparedness for ISO 17020 certification. **Ghana** PQM is reviewing 42 quality management system (QMS) documents submitted by the National Quality Control Laboratory in preparation for the upcoming ISO 17025 reassessment. **Laos** A PQM QMS team conducted a site visit to the Food and Drug Quality Control Center (FDQCC). The team reviewed the Quality Manual (QM) and seven SOP chapters for the current ISO/IEC 17025 accreditation. The team also analyzed and adjusted the roadmap for expansion of the scope of method-based accreditation. These steps lay the foundation for the FDQCC to submit an application to an international accrediting body anticipated in 2017.

Cambodia PQM continued to provide technical support to the National Health Products Quality Control Centre (NHQC) Laboratory through the development of 24 SOPs designed to meet the QMS and technical requirements of ISO/IEC 17025. **Nigeria** PQM held various trainings on key documents (Good Documentation Practices, Good Laboratory Practices, and Standard Operating Procedures, Quality Manual) in preparation towards ISO 17025 accreditation. A total of 108 professionals from three different laboratories have benefited from the training. Moreover, the ISO 17025 accredited laboratory received onsite mentoring on preparatory activities towards the American National Standards Institute-American Society for Quality National Accreditation Board (ANAB) surveillance assessment visit. **Kenya** The Kenyan NQCL was accredited ISO 17025 by the accrediting body, South African

National Accreditation System (SANAS), in June 2015. SANAS conducted a pre-surveillance audit of the NQCL to determine the maintenance of the accreditation. The audit revealed 26 major non-conformances and three minor non-conformances. PQM developed corrective and preventive actions (CAPAs) to address SANAS' non-conformances and provided technical assistance to update key documents.

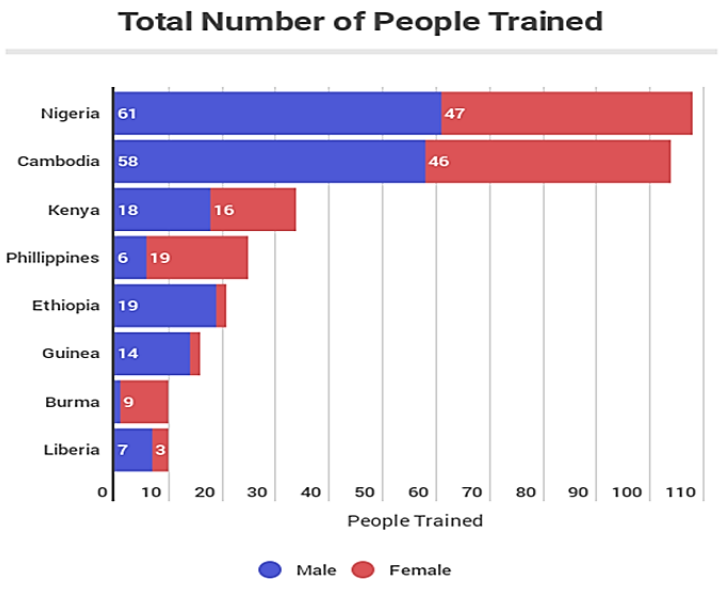


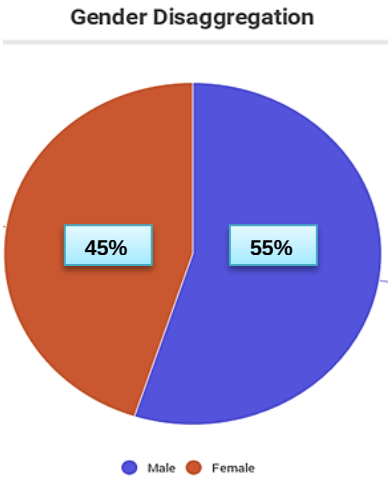
Mali In preparation of a consultation with Laboratoire National de la Santé (LNS) and its direct clients and partners, PQM reviewed assessment reports by Initiative 5% and the Center for Pharmaceutical Advancement and Training (CePAT), bodies that conducted recent assessments of LNS on behalf of Expertise France and the World Bank, respectively. Many of the issues identified in these reports were previously identified by PQM. The approach of PQM is to have LNS and key stakeholders directly involved in developing the LNS five-year strategic plan. PQM will organize a roundtable to reflect on future steps required to develop the plan. Additionally, since the microbiology laboratory of LNS is ISO 17025 accredited, several QMS documents are in place; however, a large number of documentations specific to Medicines Quality Control are lacking. PQM assisted LNS in drafting new SOPs and LNS submitted 22 SOPs to PQM for review. **Burkina Faso** PQM reviewed a Medicines Quality Control Laboratory's (LNSP) recent lab quality assessment that CePAT conducted on behalf of the World Bank. PQM drafted steps towards the implementation plan for strengthening the laboratory's QMS. **Thailand** PQM made an initial assessment on the status of QMS at Chula Pharmaceutical Technology Service Center (PTSC). The team developed: a strategic plan towards WHO PQ, CAPA plan and implementation, the Quality Manual, and 25 major SOPs were reviewed and translated. **Benin** PQM developed an implementation plan of 16 revised QMS documents for the national laboratory. **Burma** The national quality control laboratory, Nay Pyi Taw (DFDA), finalized its QM and submitted it to DFDA Senior Management for approval. A total of 25 key SOPs were also finalized and submitted to DFDA Senior Management for approval. **Indonesia** PQM QMS support of the Indonesian National Agency of Drug and Food Control (BPOM) provincial quality control laboratory in Manokwari was recognized by the government of West Papua through a national radio program broadcast, as well as through acknowledgement on BPOM's website.

Capacity of Lab Staff to Conduct Quality Assurance and Quality Control (QA/QC)

PQM provides continuous training opportunities to strengthen human resources for medicine quality management systems.

Nigeria PQM is in the initial stages of developing content for the e-learning platform 'PQM Academy.' The course is intended for policy makers, regulatory managers, government officials, local manufacturers, and others interested in learning more about the processes of GMP in pharmaceutical systems, problems that can occur as a result of poor manufacturing practices, and how it can impact on the quality of medicines. During the quarter, PQM also trained 128 professionals in several key areas of QA/QC and GMP management in Nigeria. **Mozambique** PQM trained four National Quality Control Laboratory (LNCQM) staff members on high performance liquid chromatography (HPLC) and eight staff on SOPs, as well as reviewed SOPs and the QMS. **Guinea** PQM provided training on the proper use of the recently procured HPLC system. The training included theory and hands-on training on how to conduct an assay using compendial method, as well as a refresher training on good laboratory practices (GLP) and good documentation practices (GDP) to 16 technical staff. **Cambodia** PQM delivered presentations at two workshops on good regulatory practices (GRP) and also on ISO/IEC 17025 accreditation attended by 104 Department of Drugs and Food (DDF) inspectorates from the central and provincial level. **Burma** A workshop on ISO/IEC 17025 on Internal Audit and Management Review was held for DFDA staff to reinforce QA/QC competency. **Indonesia** The PQM team participated in BPOM's workshop for QC laboratory supervisors from 32 provincial QC laboratories.





Training Areas:

i. GMP

ii. QMS

iii. GLP and GDP

iv. Good Regulatory Practices

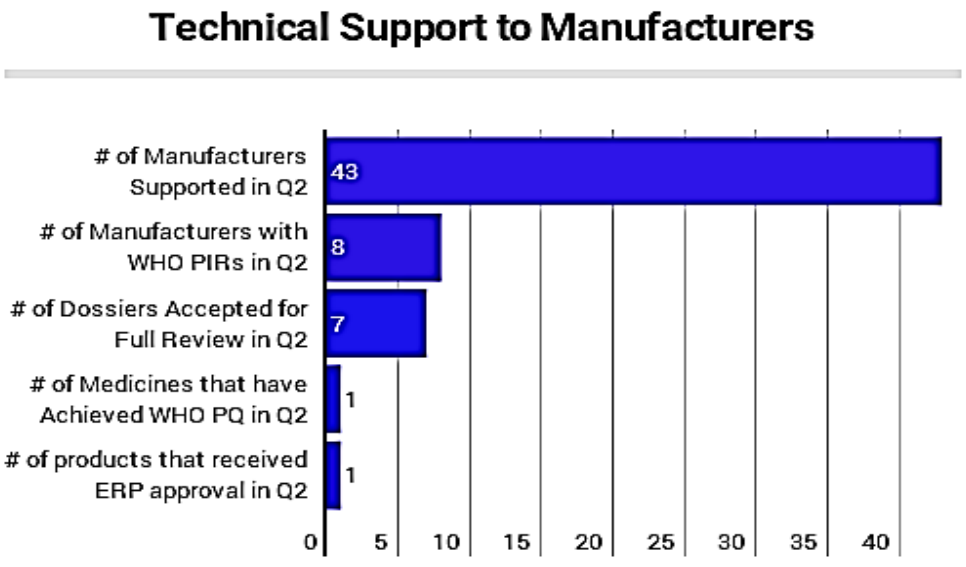
IR 2: Availability of Quality Medicines Increased

To increase the availability of quality-assured medicines in the global market, PQM supports select medicines manufacturers to become compliant with internationally accepted standards.

Technical Assistance to Manufacturers towards WHO PQ, Stringent Regulatory Authority (SRA), and Local National Regulatory Authority (NRA) Approval

PQM delivered broad technical assistance to manufacturers to address GMP and other quality-related issues. Technical assistance ranges from early initiatives to the final submission of the application, or dossier, to WHO, SRA, or local NRA.

Ethiopia PQM provided extensive technical support to Cadila Pharmaceuticals, which received WHO acceptance for full review of the tuberculosis medication, Ethambutol (400mg tablet). PQM reviewed the manufacturer's site master file and QMS in preparation of the WHO site approval visit. In addition, the manufacturer's bioequivalence (BE) and dissolution profile data for the product were also accepted. **Pakistan** With the objective of increasing the number of manufacturers obtaining WHO PQ, PQM visited four manufacturers (ATCO, Friends Pharma, ZAFA**,** and Akhai) to prepare dossier submission of chlorhexidine (CHX) gel, a WHO essential medicine widely used to prevent umbilical cord infection that can result in deadly neonatal sepsis. A stability study session was performed in Karachi and Lahore with technical personnel from the manufactures to go over Pakistan's regulatory authority's (DRAP) requirements for Stability Data Analyses of CHX Gel. ATCO Laboratories completed and submitted their CHX gel stability study to DRAP as part of the registration process. **Philippines** The PQM GMP team conducted a site visit to Hizon Laboratories to follow up on a 2015 assessment conducted by WHO PQ for Levofloxacin, an anti-tuberculosis medicine. The PQM team reviewed the GMP CAPA findings and developed a strategic plan to assess the steps forward toward WHO PQ. **Nigeria** PQM supported a local manufacturer to submit a dossier for zinc dispersible tablet, an essential micronutrient, to WHO and currently awaits the outcome from WHO PQ for the product.



Maternal, Newborn, and Child Health (MNCH) Program PQM supported a manufacturer in the production of commercial batch and full characterization of Magnesium Sulfate Injection, used for eclampsia and pre-eclampsia. **Neglected Tropical Disease (NTD) Program** PQM provided technical assistance to address issues with product dossiers, GMP, and other quality-related issues identified by six manufacturers of active pharmaceutical

ingredient (API) and finished pharmaceutical product (FPP) for a priority NTD medication, Praziquantel. **Nigeria** PQM continued to provide technical assistance to local manufacturers to strengthen medicine quality education. During the quarter, 13 staff from local manufacturers were trained in GMP, QMS, and formulation of amoxicillin dispersible tablet 250 mg and 125 mg. The amoxicillin manufacturing plant was also redesigned to meet GMP standards. **West Bank/Gaza** A full GMP assessment of two manufacturers in the West Bank, Beit Jala Pharmaceutical Company (BJP) and Birzeit Pharmaceutical Company (BPC) was conducted according to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines. The assessment prepares manufacturers for inspection and approval by a member of the PIC/S, which will enable them to obtain a marketing authorization (MA) to market their product(s) in the PIC/S country and expand the sale of their products to a broader international market. **Ethiopia** PQM supported APF Pharmaceuticals to produce medicines to treat opportunistic infection (OI) and maternal and child health (MCH) diseases. PQM is currently seeking comparator products for select OI medicines such as Ciprofloxacin and Doxycycline, as requested by the manufacturer.

Indonesia PQM delivered technical assistance to private, as well as state-owned pharmaceutical manufacturers. PQM supported three private manufacturers in the production of Levofloxacin (500 mg). PQM evaluated and reviewed seven SOPs and related documents for Zenith Pharmaceutical and implemented CAPA, as well as drafted a cleaning validation protocol for Kalbe Farma Pharmaceuticals. The state-owned manufacturer PT Phapros Tbk completed an Initial Evaluation Questionnaire for their existing FPP pediatric 3 fixed-dose combination (FDC) formulation for tuberculosis (TB) as well as its pediatric 2FDC formulation for TB. The questionnaire furthers PQM's plan to conduct necessary research to identify manufacturers interested in developing pediatric TB formulations listed in the current WHO expression of interest (EOI). Additionally, Kimia Farma made considerable progress towards recertifying for current good manufacturing practice regulations (cGMP) with the Indonesian Authority and is in the process of installing a new HVAC system in line with production of TB medicines (2FDC and 4FDC) and antiretroviral (ARV) medicine. In regard to progress made toward quality-assured TB medication to combat HIV co-infection, PQM continued to support Phapros Levofloxacin production through review of dissolution study protocols and data. Phapros is planning a pilot batch of its first line TB products (2FDC and 4FDC) and second line TB product in April 2016. PQM Indonesia also continued support to PT Indofarma's 2FDC for TB product through GMP trainings.

Availability of ERP Approved Products

Tuberculosis Program Through work with manufacturers, PQM achieved Expert Review Panel (ERP) approval of the TB medication, Kanamycin (500 mg solution for injection) finished product under category 1, which mean the Shanghai Harvest Pharmaceutical's product is permitted for time-limited procurement and listed by the Global Fund. This approval has ensured availability of a quality-assured essential TB medicine in critical shortage at a deeply discounted price. The initial order from has been placed and is being processed. In addition to the finished product, the Kanamycin API manufacturer also received WHO prequalification for its sterile API.

IR 3: Incidence of falsified, substandard, and unapproved medical products reduced

PQM combats falsified and substandard medicines in collaboration with a country's medicine regulatory authority and national health programs to establish a system to regularly examine the quality of medicines circulating in its markets. PQM supports the national regulatory authorities to assess existing QA/QC systems by selecting sites to monitor based on criteria such as epidemiology, geography, border region, history of trafficking fake medicines, etc. This also includes training field staff in sampling, testing with Minilab™ methods, and data reporting, as well as training Official Medicine Control Laboratory staff in advanced test methods.

Capacity to assess medical products quality improved

RDMA The Bureau of Vector Borne Diseases Control used the robust sampling protocol developed by PQM to collect samples in malaria tier one areas in Thailand (six provinces), which resulted in alarming failure test results of antimalarials – 34% (20 out of 58 samples) in 2015 as opposed to 22% (12 out of 54 samples) in 2014 and 1% (7 out of 709 samples) in 2012. However, where the government has placed a regulatory effort to implement the quality assurance of medicines, for instance in Laos, the results suggest the quality of medicines has been well maintained. In Laos, 64 samples of antimalarials and antibiotics were collected in the last quarter of FY15 at border areas and 62 of them went through confirmatory analysis in FY16. None of the samples failed quality testing. **Ethiopia** The PMS findings carried out by EFMHACA in collaboration with PQM showed six sampled medicines were substandard. Accordingly, EFMHACA sent an official letter to the respective importers and initiated recall of the substandard medicine samples. Similarly, as a result of PQM's support to EFMHACA branch laboratories, for the first time, a round of medicine samples collection and testing has been completed for 158 samples of five types of medicines as part of their PMS activities. These products are not among those that are supported by the PQM program. The PMS system is replicated for other non-PQM supported products, which demonstrates sustainability of the PMS program. Based on the findings, six samples of medicines were found to be substandard resulting in an EFMHACA initiated recall. The branch labs have also started a second round sample collection for PMS during the quarter. **Kenya** Four rounds of sampling and testing have been completed at five sites. The main findings identified substandard and falsified medicines, as well as expired and unregistered antimalarial medicines. Throughout the three first rounds, the monitoring of antimalarial medicines in these sites showed a decrease in non-conforming samples. **Amazon Malaria Initiative (AMI)** PQM provided technical assistance to strengthen in-country capabilities to perform PMS of medicines in the field through the implementation of a stepwise method known as the Three-Level Approach and also coordinated quality monitoring activities with the relevant country stakeholders. In collaboration with national stakeholders, PQM began collecting QC information of antimalarial medicines. This information will be presented at the annual AMI partners meeting in Q3 and discussed in the context of countries needs and capabilities towards sustainable QC programs. **Core Malaria** PQM began information collection at country levels on the extent of diversion of malaria medicines from the public to the private sector. The information obtained will be used by donors to identify risk areas for diversion and recommend follow-up actions.

Ghana Strides towards improvement of post-marketing surveillance were made in two areas: testing for Zinc formulations to initiate post-marketing surveillance of antimalarial and MCH-related medicines, and contract with Sproxil mobile technology company for field surveillance of medicines. Ghana FDA provided PQM with a spreadsheet of antimalarials that are registered in country; quality testing and improvements of tools will follow. **Amazon Malaria Imitative** To facilitate field comparison, PQM continues to support the development of an application for computers and mobile devices to enable inspector's access, online and

off-line, to a database of a country's registered medicines, thus supporting visual and physical inspection of medicines in the field. During this quarter, development of the tool by a contractor has advanced and completion is expected by the end of the third quarter. Initial databases for two countries have been finalized based on input provided by medicines regulatory authorities (MRAs) and will be integrated into the application for pilot studies.

Philippines PQM conducted a 5-year program review of the PMS program to identify the program development and implementation gaps, propose the strategies to program planning and maximize impact of PMS activities, and elucidate program highlights and lessons learned. The dissemination meeting was conducted in March with implementing partners and stakeholders to discuss the result of the program review and hear feedback on novel approaches to achieve PQM's objectives in the Philippines. The recommendations of the program review have been included in the revised work plan. **Nigeria** The review process of antimalarial PMS Protocol from the National Agency for Drug and Food Control (NAFDAC) was completed. Sensitization meetings were held with the directors of Laboratory Services and Post-Marketing Surveillance/Pharmacovigilance to consolidate the implementation plan for the first round of antimalarial MQM, which is expected to commerce next quarter.

IR 4: Actions Taken to Support Quality Medicines at Regional and Global Level Increased

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 entails contributing to expanding pharmaceutical quality-related health systems research, as well as developing innovative and efficient 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.

Technical Leadership

PQM strives to develop novel approaches to medicines quality by interfacing with academia and other actors active in the health systems field.

Cross Bureau PQM collaborated with Boston University (BU) to develop and test a multichannel chip for analysis of fixed-dose combinations. PQM reviewed progress on the project and provided feedback. One sample of Northrop (artesunate-amodiaquine) underwent testing using HPLC at the USP laboratory. The same sample is currently being tested using PharmaChk. BU tested a different batch of the same product to test a probe for amodiaquine. A new probe for Methoprim is currently being investigated using systematic evolution of ligands by exponential enrichment (SELEX) technology. **Core MNCH** PQM provided technical comments to the WHO draft International Pharmacopeia monographs for Misoprostol Dispersion and Misoprostol Tablets. The recommended suggestions will increase the user's capacity to access misoprostol product quality.

Advocacy on Quality of Medicines

PQM raises awareness about the dangers of falsified and substandard medicines and provides information to ensure access to the public and respective governments.

Cross Bureau To raise awareness about fake and substandard medicines, PQM co-authored an article in the *Malaria Journal*, "Fake Anti-Malarials: Start with the Facts" (DIO 10.1186/s12936-016-1096-x). This article is a report on key findings and discussions points of a meeting entitled 'Fake Antimalarials: Start with the Facts' held in May 2015, in Geneva, Switzerland, to disseminate the findings of the artemisinin combination therapy consortium's drug quality program. PQM was invited to the meeting as part of ongoing collaboration between PQM and the London School of Tropical Medicines and Hygiene.

Regional and Global Collaboration for Medicine Quality

PQM supports regional and global initiatives to promote medicines quality via regional partner meetings, development of regional databases and alert systems, as well as encouraging collaboration among stakeholders.

Cross Bureau PQM participated in the East African Community (EAC) regional workshop on post-market quality surveillance (PMQS). PQM supported the EAC initiative on harmonization of regulatory functions and made gains towards formalizing its relationship with the EAC Secretariat. At the workshop, PQM staff shared best practices in PMQS and provided guidance and advice for developing a regional pilot PMQS plan. Technical expertise was provided by PQM staff, and as a result of participation in this workshop, PQM continued to strengthen its relationship with the EAC Secretariat and other partners. PQM has established a partnership with Physikalisch Technische Bundesanstalt (PTB) in support to the EAC initiative to establish regional PMS. **Amazon Malaria Initiative** Regulations provide the contextual framework for sustainable implementation of the Three-Level Approach, which at the field level requires personnel that is trained in medicines' sampling procedures and quality control. In addition, screening methodologies employed in the field need to be updated or adapted to properly address a country's needs. With PQM support,

collaboration was established between one country (Peru) and an international (Global Pharma Health Fund - GPHF) stakeholder. This collaboration frames the work that will enable global utilization of methodologies developed initially by Peru to address its own needs. Peru's OMCL already developed and validated one method that will be included in GPHF Minilab™ Manual of Procedures.

Core Malaria The PQM Core Malaria team has begun preliminary trend analysis of antimalarial medicines quality control data from the medicines quality database. Data analysis is organized by region, including countries in Africa, Asia, and Latin America for the period of 2005 to 2015. Also, PQM is working on developing country profiles in terms of available trends, tools, and systems to support quality-assurance of malaria medicines in the countries. **RDMA** PQM facilitated the dissemination of case information obtained from the Greater Mekong Sub-region and through WHO-led Substandard/Spurious/Falsely Labeled/Falsified/Counterfeit (SSFFC) alert system via BREMERE Network. PQM took part in discussion on the implementation of the Quality Assurance framework together with implementing partners (Emergency Response to Artemisinin Resistance coordinated by WHO, The Asia Pacific Leaders' Malaria Alliance (APLMA), and Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM)/Regional Artemisinin Initiative) to identify areas for potential cooperation.

Pakistan Partner meetings fostered regional cooperation and increased opportunity for collaboration in support of medicines quality assurance. Two meetings were held to exchange and expand knowledge surrounding PQM activities: JSI Deliver, as well as the CORE Group Meeting organized by DRAP and attended by: USAID, UNICEF, WHO Ministry of Mother and Child, and potential CHX manufacturers. **Burma** PQM coordinated a visit to USP-India by five Senior Management staff from DFDA in February 2016. The visit strengthens regional cooperation on medicines quality assurance.

Mozambique PQM explored collaboration opportunities with WHO, the MISAU Pharmacovigilance Unit and the LNCQM to create a jointly shared database of adverse drug reactions and medicines that fail quality control testing. PQM also made plans to facilitate the government of Mozambique and LNCQM to request technical assistance from the Global Fund to improve the temporary working space of the LNCQM staff. **Philippines** A meeting with FDA, Department of Health (DOH)- National Tuberculosis Program (NTP), and Global Drug Facility (GDF) on the WHO's Collaborative Registration Procedure was held to facilitate a fast tracking of TB product registration of GDF donated medicines for the NTP. The confidentiality agreement was submitted to GDF for final review and PQM for approval. PQM headquarters (HQ) and the field office also participated in the 2016 Joint National Tuberculosis Program Review (JPR); PQM provided impactful recommendations to the JPR, particularly on Drugs and Supplies Management for Medicine Quality Monitoring and Quality Assurance system. The joint review supports quality assurance efforts among partners.

Indonesia PQM leveraged $3 million US dollars (USD) of Global Fund financing to support PQM priority provincial QC laboratories. The sampling and testing of these medicines will also be supported via the PQM-initiated Global Fund project to support procurement and training of BPOM quality control laboratories under the National TB Program's PR grant. The initial $1 million USD of reprogrammed TB funds supported procurement of ion chromatography machines and other equipment needed for testing certain TB medicines, such as amikacin, kanamycin, and streptomycin. **Cambodia** PQM leveraged funds to make its work possible, as well as the work of implementing technical and development partners (WHO, GFATM, and others). Most immediately, two trainings were held as a direct result of leveraged funds. The WHO country office held the trainings on Regulatory Inspection in the Pharmaceutical Distribution Chains for Inspectors and Good Laboratory Practices for the NHQC Staff.

Challenges

Both unforeseen as well as known challenges are an inevitable part of program implementation and are an important source of strategy recalibration and experiential-based growth. Aggregated program challenges encountered during the quarter are specific to manufacturers, laboratories, and regulatory authorities.

Challenges encountered working with manufacturers center around delays in addressing required actions, as well as in product delivery. In spite of PQM recommendations, various manufacturers delayed decision making as to how to address assessment findings which further impeded implementation of relevant CAPAs. At another manufacturer, delays originated upstream. An API supplier changed the production site and scheme of the API synthesis which posed significant delays in product development, validation, and dossier preparation. Some of the supported countries experienced delays in the delivery of procured consumables to conduct MQM activities for antimalarial and MNCH priority medicines.

Laboratory challenges encountered include high staff turnover, unresponsiveness, and procurement difficulty. The National Quality Control Laboratory in Kenya identified its main difficulty maintaining accreditation as high staff turnover, which also impacts PQM implementation, as turnover of staff often leads to the loss of the well-trained staff PQM collaborates with.

Finally, in some instances complex internal structures of national regulatory agencies impeded expeditious program delivery. Some authorities redefine or lack clarity in roles and responsibilities, which causes confusion and delay when delegating roles across regional and local administrations. Still other agencies are nascent and have yet to determine the agency's position within or independent of the government.

Lessons Learned

The experience of various PQM portfolios has illuminated lessons learned during the second quarter. The lessons highlight the importance of high-level regulatory agency buy-in to facilitate enhanced collaboration, as well as greater understanding of manufacturer capabilities and limitations. These lessons encourage program learning, as the lessons are integrated to improve program performance. In addition, lessons are transferrable to other current PQM programs and can also be incorporated during the planning stage of programs and work plans.

PQM managers identified high-level regulatory authority engagement as key to success of program implementation. The buy-in demands a high degree of diplomacy, communication, and collaboration on the side of PQM to effectively navigate relationships, reach agreement on intended actions, and execute program deliverables from the federal to the local levels. Specifically, the Nigerian portfolio was able to mitigate communication issues with the national regulatory agency by holding standing quarterly meetings to review shared commitments and clearly outline roles and responsibilities. The Pakistan portfolio, working with a newly formed agency, maintained a strong line of communication with the agency and together with PQM, worked to etch out their respective roles and areas of collaboration.

Flexibility to adjust to unique manufacturer circumstances was identified as a key lesson learned relevant to the PQM program as a whole. In the area of GMP, understanding the specifics of a manufacturer early on was found to greatly assist future interventions.

Sustainability

PQM strives to embed sustainability in its programming in an effort to create systems strengthened to the point that they may one day be self-sustaining. Sustainability in this context is defined as the set of physical resources, processes, regulations, and partnerships facilitated by PQM that enable the eventual independent operation and full function of the institution or program in compliance with its mandate. During the second quarter, PQM made gains in sustainability efforts in two main areas: in diversifying partnerships and funding streams, as well as strengthening national medicines authorities and local manufacturing capabilities where feasible. The latter enables countries to take steps towards eventual ownership of their quality assurance systems and guarantees supply of high quality and locally sourced medicines. The former allows authorities a contingency plan in the case that a funding stream becomes jeopardized.

During the quarter, PQM accomplished sustainability measures towards building competent national medicine regulatory authorities poised to operate without external assistance. PQM made headway in advancing sustainability through its work in developing pharmaceutical policies, bolstering of medicines registration, preparing laboratories for international accreditation, building laboratory capacity in QA/QC, supporting capacity to assess medicines quality, as well as supporting manufacturers to increase the supply of quality assured medicines.

Sustainability highlights related to building strong national regulatory bodies include: technical assistance in the development of the national QAP adopted by Nigeria's National Council of Health; enhancement of the information management system related to the registration processes of the Guinean Regulatory Authority; and preparation for ISO 17020 certification in Ethiopia through a rapid gap assessment of the EFMHACA inspection system and associated training. Highlights related to manufacturer support include: ERP approval of the TB medication, Kanamycin, finished product under category 1 for Shanghai Harvest Pharmaceuticals; support to a Nigerian manufacturer to submit a dossier for zinc dispersible tablet; and extensive technical support to Cadila Pharmaceuticals in Ethiopia for acceptance by WHO for full review of the tuberculosis medication, Ethambutol.

In the area of expanded and strengthened partnerships, as well as diversified funding, PQM made numerous gains. PQM participated in the EAC regional workshop on PMQS with the objective of harmonizing and strengthening regulatory functions across the region. PQM also established a partnership with PTB in support to the EAC initiative to establish regional PMS. The Three-Level Approach in Latin America provides guidance for the transition of government ownership of medicines' sampling procedures and quality control. With PQM support, collaboration was established between Peru and the Global Pharma Health Fund that will enable global utilization of methodologies developed initially by Peru to address its own needs. In Mozambique, PQM explored collaboration opportunities with WHO, the MISAU Pharmacovigilance Unit, and the LNCQM to create a jointly shared database of adverse drug reactions and medicines that fail quality control testing. PQM also made plans to facilitate the government of Mozambique and LNCQM to request technical assistance from the Global Fund to improve the temporary working space of the LNCQM staff. Finally, in the area of leveraging funds for increased financial sustainability, PQM was able to leverage $3 million USD of Global Fund financing to support PQM priority provincial QC laboratories in Indonesia. The initial $1 million USD of reprogrammed TB funds supported procurement of ion chromatography machines and other needed equipment for testing certain TB medicines. The funds leveraged will allow PQM programs to support capacity building and training in priority BPOM QC laboratories in an unprecedented manner using Global Fund funding. In Cambodia, PQM also leveraged funds to make its work possible, as well as the work of implementing technical and development partners (WHO, GFATM, and others). Most immediately, two trainings were held as a direct result of leveraged funds.

Management Overview

March 1, 2016 served to officially recognize a significant milestone in PQM's calendar given USP's official transition of staff at two country offices in support of PQM activities following successful registration. USP–Nigeria located in Lagos, saw the transition of 7 consultants to USP contracts. USP–Philippines saw the transition of 2 consultants across to USP contracts, whilst the occasion also served to acknowledge a similar transition made by USP–Indonesia located in Jakarta earlier in 2015.

The occasion was marked by a real time "Go Live" welcome, which served to connect the four country locations involved via videoconference. Introductions to USP's Executive Team were led by Chief Executive Officer, Dr. Ronald Piervincenzi, and Senior Vice President of Global Public Health, Ms. Kelly Willis. A series of onboarding trainings in support of further orientation of field-based staff have taken place subsequent to this initial welcome message as a way to ensure staff are fully orientated to both the organization, as well as the PQM program.

During the second quarter, PQM released the FY15 Annual Performance Report. The report provides details about activities from the last fiscal year, outlined by progress toward the four Intermediate Result areas. Also included in the report are highlights of individual portfolio accomplishments. The report was submitted to the USAID Development Experience Clearinghouse and shared with various partners to convey PQM's work with a broad audience.

Collaborations with key stakeholders continued to occur in the second quarter. With WHO, successful cooperation took place towards Regulatory Systems Strengthening (RSS). Together with USAID representatives, the PQM team hosted Michael Ward, WHO Coordinator for the Department of Essential Medicines and Health Products, in February. After the visit, members of the PQM team participated in the Bangladesh meeting to create a Roadmap for Strengthening the National Regulatory System for Medicines and Health Products. Subsequently, PQM continues to engage with WHO on work in Bangladesh and reflects on the progress already made through use of WHO RSS tools.

PQM also engaged with other USAID-funding programs to identify where collaboration between implementing partners can improve outcomes. PQM continues efforts to strengthen collaboration with the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) program, a complementary program to PQM in regulatory systems strengthening, to outline areas for increased synergy. Members of the PQM leadership team met with counterparts from Chemonics, the contractor for the Global Health Supply Chain/Procurement and Supply Management (PSM) Program to introduce PQM's technical assistance activities and areas of staff expertise.

CORE PROGRAM

Cross Bureau

Objective: Provide technical leadership

Activity 1: Increase awareness of the importance of medicines quality

To raise awareness about fake and substandard medicines, PQM co-authored an article, published in the Malaria Journal. This article is a report on key findings and discussions points of a meeting entitled 'Fake Antimalarials: Start with the Facts' held on May 28, 2015, in Geneva, Switzerland, to disseminate the findings of the artemisinin combination therapy consortium's drug quality program. PQM was invited to the meeting as part of ongoing collaboration between PQM and the London School of Tropical Medicines and Hygiene.

Activity 2: Develop risk-based quality assurance systems - Models for self-sufficiency and sustainability

The pharmaceutical market is expanding in developing countries. However, the resources deployed to assure the quality of medicines is limited, presenting increased challenges. Post-marketing surveillance (PMS) is a regulatory function that requires investment but does not generate revenue. Therefore, a risk-based approach for managing pharmaceuticals has generated interest and has been applied, to some extent, to PMS. During the quarter under review PQM initiated efforts at mapping current efforts at risk-based regulatory practices that may be applicable to developing countries. Progress is also being made with the development of the risk-based tools and guidelines. To advance its work in support of post-marketing surveillance in the EAC, PQM initiated efforts to establish a partnership with PTB in support to EAC regional PMS.

Activity 3: Provide limited technical assistance to Boston University for PharmaChk

PQM reviewed progress reports from Boston University and provided feedback. One sample of Northrop (artesunate-amodiaquine) underwent testing using HPLC at USP laboratory. The same sample is being tested using PharmaChk. BU tested a different batch of the same product to test a probe for amodiaquine. The batch tested at USP is currently being tested at BU. New probe for Methoprim is currently investigated using SELEX technology. BU developed and tested multichannel chip for analysis of fixed-dose combinations. Artesunate-amodiaquine was used to test the chip.

Activity 4: Technical leadership to regional networks of medicines quality assurance Professionals

The Cross Bureau senior program manager participated in the EAC regional workshop on post-market quality surveillance held on February 11-12, 2016 in Kigali, Rwanda. Participants included representatives from national regulatory authorities or equivalent authorities, as well as a PTB consultant and representatives from the World Bank. At the workshop, PQM staff shared best practices in PMQS and provided guidance and advice for developing a regional pilot PMQS plan. This was also an opportunity to gather information on PMS in participating Partner States. Technical expertise was provided at all sessions of the workshop by PQM staff, and ultimately the workshop culminated with recommendations for moving forward in the development of PMQS activities. As a result of participation in this workshop, PQM continued to strengthen its relationship with the EAC Secretariat and other partners. Ongoing collaboration with the EAC is planned for the third quarter.

PQM has been supporting the EAC initiative on harmonization of regulatory functions and is now in the process of formalizing its relationship with the EAC Secretariat. PQM will draft a concept note defining the area of support which will include GMP, PMS, Quality Management, and Information Technology/New Technologies. The concept note will be submitted to the EAC Steering Committee prior to its next meeting to be held in June 2016. A further planned step includes establishment of a Memorandum of Understanding between the EAC Secretariat and PQM.

Activity 5: Revise Health System Assessment Approach (HSAA)
PQM participated in the 2nd Office of Health Systems (OHS) Implementing Partners meeting to discuss guidance and instructions for updating HSAA. To improve the available tools for Health System Strengthening within USAID's vision for the 2015-2019 period, technical partners specialized in WHO's Health Systems Building Blocks were requested to review and update USAID's 'Health System Assessment Approach: A How-To Manual.' In this context, PQM has been involved during Q2 in the review of the 'Module for Medical Products, Vaccines and Technologies' of the 'Guidance on Assessing Health System Building Blocks' section of the manual. This module describes the importance of a management system for medical products, vaccines, and technologies and discusses indicators to determine the strengths and weaknesses of existing systems. In the original version, elements of quality were not thoroughly discussed, and PQM revised this module to ensure that aspects of QA/QC were properly addressed at all stages of the supply chain and in all processes discussed in the chapter; particularly but not exclusively, in sections related to laws, regulations, institutions, and surveillance. PQM review of this module will be integrated and delivered during Q3 to Abt Associates, the Health Finance & Governance Project partner that is coordinating the review and update process. PQM will coordinate with SIAPS to finalize the revisions and submit a single document.

Activity 6: Develop e-Learning course on medicines quality assurance
PQM drafted sections of the e-learning course. These sections deal with general definitions, the issue of poor quality medicines, and the importance of quality monitoring.

CORE Maternal, Newborn, and Child Health (MNCH)

The following progress on the Core MNCH portfolio is described. Implementation of activities recently began just after approval of the work plan was provided on March 15, 2016.

Objective 2: Help increase the availability of quality-assured MNCH medicines
Magnesium Sulfate Injection (500 mg/mL) is used for eclampsia and pre-eclampsia in women. PQM continued to plan the initial GMP gap assessment of the Galychpharm manufacturing facility. Key milestones that have been achieved by Galychpharm include: 1) the production of a commercial batch in the amount of 1000 L, and 2) full characterization of the product, including impurities.

Objective 3: Provide technical leadership
Misoprostol tablets are used for the prevention and treatment of post-partum hemorrhaging in women. Due to the instability of the API, it is typically available as dispersion in hydroxypropyl methyl cellulose (HPMC), thus making it easier to use in manufacturing misoprostol tablets. To date none of the pharmacopeias had published a monograph of test procedures and specifications for tablets creating a gap in the ability to perform quality control testing. To address this gap, the WHO published for discussion, draft monographs for Misoprostol Dispersion and Misoprostol Tablets for Inclusion in the International Pharmacopoeia. On February 9, 2016, PQM submitted technical comments to both draft monographs. The comments included recommendations to improve key monograph sections such as the dissolution and assay. The development of robust methods will allow for accurate analysis of misoprostol tablets during registration and post-market surveillance resulting in an increased capacity to assess medicine quality.

CORE Neglected Tropical Disease (NTD)

Objective 1: Increase access to quality-assured NTD medicines
Manufacturers with pending ERP applications have been shared from the WHO NTD team. Of several companies, CSPC Ouyi Praziquantel (PZQ) FPP has been found to be a promising company selected during Q2 for full engagement into the PQM technical assistance pipeline. ERP questionnaires have been previously completed; however, due to the API source non-compliance for GMP, CSPC was not able to pursue with answering the associated question from the WHO NTD team. PQM has evaluated several available options where currently CSPC is actively collaborating with PQM and has planned for the use of SRA approved API sources. PQM will arrange an onsite CSPC GMP compliance assessment.

Specific areas of full technical assistance to address particular product dossiers, GMP, and other quality-related issues have been identified for manufactures of PZQ API and FPP. The following companies have been under continuous technical assistance during FY16 Q2:

- Minsheng Bingjiang Pharma Praziquantel FPP (onsite GMP inspection has been conducted, and the company is currently under CAPA)
- Minsheng Shaoxin Pharma Praziquantel API
- CSPC Ouyi Praziquantel FPP Project
- Jiayi Pharma Praziquantel API
- Jiangsu Chengxin Pharma Praziquantel API
- Zhejiang Hisun Phama (onsite GMP inspection is planned during April 2016).

Objective 2: Technical support for bioequivalence study
Several efforts are ongoing for identification and selection of NTD medicines for BE support. The product type is to be identified upon successful quality compliance. The USAID/NTD team, the WHO NTD team, and PQM initiated discussions to strengthen collaboration in support to NTD manufacturers.

CORE Tuberculosis (TB)

PQM staff has been working diligently with the USAID Core TB group on approval of the FY16 work plan. Monthly meetings have been scheduled for discussion of work plan activities and updates.

Under the FY16 work plan, currently the following objectives were approved by the USAID TB team:

- Framework 1: Help increase the supply of quality-assured TB medicines
    - Sub-objective 1.1: Provide GMP and dossier technical assistance to manufacturers (new and existing) of TB medicines for SRA/WHO prequalification approval
- Framework 2: Provide Technical Leadership
    - Sub-objective 2.1: Participate in technical training on GMP and dossier requirements on current WHO and SRA procedures and other strategic development needs
    - Sub-objective 2.2: Strengthen capacity of the manufacturers and contract research organizations (CROs) on GMP and pharmaceutical quality related topics in collaboration with regional programs.

For those activities still under review by the USAID TB team, PQM staff has been working to provide all requested documents. Particularly, PQM submitted a concept note as requested by the USAID TB team. This concept note outlines PQM's collaboration with global and regional partners to ensure availability of quality-assured TB medicines in countries. The concept note includes the following activities:

- Work with WHO to identify countries and manufacturers that are part of or are planning to join the WHO's Collaborative Registration Procedure but lack capacity to fully utilize the system to allow the fast track registration
- Identify the regional initiatives for future technical assistance, ensuring registration of quality-assured medicines in the member countries of the region
- Collaborate with GDF to identify and provide a technical assistance to the countries where delay with registration of GDF TB medicines leads to interruption of supply including the new medicines and new formulations of pediatric fixed dose combinations.

Sub-Objective 1.1:
PQM provided assistance to manufacturers of priority TB products toward WHO prequalification or ERP approval.

Through the work with manufacturers, PQM was able to achieve two important successes. The Expert Review Panel approved of the 500 mg Kanamycin solution for injection finished product under category 1. Achieving this success has ensured availability of quality-assured essential TB medicine that is potentially in critical shortage. In addition to the finished product, the Kanamycin API manufacturer also received WHO prequalification for its sterile API.

Also during the quarter, PQM GMP staff provided assistance for WHO prequalification of the following products:

- Para-Aminosalicylate Sodium API: API Master File was submitted for prequalification at the end of March, but has not yet been accepted for review.
- Rifampicin API: Initial meeting to discuss the status of the dossier submitted and inspection outcome was held.
- Kanamycin API, non-sterile: Assistance in process development was provided.
- Clofazimine API and FPP: Comments on proposed bioequivalence protocol has been provided; originally, the GMP assessment for API and FPP facilities were to be held in March, but due to heavy process development work, PQM's assessment is

postponed to May/June 2016. The manufacturer currently is working on revising the BE protocols to include pilot studies and confirming a CRO to execute the BE study.

- Moxifloxacin and Gatifloxacin API: Preliminary walk-through of the facility discussion of technical assistance was held.
- Gatifloxacin FPP: Initial meeting to discuss technical assistance to manufacturers was conducted.

Sub-Objective 2.1:

PQM staff applied to participate in the WHO Quality Assessment Training Workshop. On March 31st, PQM staff members were notified that they were selected to participate in the training. This training is to occur May 16-19, 2016.

Sub-Objective 2.2:

USAID approved one workshop to be conducted in the Eastern Mediterranean region. PQM is proposing to hold the workshop in July 2016. PQM staffs are currently working on preparation of the workshop.

CORE Malaria

Objective 1: Identify countries where the extent of antimalarial medicine diversion from the public to private sector is occurring and use data for evidence based decision-making

PQM has begun planning to obtain information at country levels on the extent of diversion of malaria medicines from the public to the private sector. The information obtained will be used by the respective donors to identify risk areas for diversion and recommend follow-up actions.

Studies will begin in May 2016, and reports generated from the studies will be submitted one month after each study is completed.

Objective 2: Provide technical leadership & global advocacy to raise awareness about the potential dangers of using falsified and substandard antimalarial medicines

The PQM Core Malaria team has begun preliminary trend analysis of antimalarial medicines quality control data from the medicines quality database. Data analysis is organized by region, including countries in Africa, Asia, and Latin American for the period of 2005 to 2015. Also, PQM is working on developing country profiles in terms of available trends, tools, and systems to support quality-assurance of Malaria medicines in the countries.

On January 20, 2016, PQM's Core Malaria team attended and presented at a meeting planned by OHS/USAID and President's Malaria Initiative (PMI) to review the work of OHS implementing partners funded by PMI. At this meeting, the following was presented and discussed by PQM:

- PQM's mandate and how it relates to PMI's overall objectives for a world without malaria
- PQM's activity, results achieved, and outcomes from PMI funded field support activities for FY15/FY16
- Directed Core Malaria, field support, and Cross Bureau status updates, with a comparison of FY15/16 activities and recommendations for future work.

AFRICA & MIDDLE EAST

ANGOLA

Objective 1: Strengthen the capacity of the MOH/Divisão Nacional de Medicamentos e Equipamentos (DNME)

During the quarter, the results from the baseline medicine quality monitoring study conducted previously in Q1 in Luanda were reported to USAID and shard with DNME and IG. The results will also be disseminated to key stakeholders and partners during the next quarterly PQM trip proposed in June. A training session has been planned for the June/July timeframe to expand the scope by procuring Minilabs™ for additional sentinel sites sample screening.

Objective 2: Expand and support sustainable local capacity to monitor the quality of medicines in the country

Quotes for Minilab™ were received and the order was placed; a training session for the additional sentinel sites added for MQM is planned for June 2016.

BENIN

Objective 1: Strengthen the capacity of the National Quality Control Laboratory

PQM technical assistance for the NQCL is focused on building its technical and managerial capacities. Technical capacity building deals with equipping the lab, maintaining existing lab equipment, and training lab staff on analytical methods. Currently, the lab lacks a single functional HPLC system, essential equipment used for testing medicines following international standards. Due to the level of funding, a new HPLC system could not be procured for the lab. Instead, PQM attempted to replace the detector of an existing HPLC. Unfortunately, the manufacturer discontinued the series of HPLC that NQCL has. PQM negotiated a steep discount with another HPLC manufacturer to procure a new HPLC system. This final decision on the discount is currently pending approval from management of the manufacturer. USP is willing to contribute to the cost of the HPLC and PQM will cover the remaining cost. The procurement of the new HPLC system will include installation, qualification, and training of lab staff on the use of the equipment.

Managerial capacity building is focused on establishing a strong QMS. PQM assisted NQCL in developing an implementation plan for strengthening its QMS. The lab developed 16 QMS documents which include: Quality Statement, Quality Policy, Quality Manual, Organigram, three SOPs (Document Control, Confidentiality, and Conflict of Interest), five instructions (documents writing, approval and distribution, documents coding, and documents archiving), change control, list of internal documents distribution, list of revisions, evaluation form, recording form, and observations form.

Objective 2: Establish and support sustainable local capacity to monitor the quality of medicines in the country

PQM collaborated with NQCL to conduct a survey on the quality of antimalarial medicines especially artemisinin-based combination therapies (ACTs). To expand the capacity of NQCL in monitoring the quality of antimalarials to other departments, PQM procured Minilab™ supplies. Delivery of these supplies is expected in April. PQM will facilitate the sampling and screening of 400 samples.

BURKINA FASO

Objective 1: Strengthen the capacity of Medicines Quality Control Laboratory of LNSP
PQM shared this year's work plan with the management of LNSP and Directorate General of Pharmacy and Drug Laboratories (DGPML). PQM reviewed a recent assessment of the quality lab that CePAT conducted on behalf of the World Bank and drafted steps in the implementation plan for strengthening the quality management system of the lab. Further steps and timelines will be determined in collaboration with LNSP.

Objective 2: Establish baseline for the quality of antimalarial medicines
PQM procured one Minilab™ kit and supplies to be used for training staff from the LNSP, DGPML, Central Medical Store, and Ouagadougou University. The kit and supplies are expected to ship to LNSP in April. In preparation of the training, PQM coordinated with LNSP and DGPML to finalize the list of participants and clarify some logistics. The training is planned for May 16-20, 2016 followed by sample collection and screening. The training manual will ship to LNSP in April to give participants enough time to become familiar with the training content.

ETHIOPIA

PQM continued efforts to strengthen the capacity of Ethiopia's national regulatory authority, EFMHACA, to ensure the country's medicines and medical devices are reliable and safe for public consumption. PQM supported the authority's governance structure, branch laboratory functions, inspection capacity for authorities, and medical product registration system. Other areas of focus include supporting good manufacturing practices among local medicines manufacturers and deepening the post-marketing quality monitoring of medicines circulating in both the public and private markets.

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

The PQM program engaged in activities to improve the Ethiopian authority's medical product registration, thereby extending the reach of public health medicines. Registration related document improvements accomplished in Q2 include: revised clinical trial approval guidelines, development of medical device evaluation checklists submitted to EFMHACA, drafting of training SOPs for medicine registration, drafting of guidelines for registration of biological products, and provision of reference books on various registration and inspection topics (USP, Martindale, Goodman and Gillman, Book of Excipients) to EFMHACA. PQM also provided technical support to EFMHACA staff prior to their dossier assessment initiative, where over 300 medicine dossiers were assessed. In partnership with SIAPS, PQM co-developed the EFMHACA Medicine Regulatory Information System (MRIS). Lastly, PQM led a three-day training on assessment of food supplement dossiers to 16 EFMHACA staff in Adama.

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

PQM engaged in the strengthening of the authority's inspection system for regional and city authorities through assessment and guidance. A rapid gap assessment of the EFMHACA inspection system was conducted in preparation to ISO 17020 certification; development of a concept note and terms of reference related to the certification process has been completed and approved. A rapid inspection assessment was also conducted at the regional level at the Afar State Medicine Regulatory Authority. A 10-day training on Advanced GMP to EFMHACA staff was funded and conducted by PQM. The PQM team also prepared training materials on inspection of good distribution practice and good regulatory inspection techniques. The materials are in preparation for a training next quarter. Materials (GDP, good storage practices, and recall guidelines) were also completed and distributed to five regional and one city regulatory authorities. Additionally, PQM facilitated the procurement of nine global positioning system (GPS) devices to regional and city authorities.

Objective 3: Strengthen product quality testing system of EFMHACA

At four EFMHACA branch laboratories (Diredawa, Mekele, Bahir Dar, and Hawasa), PQM supported supervisory efforts to determine individual laboratory capacity. The supervisory activity was a joint effort conducted by PQM, the USAID-PMI Malaria Advisor, and EFMHACA staff. The findings include common strengths: competency to conduct compendia testing, active collection and PMS testing of samples, consistent use of Minilabs™ as part of lab inspection activities, HPLCs installed, and adequate related training provided; as well as common challenges: shortage of reference standards to conduct compendia testing, shortage of chemical and sample storage shelves, power fluctuations, missing laboratory inputs- performance verification test (PVT) glassware, and staff not fully trained on quality management system.

PQM led the second round of CAPA response for WHO PQ of the Product Quality Assessment Directorate (PQAD) laboratory and supported the development of eight new branch laboratory SOPs for instrument operation and seven laboratory log books for verification record and daily use of instruments.

PQM supplied proficiency testing (PT) samples to the agency; the samples include: HPLC, pH, loss on drying, Karl Fischer, water determination atomic absorption spectroscopy (AAS), Fourier transform infrared spectroscopy, AAS, and conductivity. The latter three PT samples are relevant to comply the requirement of ISO 17025 accreditation scope expansion. The samples are currently undergoing analysis at the EFMHACA main laboratory. PQM also supports the Regional Bioequivalence Center (RBEC) and provided HPLC equipment to the Addis Ababa University School of Pharmacy.

In human resources development, PQM arranged training for two individuals from EFMHACA's food laboratory in India and provided financial support to hire four branch laboratory staff.

Objective 4: Assist to build national capacity for human resource development in medical products, regulatory sciences
No activity implemented in this quarter.

Objective 5: Support to improve the GMP knowledge and skills of local medicine manufacturers to increase the availability of quality-assured medicines
PQM supported expanded GMP knowledge and skills of local medicine manufacturers with the intention of increasing the production of locally sourced quality-assured medicines throughout the country. PQM conducted a follow-up assessment of Cadila Pharmaceuticals master file and quality management system with the aim of preparing the manufacturer for a WHO site approval visit. PQM delivered technical assistance to APF Pharmaceutical Company to increase production of medicines for OI diseases. Currently, PQM is seeking comparator products for some OI medicines, such as Ciprofloxacin and Doxycycline, based on the request from the manufacturer. Preparatory work has been completed to conduct an awareness raising workshop on GMP in collaboration with Ministry of Industry, EFMHACA, Local Pharmaceuticals Association, WHO, and other stakeholders.

Objective 6: Strengthen survey/PMS of the quality of medicines circulating in the national market
PQM participated in the preparation of PMS protocols for OI, antimalarials, and MCH medicines and completed a survey of areas as input for a database cataloguing private and public facilities. Finally, a procurement request for laboratory consumables to be used for testing of FY16 PMS is being processed.

Objective 7: Strengthen the governance structure and program effectiveness of the food and medical products regulatory authorities
PQM participated in the review of Proclamation 661; the document was submitted to the authority's management team for further discussion and approval. The proclamation defines the power and structure of the Administration in terms of its ability to regulate food and medicines trade, as well as health care services in the country. Proclamation number 661 delegates any activity that is not given to the federal authority to regional/state governments and city administrations.

GHANA

Objective 1: Strengthen the capacity of the National Quality Control Laboratory Ghana FDA

To strengthen the capacity of the National Quality Control Laboratory, a total of 42 quality management system documents were submitted and reviewed in preparation for the upcoming ISO 17025 reassessment by ANAB. Training on relevant topics for the individual units undergoing assessment is planned for April 2016.

Objective 2: Support and strengthen post-marketing surveillance of medicines (PMI and MCH)

Testing for Zinc formulations was started at the laboratory and results will be finalized by Q3. The target was about 60 tablets and five different brands in 10 sentinel sites; due to delay in the fixed amount award (FAA), the MQM for FY16 is pending.

Objective 3: Support FDA registration and enforcement unit (PMI)

The Sproxil contract was finalized in Q2, and Ghana FDA has provided PQM with a spreadsheet of antimalarials that are registered in country. Quality testing and improvements on the L1 tool is planned for April-June 2016.

Objective 4: GMP Compliance (PMI)

A GMP compliance activity was planned during the quarter in anticipation for a Q3 discussion with Senior FDA Ghana on a workshop (April 2016), which will include the finalized GMP roadmap.

GUINEA

The outcomes of a past QA assessment revealed the immediate need to begin introducing initiatives in support of strengthening the capacity of the national quality control laboratory, Laboratoire National de Contrôle de la Qualité des Médicaments (LNCQM) and the regulatory authority, Direction Nationale de la Pharmacie et des Laboratoires (DNPL).

Objective 1: Continue building the technical capacity of the national quality control laboratory (LNCQM)

The LNCQM has a very limited technical capacity and limited resources to undertake the appropriate quality control of medicines. Consequently, the lab cannot provide concrete data to DNPL to adequately support regulatory actions.

To continue strengthening LNCQM's capacity, PQM procured one HPLC system. This instrument is used to conduct assay, a compendial method required to determine the quality and quantity of the API in a pharmaceutical product. Assay results obtained from this HPLC can be used as evidence to support regulatory actions. The newly procured HPLC was installed in November, 2015 by a technician from the manufacturer with support from the PQM technical consultant.

Also during the quarter, PQM provided training on the proper use of the HPLC system. The training included the theory and hands-on training on how to conduct an assay using compendial method. During this training, PQM also provided a refresher training on GLP and GDP. The HPLC, GLP, and GDP training were given to 16 technical staff (2 females and 14 males). The participants were given pre- and post-training quizzes on the HPLC. Prior to training, the mean assessment score was 18.3%. The post-training the score increased to 64.3%.

To be able to conduct testing routinely, PQM provided preventive maintenance training to three staff from the lab and repaired some lab equipment. The main activities conducted include the following:

- Assess the condition and update on the status of laboratory equipment since the last laboratory inspection visit;
- Conduct troubleshooting and repair non-operational equipment (balance, water pump, installation of transformer for the gas chromatograph donated by USP);
- Train users on basis troubleshooting for the HPLC and how to conduct preventive maintenance on the newly installed equipment.

Objective 2: Strengthen the DNPL functions by improving the existing registration and processes and reviewing pharmaceutical law documents

PQM plans to ensure that the DNPL has the necessary regulatory tools for its registration components to become fully operational elements of a strong quality assurance system. For registration, PQM proposed to assist DNPL in developing robust registration systems to ensure that all medicines entering the country are registered.

Putting adequate medicines registration in place will allow DNPL to improve its efficiency in processing marketing authorizations and better control the quality of medicines available in the country's markets. In line with this objective, during this quarter PQM evaluated the existing registration system and enhanced its capacities.

PQM interventions during Q2 improved partially the existing system but still more assistance needed to be fully operational by each staff of the registration department. Once the existing system is improved, DNPL will be able to generate additional income from registration fees. This income could be invested to bridge existing gaps in human and technical resources and to sustain this activity as part of strengthening the country's health system.

In FY15, PQM reviewed DNPL law documents and submitted a first draft of recommendations to the DNPL Director for review. As a follow-up to this activity, PQM conducted a workshop and reviewed the first draft with key stakeholders during the quarter. The main outcomes of this intervention include the following provisions:

- Provisions related the medicines registration:
  The Committee should decide the approaches and procedures it needs to ensure product efficacy, quality and safety. It is recommended to use a risk-based approach, including the use of a medicines evaluation committee, quality control procedures, fees for DPNL services, and good registration practices based on WHO models. DPNL lacks qualified human resources to carry out these tasks effectively at the present time;
- Provisions related to the registration of products other than medicines for human use, such as non-pharmaceutical health products, cosmetics, and medical devices;
- Provisions about the organization of the regulatory functions of DNPL, in particular the inspection of medicines in the supply chain/ on the market:
  Given the size of the informal market in Guinea, it is important that a unit of inspectorate be established under the authority of DNPL in order to ensure the application of the law and regulations;
- Provisions about the regulation of clinical trials in human and animal subjects and organ donations;
- Provisions related to governance and prevention of conflicts of interest.

KENYA

Objective 1: Continue strengthening the post-marketing surveillance of medicines in Kenya by improving the monitoring the quality of antimalarial and rapid diagnostic tests (RDTs)

Recently, Kenya's constitution decentralized many powers, including delivery of health services, to the counties. Key stakeholders are concerned about the ability of counties to procure medicines that meet the regulatory requirements of the national government. To prepare the counties to undertake their new role in procuring quality medicines, PQM collaborated with stakeholders to scale up the MQM program, expanding it to include new counties and ports of entry. Subsequently, the fifth round of MQM was expanded to six additional sites. Kenyan port sites were selected in endemic malaria zones based upon the large quantities of medicines that enter via air or sea.

As part of PQM's vision to support Kenya's overall strategy of attaining sustainability of established capabilities, during the second quarter, PQM conducted a trip to Kenya where the team from PQM and from Minilab™ company (Richard Jahneke) supervised the preparation of MQM round activities that include the following tasks:

- Selection of samples to be collected and tested;
- Sampling strategies (distributing on the number of samples to be collection from each sector: public, private and illicit market);
- How to collect good samples taking into account the challenge encountered during the previous MQM round;
- Conduct Refresher Minilab™ basic tests;
- Reporting data.

The above MQM activities were conducted by team leaders previously trained by PQM staff. The training was provided to 34 participants (16 males and 18 females). The training was new to some of the participants and a refresher for others. Thirty participants were sponsored through USAID PMI funds, while four participants were funded directly by their respective counties: Uasin Gishu (Eldoret), Migori, Kajiado, and Kakamega. This government initiative is part of sustaining MQM activities at the county level.

Objective 2: Strengthening the quality control of medicines in Kenya by sustaining ISO 17025 at NQCL

On June 2015, the Kenyan NQCL was accredited ISO 17025 by the accrediting body SANAS. To maintain this accreditation, during Q2, PQM conducted an assessment of the implementation of the ISO 17025:2005 quality management system program and preparation for the SANAS pre-surveillance audit of NQCL.

Prior to the SANAS audit, PQM conducted the following activities:

- Reviewed the QMS at the NQCL;
- Identified corrective and preventive actions;
- Prepared the NQCL staff for the SANAS assessment.

The SANAS audit revealed the following findings:

- 26 major non-conformances
- 3 minor non-conformances.

This high numbers of non-conformances were due to the instability of lab staff (more than seven staff left the lab) and managerial issues. Post-SANAS audit, PQM staff developed CAPAs to address SANAS non-conformances. As part of maintaining NQLC accreditation, PQM provided the following technical assistance:

- Quality Manual: updated and submitted
- Corrective and Preventive Actions: updated and submitted
- Internal Audit: updated and submitted

- Measurement Uncertainty: updated
- Purchasing: updated
- Document Control: reviewed/updated
- Document Master List: updated.

LIBERIA

Consistent with the 2015/2016 work plan, PQM has expanded MQM activities, supported the Liberian Medicines and Health Products Regulatory Authority (LMHRA) quality control capacity by establishing an action plan toward ISO accreditation and promoted appropriate regulatory actions.

Objective 1: Continue strengthening the LMHRA's Quality Control capacities
In accordance with the PQM established action plan to prepare the LMHRA QC laboratory for ISO 17025 accreditation, 45 SOPs have been reviewed, approved, and are now functional. Remote QMS training is ongoing, and the lab is gradually conforming to ISO 17025 requirements for accreditation. Presently at the QC lab, sample collection and testing are well documented, equipment is used in accordance with SOPs, and analyst reporting method has improved.

In continuation of PQM technical assistance to enable the lab gain ISO accreditation, PQM identified the following gaps, which are currently being addressed by the LMHRA and PQM:

- Structuring of lab personnel in accordance with ISO standard (model provided);
- Training in advance compendia method (quality control manager to be trained at USP);
- Train the lab staff on internal audit and management review;
- Review of the following 8 SOPs:
  - Use of Oven
  - Use of Water Bath
  - Use of Sonicator
  - Use of Centrifuge
  - Use of Water Purification System
  - Use of Hot Plate
  - Use of Vacuum Filtration Pump
  - Use of Safety Fume Hood.

Objective 2: Continue strengthening the LMHRA's Regulatory capacities

- LMHRA regulatory capacity strengthened using evidence-based data to support enforcement action. With support of PQM technical assistance, 40 new regulatory actions were taken.
- From February 29 - March 12, 2016, two of five registration department staff were trained at CePAT in dossier evaluation.

Objective 3: Monitoring antimalarial medicines quality (MQM) and promoting LMHRA to take appropriate regulatory actions based on evidence data
In January 2016, a team comprised of inspectors from the LMHRA, a PQM consultant, county pharmacist (representing the County Health Team), representatives from Liberian National Police (LNP) and local authority carried out a 10-day regulatory action in five counties. The team, acting on results from Minilab™ and compendia testing of MQM round five (MQM-5), removed several poor quality medicines from circulation. The team also seized the occasion to provide updates to stakeholders at the county level on poor quality medicine in circulation.

- **Monsterrado**: About 100 medicine shops and pharmacies were inspected. Several substandard medicines were removed from the market, especially in the Paynesville/Gardnerville belt. Amodaiquinie montherapy were found mainly in the Paynesville red light area. Storage facilities of hospital were found to be in good condition. Pharmacies were observed to be in compliance with LMHRA requirements. Thus, the major challenge with regulating medicines in Monrovia has to do with medicines shops in slum communities. Moreover, drug peddling was observed to be on the decrease in Monrovia and parts adjacent.

- **Bomi**: There are few medicine shops and pharmacies in Bomi County compared to all five counties. Ninety percent of the shops and pharmacies can be found in Tubmanburg. Fake quinine sulphate, manufactured by Sheechem was found in Gbah. The products were observed to contain the same batch numbers, but manufacturing and expiring dates were missing.
- **Margibi:** In Margibi, the County Health Team (CHT), Liberia Maritime Authority (LMA), and LNP joined the LMHRA/PQM team to remove several poor quality medicines from private medicines shops and open markets; Amodiaquine monotherapy and chloroquines in large quintiles were removed from shelves. To ensure that these products do not return on shelves, a team made up of CHT, LMA, and LNP were constituted to keep the surveillance ongoing even in the absence of the LMHRA.
- **Bong**: The team observed more poor quality medicines to be in circulation in Bong County. The Acting Superintendent of Bong County led the team that confiscated more poor quality medicines from Gbarnga general market and medicine stores. Amodiaquine monotherapy syrup was found in four medicines shops. Over 50 medicines shops were inspected in Gbanga, Phebe, and Totota. Substandard Lamivudine-Zidovudine-Nevirapine and Nevirapine manufactured by Strides ArcoLab Ltd. and Aurobindo Pharma, respectively were observed in Phebe hospital. With support from the superintendent's office, a team was set up, headed by the county pharmacist to keep the surveillance ongoing even in the absence of LMHRA.
- **Nimba**: MQM round five suggests Nimba County as the hot spot for poor quality medicines. This is largely owing to the fact that the county borders Guinea and Ivory Coast, where most of the unregistered products circulating in Liberia are smuggled from. 140 medicine stores were inspected and over 1000 boxes were removed.

Registration Status

MQM activities this quarter also discovered that more than half (58%) of the medicines circulating in Liberia are unregistered. This is because all public sector medicines brought in via National Drug Services (NDS) do not go through the LMHRA registration process. Thus, the LMHRA has little or no information to public sector medicine quality. Substandard Lamivudine-Zidovudine-Nevirapine and Nevirapine manufactured by Strides ArcoLab Ltd. and Aurobindo Pharma, Artesunate from Guilin Pharmaceutical, and Chloroquine manufactured by Syncom Formulation Ltd., found in the public sector during MQM-5, send out a clear warning that public sector medicines need to be quality-assured.

MALI

Objective 1: Strengthen the capacity of the National Laboratory of Health (LNS)

Activity 1: Develop a five-year strategic plan for LNS

In preparation of a consultation with LNS and its direct clients and partners, PQM reviewed assessment reports by Initiative 5% and CePAT who recently conducted assessments of LNS on behalf of Expertise France and World Bank, respectively. Many of the issues identified in these reports were previously identified by PQM. The approach of PQM is to have LNS and key stakeholders directly involved in developing the LNS strategic plan. PQM will organize a roundtable to reflect on the steps to be taken to develop the plan.

Activity 2: Strengthen technical capacity

PQM reviewed the status of lab equipment and their use. Several lab instruments are not in service and need maintenance and repair. Other lab instruments are underused due to the lack of qualified staff. A plan has been establish to repair and maintain the lab in May 2016.

Activity 3: Strengthen QMS

Since the microbiology laboratory of LNS is ISO 17025 accredited, several QMS documents are already in place. However, a large number of documents specific to medicines quality control have been lacking. PQM assisted LNS in drafting new SOPs, and LNS submitted 22 SOPs to PQM for review. They include the following:

Calibration of pH meter	Balance Sartorius	UV Visible Spectrophotometry
Methods selection, validation and transfer	Balance Scaltec	Laboratory notebook
Filtration of solutions	Laboratory cleaning	Use of Logbooks
Columns management	Preparation of solutions	Reference materials
Management of equipment	Laboratory safety	Thin Layer Chromatography for identification test
Out of specification results	Procedure of procedures	Dissolution tester
Glassware cleaning	Labelling	Use of pH meter
		Use of sonicator

Objective 2: Strengthen pre and post-market quality control of antimalarial medicines

PQM conducted inventory of Minilab™ supplies to identify the needs for the next round of sampling and testing of antimalarial medicines. Lacking supplies and consumables were procured and expected to ship by April 2016. To strategize the sampling during this round, PQM reviewed data from previous rounds. A new sampling plan is currently under development.

The lack of action taking when poor quality medicines are identified was previously discussed with the Directorate of Pharmacy and Medicine (DPM). The latter shared with PQM its 2016-2018 action plan, which includes support to the National Commission against Illicit Sale of Medicines and Counterfeit.

MOZAMBIQUE

Objective 1: Strengthen the capacity of the National Quality Control Laboratory LNCQM

PQM contracted Microsep, the qualified vendor of HPLC, to conduct training to four LNCQM staff on the use of the new HPLC. Four different dosage forms were used for the hands-on practical exercise of the HPLC training. PQM also conducted training to eight LNCQM staff on technical SOPs – how to use the weighing balance and perform daily calibration using external calibrated weight sets, investigation of out-of-specification results, and SOP on pH. Procurement of laboratory key consumables, reagents, supplies, and equipment were completed and shipped to the lab.

Objective 2: Support and strengthen post-marketing surveillance of medicines

The FY16 activity for MQM is delayed until there is clarity on FAA requirements.

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

A meeting was conducted in February/March 2016 with the head of the MRA regarding assistance with the pharmaceutical law. PQM obtained a copy of the law, and a working group session is planned for Q3 to assist the PD with drafting the regulations.

NIGERIA

Overall Quarter Progress
PQM made significant progress on strengthening NAFDAC regulatory capability. Follow up was completed on a prior gap analysis and basic trainings were conducted in preparation for ISO 17025 accreditation of three laboratories. A total of 128 participants from three regional laboratories and the central office were trained on Advanced GMP and QA.

In line with the preparation for accreditation, strategic equipment were procured for one of the laboratories including: Traceable pH Standard pH4.005, Traceable pH Standard pH7.000, Traceable pH Standard pH10.012, Buffer solution standard pH 12±0.05, Buffer solution standard pH 2±0.02 weighing bottle, Pyrex glass 40x80 weighing bottle, Pyrex glass 40x80 weighing funnels, borosilicate glass 3 ml weighing funnels, borosilicate glass 3 ml HYDRANAL Composite 5, HYDRANAL solvent, and HPLC reagents.

In an effort to sustain technical capacity and strengthen QMS and maintain ISO 17025 accreditation for NAFDAC Central Laboratory, Yaba, a surveillance audit was conducted by ANAB, which was a huge success. An ultrasonic bath was procured for the laboratory along with other relevant supplies such as HPLC grade water (columns), calibration service, and dissolution PVT kits.

GidiMobile, the technology firm responsible for the developing the e-learning platform (PQM Academy), presented the first demonstration on thin-layer chromatography (TLC) to the PQM Nigeria team. Next steps include provision of the narrative content and video recordings of six GMP modules (as a start) in batches within the next six months. Expected completion for each module may take about four weeks.

As a follow-up to the initial desk review conducted in the post-marketing surveillance directorate to ensure coordinated national post-market surveillance practice, the first draft of the PMS document was designed and is currently under review. Next steps include compiling and rolling out of the implementation plan to encourage regulatory action and facilitate a round of PMS activity.

PQM, as a major partner for the Pharmacists Council of Nigeria (PCN), promoted the Pharmaceutical Quality Assurance Curriculum review. The inaugural meeting was conducted to formally inaugurate the committee of 10 Nigerian academics to discuss opportunities to drive the incorporation of pharmaceutical quality assurance within the curriculum of Nigerian University programs. Gap analysis on the curriculum has been conducted by the committee.

The National QAP document, developed by the Federal Ministry of Health (FMOH) with support from PQM, was adopted by the National Council on Health, the highest health policy authority in Nigeria. This policy document mandates quality assurance and quality control considerations throughout the pharmaceutical supply chain. To operationalize this document, PQM has commenced meetings with the Director of the Food and Drugs Department of FMOH in this quarter. FMOH is partnering with PQM to draft the guidelines and SOP for implementation, which will bring together all stakeholders on purpose and modalities for implementation.

During this quarter, technical assistance was provided to local manufacturers through capacity building on Advanced GMP. Topics included:

- Quality management,
- Sanitation and hygiene
- Complaints and Recalls
- Contract Production and Analysis
- Self-inspection
- Personnel

- Premises
- Equipment
- Materials
- Documentation.

The listed topics were geared towards improvement of GMP compliance to work on their quality management system and processes in line with the mission's goal to increase local manufacturing for MNCH priority medicine and antimalarial medicine. A total of 108 professionals (61 males and 47 females) participated in this training. PMQ also identified an expert in water qualification and validation to assist one local manufacturer in improving the water qualification and validation process used in the manufacturing premises.

In response to ERP submission to UNICEF by manufacturers (Chi Pharmaceuticals, Drugfield Pharmaceuticals, and Daily Need Group for Zinc dispersible tablet, Chlorhexidine gel, and amoxicillin dispensable tablet), PQM accompanied UNICEF to conduct an audit of the GMP status of the listed companies. Chi was successful while the other two local manufacturers had few corrective and preventive actions which were raised and PQM has continued to support the identified local manufacturers to close the gaps.

Objective 1: Strengthen NAFDAC Regulatory capacity
Sub Objective 1.1: Build technical capacity towards ISO 17025 Accreditation for NAFDAC's regional laboratories-Agulu and Kaduna regional Laboratories
Activity 1.1.2: Provide Basic trainings on GDP, GLP to Kaduna laboratory staff
One-week intensive training was delivered to 24 NAFDAC Kaduna Regional Laboratory staff members (11 females and 13 males) on preparatory activities towards ISO 17025:2005 laboratory accreditation. Staff members were trained on the following topics:

- ISO 17025:2005 basic requirements
- Good Documentation Practices
- Good Laboratory Practices
- Standard Operating Procedures
- Quality Manual.

After each training session, participants developed their post-training action plans to implement the gained knowledge. Post training discussions, the trainees appreciated the need to review and adjust their standard of operation, in keeping with the training approach of Cooperating, Learning, and Adjusting (CLA), as preparations are geared towards ISO 17025 accreditation.

Activity 1.1.5: Procure relevant reagents as need
PQM, in line with the work plan, procured relevant reagents for Agulu regional laboratory. The procured items include:

Description of Goods	Quantity
Traceable pH Standard pH4.005	10
Traceable pH Standard pH7.000	10
Traceable pH Standard pH10.012	10
Buffer solution standard pH 12±0.05	10
Buffer solution standard pH 2±0.02	10
Weighing bottle, Pyrex glass 40x80	1
Weighing bottle, Pyrex glass 40x80	1
Weighing Funnels, borosilicate glass 3 ml	1
Weighing Funnels, borosilicate glass 3 ml	1
HYDRANAL Composite 5	3
HYDRANAL solvent	3
Visitor spectacles	3

In addition, more items were procured for NAFDAC central laboratory situated in Yaba, Nigeria to maintain the accreditation status of the laboratory. These items include:

Description of Goods	Quantity
Ultrasonic Bath	2

Activity 1.3: Strengthen NAFADAC's post marketing surveillance directorate technical capacity for effective PMS

Following PQM's technical assistance to NAFDAC's post-marketing surveillance, the first draft of the document has been designed and is being reviewed. Next steps include compiling and roll out of the implementation plan to encourage regulatory action and facilitate additional rounds of PMS activity, including MQM.

Activity 1.5: Enhance NAFDAC personnel technical capacity

The concept of an e-learning platform is in the work plan as NAFDAC Academy. The first demonstration on TLC has been presented. Next steps include provision of the narrative content and video recordings of six GMP modules (as a start) in batches within the next six months. Expected completion for each module may take about four weeks.

Activity 1.8: Collaborate with Academia to support pipeline for skilled professionals

In line with the approved work plan, PQM supported PCN to facilitate an inaugural workshop consisting of 10 Nigerian Academics on Pharmaceutical Quality Assurance Curriculum review held on Tuesday, January 12, 2016 in Abuja, Nigeria. This was conducted to formally inaugurate the committee and discuss opportunities to drive the incorporation of pharmaceutical quality assurance within the curriculum of Nigerian University programs.

The constituted committee conducted a gap analysis on the current curriculum and presentations on findings in QA, curriculum development, and training/collaborating center. The PQM team provided additional content, which will be reviewed by the committee.

Activity 1.9: Operationalize the recently developed Quality Assurance Policy QAP in geo-political zone

One of the key milestones achieved this quarter includes the National Council of Health approving the Assurance Policy for Nigeria developed by PQM. The preparation for operationalization of the QAP document commenced with meetings held with the Director of the Food and Drugs Department of the Ministry of Health. The agreed first step in the operationalization exercise has commenced, which is to draft the guidelines and SOP for implementation, as this will inform all stakeholders on purpose and modalities for implementation. Next steps will include concluding the draft and review process of the guidelines and SOPs and facilitate implementation in six states by next quarter.

Activity 1.11: Human capacity building for Local manufacturers

PQM continued to help strengthen the capacity of local manufacturers. During the quarter, the PQM GMP team visited 13 local manufacturers to identify areas of common need in the industry. The identified areas of need provided the platform for two onsite quarterly trainings. GMP topics of discussion during the trainings include: introduction to validation and qualification and process validation.

As a result of the identified needs, one of the local manufacturers visited requested PQM's technical assistance in collaboration with a GMP expert from India to redesign their plant to meet international standards. The process of redesigning the plant was completed and construction is expected to commence shortly. Also, two visits were made to two local manufacturers: Daily Need Group and Drugfield Pharmaceuticals.

Activity 1.12: Strengthen Technical Capacity for PQM Staff

In line with the work plan, internal trainings were held, consisting of eight local PQM staff, (four males and four females), on USAID procedures. The trainings included:

- Total Time Accounting
- Petty Cash Management
- Human Resource

- Procurement and Inventory.

Objective 2: Increase the supply of Quality-assured medicines locally

Activity 2.1: Provide Technical Assistance to local manufacturers of MNCH priority medicine

In line with the work plan to scale up the increase of local manufacturers for MNCH priority medicine, technical assistance was provided to local manufacturers in formulation, documentation, design to meet GMP requirements, management system, and processes. PQM also identified an expert in water qualification and validation to assist one of the companies to improve the water qualification and validation process used in the manufacturing plant.

The UNICEF/PQM audit of companies that manufacture Zinc dispersible tablet, Chlorhexidine gel, and amoxicillin dispersible tablet resulted in recommended CAPAs for two companies. During this quarter, the PQM GMP team continued support to ensure the identified manufacturers complete the process of CAPAs identified during the audit.

Activity 2.2: Provide Technical Assistance to local manufacturers of Antimalarial medicine

During the quarter, advertisement placement for the production of antimalarial medicine was distributed to interested local manufacturers. Thirteen local manufacturers responded to the advertisement. After cross examination of the GMP status of the interested manufacturers, four companies met the required standard, as three of the selected have WHO GMP prequalification, while one of the companies is in the process of acquiring the WHO GMP prequalification. The process of gap analysis commenced immediately after selection process and will be completed before the end of the next quarter.

Activity 2.3: Provide Technical Assistance to NIPRD Analytical Lab towards ISO 17025 accreditation to support local manufacturing

In this quarter, a four-day training workshop on preparatory activities towards ISO 17025:2005 laboratory training was provided to staff of the National Institute for Pharmaceutical Research and Development Agency (NIPRD) held on March 21-24, 2016 at NIPRD in Abuja, Nigeria. A total of 85 staff (34 females and 51 males) were trained on the following ISO 17025:2005 basic requirements:

- Good Documentation Practices
- Good Laboratory Practices
- Standard Operating Procedures
- Quality Manual.

Post training sessions, trainees developed their post-training action plans to implement the gained knowledge in preparation for accreditation.

SENEGAL

Objective 1: Strengthen capacity of DPM and support enforcement of its regulatory actions

No activity has been implemented during this quarter.

Objective 2: Continue strengthening the capacity of Laboratoire National de Contrôle des Médicaments (LNCM) and assist the lab to reach ISO 17025 accreditation

To support LNCM in reaching its milestone of attaining ISO 17025 accreditation, PQM proposes the following activities: procurement of new HPLC system, calibration of all newly procured equipment, compendial training, accrediting body visits, and cost of Tunisian Accreditation Council (TUNAC) accreditors. To this end, during the quarter, PQM assisted the lab in procuring new HPLC delivered to the lab. The installation of the new HPLC and training on its proper use is scheduled for Q3**.** Upon installation of the new HPLC, PQM will organize an assessment visit by auditors from TUNAC.

Objective 3: Continue sustaining an integrated post-marketing surveillance of medicines in nine sites

As part of sustaining PMS activity by LNCM and DPM, PQM initiated two FAAs during the quarter. The FAA will prepare the two government organizations (LNCM and DPM) to receive USAID funds and build their capacity to effectively manage USAID fund.

The FAA of DPM and LNCM include activities pertaining to conducting one round of MQM activities. The main activities to be conducted by LNCM and DPM include:

- Minilab™ supplies, reagents, and chemicals to conduct one round of sampling and testing of antimalarial samples and other essential medicines in nine sites
- Technical assistance to collect good samples
- Travel logistic coordination for sampling and testing with focal point and PNLP
- MQM dissemination meeting
- Regulatory actions to be taken by DPM according to the new inter-ministerial workshop August 2015 recommendations.

PQM submitted all required documents and provided guidance to LNCM and DPM on how to fill in the forms. The final drafts of the two FAAs will be shared with USAID HQ and the USAID Mission in Senegal in Q3 for final review and implementation by LNMC and DPM.

WEST BANK/GAZA

Palestinian pharmaceutical companies manufacture a wide range of generic products. The Palestinian Authority and pharmaceutical industry sources suggest that the local industry covers 35-40% of the Palestinian pharmaceutical market, while the remainder is imported from other countries, including Israel. The total value of the country's annual supply is estimated at $65 million, of which $25 million constitutes local products and $40 million is sourced from abroad. A potentially important market for Palestinian products is East Jerusalem, which currently is not accessible due to the lack of a mutually acceptable regulatory harmonization that would assure the quality of the products. Although some local manufacturers sell selected products outside Palestine, their share of sales is very small. To be competitive and expand their sales, all manufacturers are seeking other potential markets including Middle East and North African (MENA) countries, European countries, and, for some manufacturers, the United States.

Objective 1: Provide technical assistance to Palestinian pharmaceutical manufacturers to meet WHO and/or PIC/S GMP standards

During Q2, PQM staff and a consultant conducted a full GMP assessment of two manufacturers in the West Bank. These included Beit Jala Pharmaceutical Company (BJP) and Birzeit Pharmaceutical Company (BPC). The full assessment was carried out according to the PIC/S guidelines. This will prepare manufacturers for inspection and approval by a member of the PIC/S, which will enable them to obtain a marketing authorization to market their product(s) in the PIC/S country and expand the sale of their products to a broader international market.

PQM staff is planning to conduct similar full assessment for two other pharmaceutical companies in Q3, in addition to training the Palestinian Authority staff in inspection according to PIC/S guidelines.

ASIA

BURMA

Objective 1: Build and strengthen the capacity of DFDA laboratories in Nay Pyi Taw and Mandalay

Progress toward achieving ISO/IEC 17025 of DFDA Nay Pyi Taw laboratory was made during the quarter. The PQM team depends on the availability of funding and dedication of DFDA towards ISO. This quarter, PQM's technical assistance was prioritized and allocated towards strengthening the lab's resources and capacity enduring the implementation of the Good Practices of Pharmaceutical Quality Control Laboratory and Quality Management System.

Activity 1.4: Train the Nay Pyi Taw laboratory staff on ISO/IEC 17025 clause 5, Internal Audit and Management Review

PQM trained the laboratory management and QA team on the Internal Audit procedures and Management Review by the top management of DFDA Laboratory, both of which are essential for ISO/IEC accreditation. This training will be combined with ISO/IEC 17025 clause five training, which encompasses technical requirements for the accreditation.

Objective 2: Strengthen the national surveillance system to detect substandard, falsified and counterfeit medicines and halt the banned oral artemisinin-based monotherapies from the market.

Activity 2.1: Conduct training on Pharmaceutical supply chain inspection to DFDA inspectorates

PQM began planning for a training of 10-15 DFDA inspectorates on techniques involved in pharmaceutical supply chain inspection practices, process, procedures, proper recording of findings, and reporting. This training will be considered as training for trainers so the participants will be able to train the new inspectorates entering the DFDA. In this way, the outcome of the training will have significant impact on strengthening the inspection systems of DFDA.

Objective 3: Provide technical leadership in medicines quality and reinforce the program effectiveness and visibility in the Burma as well as improve connection with the regional activities

Activity 3.3: Participate and present PQM data and findings in relevant regional and international arena.

PQM sponsored a team of DFDA staff to visit the USP-India facility. The visit took place on February 17, 2016. The purpose of the visit had three main objectives: strengthen the relation between DFDA and US; gain exposure and knowledge of the functions and working environment of an internationally recognized USP laboratory, which is operating at the highest standards; and understand the key components and standards of an ISO 17025 accredited laboratory and incorporate the gained experience in preparations towards ISO 17025 accreditation of DFDA laboratories.

Activity 3.4: Maintain country consultants for effective coordination, communication with the PMI – USAID/Country Mission, and follow up of program implementation, monitoring, and evaluation

PQM maintained effective coordination, communication, and interaction with the PMI-USAID country mission, as well as with other partners in Burma for successful program implementation. The unique political environment in the country continues to change; in spite of this, PQM's program continues to be present and relevant in Burma's public health environment.

CAMBODIA

Objective 1: Build Capacity and Strengthen QA/QC Systems

Activity 2: System for Document and Record Control implemented. This requires NHQC to have a written procedure for activities and objective evidence the procedures are being followed.

During the course of the second quarter, PQM continued to provide technical support to the National Health Products Quality Control Centre (NHQC) laboratory with the development of their documents toward meeting the QMS and technical requirements of ISO/IEC-17025.

Activity 3: System for Equipment maintenance and calibration implemented.

This requires NHQC to have a written procedure for activities and objective evidence the procedures are being followed.

Activity 4: System for Non-Conforming Work and Out of Specification Identification, Documentation and corrections implemented.

This requires NHQC to have a written procedure for activities and objective evidence that the procedures are being followed.

INDONESIA

Note**:** PQM Indonesia activities under approval of the MRA (BPOM) have been on hold pending US Government–Government of Indonesia negotiations on implementing the terms of the Assistance Agreement. PQM Indonesia anticipates resuming activities during Q3.

Objective 1: To increase the local supply of quality-assured TB and HIV medicines in Indonesia by providing technical assistance to selected pharmaceutical manufacturers and contract research organizations to achieve international standards, including WHO Prequalification

Zenith Pharmaceuticals levofloxacin 500 mg product: PQM evaluated/reviewed seven SOPs and related documents for Zenith Pharmaceutical's levofloxacin 500 mg product currently under development through the WHO PQ program in Indonesia. PQM is also in the process to review the draft Dossier Module 3 and QOS Module 3 in common technical document (CTD) format, as well as following-up on CAPA progress following PQM's audit. PQM also provided laboratory consumables for QC testing at Zenith's recently renovated laboratory. Zenith Pharmaceutical is optimizing the levofloxacin 500 mg product formulation with PQM Indonesia's support and aims to submit its dossier to WHO towards the end of 2016.

Sanbe/Caprifarmindo levofloxacin 500 mg product: PQM provided reference materials (chemical and documentary standards including levofloxacin related compounds A, B, C and prednisone tablets) according to WHO requirements, as well as needed laboratory equipment for HPLC analysis. Sanbe/Caprifarmindo anticipates submitting its product dossier to WHO by the end of 2016.

Kalbe Farma levofloxacin 500 mg product: PQM continued following up on progress towards CAPA implementation/completion and preparation for drafting the cleaning validation protocol.

Pediatric FDCs for TB: To conduct necessary research and identify manufacturers interested in developing pediatric TB formulations listed in the current WHO EOI, PQM requested local state-owned manufacturer PT Phapros Tbk to complete an Initial Evaluation Questionnaire (pediatric 3FDC formulation Rifampicin 75 mg/Isoniazid 50 mg/Pyrazinamide 150 mg and pediatric 2FDC formulation Rifampicin 75 mg/Isoniazid 50 mg). The Initial Evaluation Questionnaire was completed by PT Phapros Tbk and submitted to PQM for review and consideration.

Kimia Farma's TB Medicine (2 FDC and 4 FDC) and ARVs Medicines: Kimia Farma has made considerable progress towards re-certifying for cGMP with BPOM and is in the process of installing a new HVAC system for the non-beta lactam area (which currently has a suspended cGMP certificate from BPOM), as well as installing new equipment for granulation, weighing, tableting, and packaging in the FDC production area (machine FBD, dehumidifier, super mixer, tableting machine, and blistering). In their ARV facility (which has a current GMP certificate from BPOM), they have installed a new weighing booth, sampling booth and metal detector. The WHO PQ projects with Kimia Farma are currently on hold, but PQM continued to support them on GMP-related assistance in-line with USAID mission objectives for supporting TB and HIV quality in Indonesia.

PT Phapros Tbk 1st line TB products (2FDC and 4FDC) 2nd line TB products (Levofloxacin 500 mg): PQM continued to support Phapros through review of dissolution study protocols and data, and Phapros is planning a pilot batch in April 2016 for levofloxacin product. A validation report is estimated to be finalized in July 2016. The registration department is working on dossier preparation with CTD format for module three and quality overall summary and will submit to PQM for first review by the end of June 2016.

PT Indofarma's 2FDC for TB product*:* PQM Indonesia continues to support PT Indofarma's involvement in GMP trainings conducted in Indonesia, although their active pursuit of WHO PQ for their 2FDC is currently on hold since they are in the process of constructing a new manufacturing facility for their solid dosage products with an estimated completion date of July 2017.

Objective 2: To strengthen Indonesia's medicines Quality Assurance system by supporting the National Agency for Food and Drug Control's regulatory, inspection, post-marketing surveillance, anti-counterfeiting investigations, and quality control (national and provincial laboratories) functions with a focus on TB and essential medicines to achieve international standards of practice

PQM supported two provincial BPOM quality control laboratories in Papua and West Papua provinces of Eastern Indonesia by providing needed calibration services for HPLC equipment used in the testing of AIDS, TB, and malaria (ATM) medicines. Calibration of equipment is essential to ensure the equipment providing accurate and valid data in measurement and it is mandatory requirement for ISO/IEC 17025. This support is part of continuing FY15 PQM activities. Papua province is one of two pivot provincial sites under President's Emergency Plan for AIDS Relief (PEPFAR) support in Indonesia and is a high-priority area for conducting QA activities on ARV medicines.

A total of fourteen provincial and national BPOM quality control laboratories agreed to join the Inter Laboratory Proficiency Testing scheme under USP's Network of Medicines Control Laboratories (NOMCoL) Asia Pacific program. Shipment of sample and reference standards (ILT test kits) is in process to be sent to each province laboratories. The ILT is an external quality assessment or quality control procedures for monitoring the validity of test undertaken by the laboratory and part of ISO/IEC 17025 requirement, and this activity will be conducted during Q3.

West Papua provincial QC laboratory recognized PQM support to Papua and establishment of the WHO PQ program. PQM Indonesia was recognized by the government of West Papua for its support of the BPOM provincial quality control laboratory in Manokwari through a radio program broadcast by RRI (Radio Republik Indonesia). This information also has been published in the BPOM national website:

http://www.pom.go.id/new/index.php/view/berita/10246/Semangat-Menuju-Laboratorium-Unggulan-ATM-diangkat-melalui-Siaran-Radio-RRI-Manokwari.html.

With PQM's support and the establishment of a formal program in West Papua, the Director of the provincial quality control laboratory of West Papua secured government funding to construct a new provincial BPOM QC laboratory that complies with WHO recommendations as part of its strategy to become a WHO PQ laboratory by 2020. Resources will be directed to establish this site as a Center of Excellence, and considerable progress has been made following PQM's technical assistance during 2015 and continuing into 2016. This is a major achievement and recognition of the importance of PQM support in this province. The laboratory has been trained on testing tenofovir-based ARVs using USP monographs and reference standards and will be an important site for quality control of ARVs in this area, where there is a generalized HIV epidemic in Indonesia.

The PQM team participated in BPOM's workshop for QC laboratory supervisors from 32 provincial QC laboratories (BBPOM). The main purpose of the workshop was to introduce the participants to changing the overall scope of accreditation for laboratories from product-to process-based and how the staff can implement and improve their competency on testing. The representative from the national agency of professional certification (KAN) explained the importance of testing competency and how to evaluate and prepare for entry into the Association of Southeast Asian Nations (ASEAN) regional market.

PQM expanded the focus area of the program by involving and supporting the government's provincial QC laboratory in DKI Jakarta province. DKI Jakarta, the second provincial pivot site of highest priority under PEPFAR, will be an important site for conducting quality control activities on ARVs in the public sector. The PQM team met with the Head of BBPOM DKI Jakarta and her team to establish a focus for technical assistance to be provided under HIV funding, especially through capacity building on testing, as well as sampling/post-marketing surveillance. BBPOM DKI Jakarta's catchment area is large and consists of roughly 40 pharmaceutical manufacturers. BBPOM DKI Jakarta currently has a Minilab™; however, it has not yet been operationalized. Discussion also centered around equipping the mobile food testing lab (a van with wet lab capacity) with Minilabs™ to conduct remote, on-site sampling and testing using Minilabs™ following PQM training in 2016.

In FY16, PQM will support the Center for Research and Development at BPOM to work on developing BPOM protocols for baseline surveys on quality of medicines available in the markets in tandem to the national PMS system.

Objective 3: To enhance the technical capacity of the government of Indonesia to develop and implement inter-agency (MOH, BPOM, donors, professional associations, and other stakeholders) policies and procedures for medicines quality assurance, including coordination, advocacy, and developing appropriate public awareness tools

Following a year and a half process from development to approval, the Minister of Health of Indonesia has signed the Ministry of Health Regulation Number 02/2016 entitled "Guidelines for Sampling and Testing Medicines from Government/Public Facilities." The signing of the official Guidelines by the Minister of Health is a major achievement for the government of Indonesia, which was initiated by a joint cooperation between PQM and WHO beginning in 2014. Following a series of meetings convened by PQM and WHO, the Guidelines were recognized as an important step forward in facilitating cooperation between the Ministry of Health and the national MRA (BPOM) towards ensuring that public program medicines are routinely sampled and tested per government policy. Previously, no such formal guide for cooperation existed, and traditionally the national post-marketing surveillance system of BPOM only covered the private sector markets, and thus could not access TB, HIV, malaria, and other priority disease medicines for quality control purposes.

PQM recognized the crucial need to facilitate and develop a formal policy which the government could use to ensure that public medicines were being sampled and tested using government budgets on a routine basis. These guidelines will also serve to ensure ongoing data sharing and follow up between the MOH and BPOM in the event of non-compliant or failed products being discovered.

Further commitment by PQM in facilitating the drafting and dissemination of these Guidelines by the government of Indonesia will include a number of PQM supported socialization workshops in which officials from BPOM and MOH will be brought together to establish implementation protocols to roll out the Guidelines. PQM will also continue to support the implementation of the sampling and testing of priority medicines by providing much-needed chemical and documentary reference materials for the public medicines, many of which do not have a current testing method under the official Indonesian Pharmacopeia.

The sampling and testing of these medicines will also be supported via the PQM-initiated Global Fund project to support procurement and training of BPOM quality control laboratories under the National TB Program's PR grant.

Initially, PQM leveraged $1 million USD of reprogrammed TB funds under the NTP in Indonesia for the purpose of supporting procurement of ion chromatography machines and other needed equipment for testing certain TB medicines (amikacin, kanamycin, and streptomycin). During 2016-2017, an additional $2 million USD has been allocated to the PQM-supported projects for procurement and training purpose for all BPOM QC laboratories via the new funding mechanism. In total, the $3 million USD funds leverage will be used by

the PQM program to support capacity building and training in priority BPOM QC laboratories in an unprecedented project using Global Fund funding. Final procurement is being conducted for the initial $1 million USD during Q2-Q3, and the next procurement and training will begin sometime in 2016.

PQM continued to provide input and involvement in various USAID partner projects on TB and HIV/AIDS, such us Decentralization of ARV to the district level, an approach of supply chain management led by the John Snow, Inc. (JSI) USAID/Deliver project and United Nations Development Program (UNDP) projects on procurement mapping and assessment of ATM medicines, as well as FHI360's LINKAGES project on care services provision.

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

A two-week external Mid-Term Program Review (MTPR) was conducted during Q2 consisting of data collection (field site visits, focus group discussions, and one-on-one interviews) with partners and donor. The MTPR focused on two primary areas of the PQM Indonesia technical assistance portfolio: 1. Training and Technical Assistance (TTA), and 2. Advocacy, sensitization, and awareness raising (ASA).

Additionally, following initial data collection, a stakeholder consultation workshop was convened to bring together representatives of all PQM Indonesia partners for feedback and discussion. The workshop, attended by 42 participants from manufacturers, CROs, MOH, USAID, BPOM, and non-governmental organization (NGO) partners, identified a number of important recommendations, as well as facilitating exchange and discussion between ministries and sectors for a fruitful conversation.

Highlights from the PQM Indonesia program included reporting on achievements of the program to date, as well as the work plan activities for FY16 to disseminate to relevant partners. Recommendations from stakeholders for improving the effectiveness of training and the delivery of the technical assistance of the PQM program were highly appreciated and will be taken in consideration for further implementation of PQM program.

Key documents/strategic plans to come out of the MTPR, which will be finalized during Q3, include:

- A comprehensive Mid-Term Program Review Report, including data analysis and presentation of recommendations arising from the review;
- Human Resources Development Plan;
- Advocacy and Communications Plan;
- Sustainability Plan.

Final data collection and finalization of the MTPR report is due during Q3.

Staffing/Office:

The Logistics and Procurement Assistant for the PQM Indonesia field office was recruited and began working in January 2016. In addition, a candidate for the second QA/QC Specialist has been identified through two recruitment processes. The PQM Indonesia field office plans to recruit a Communications/Monitoring & Evaluation (M&E) Officer during Q3 or Q4 of FY16.

PQM Indonesia has identified potential options for a new office space for the field office. Due to growth in the staffing and space needs of the field office, PQM is conducting searches for alternatives to the current serviced office space, which will contribute to significant financial savings over the life of the program.

PAKISTAN

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

Activity 1.5: Continue to work with key stakeholders (DRAP, USAID, UNICEF, WHO, CHX/JSI/HSS Project of USAID) to expedite the registration of imported CHX gel from Lomus Pharmaceuticals and/or Drugfield Pharmaceuticals Ltd of Nigeria.

While waiting for local CHX products to become available, DRAP issued the waiver in the form of No Objection Certificate (NOC) to JSI and JHPIEGO for the importation of 2.1 million 10 g tubes of CHX gel 7.1% into Pakistan. This work plan activity is no longer necessary since a waiver was obtained from DRAP for imported CHX products. The activity was changed to support the trainings on PMS and Good Sampling Practices for provincial inspectors of drugs (PIDs) in Sindh and Punjab based on the request from the federal inspectors of drugs (FID) and PID representatives attending the April 11-13, 2016 training.

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

Activity 2.1: Provide essential RS, DM, and other chemical supplies to each of the labs above. Some additional supplies will also be provided for use in the training workshop.

PQM maintained close contact with the Division of Registration and provided input and advocacy on improvement of the registration process. Part of this process was to develop a draft of a strategic plan with DRAP. The review is still in progress, and it is expected to be finalized during Q3 of 2016.

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

No activity has been implemented during this quarter.

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

No activity has been implemented during this quarter.

Objective 5: Strengthen the USP PQM program performance and operations in the country

Activity 5.1: Country Office Registration, Operations and Staffing

USP Pakistan business registration was submitted on Staffing:

Role	Headcount	Individuals	Remarks
Senior Regional Manager	1	Souly Phanouvong	Existing (USP HQ)
Country Program Coordinator/ Consultant	1	Nadeem Alamgir	Existing – based in Islamabad
Country Program Director "Chief of Party"	1	Being recruited – on boarding March – May 2016	Candidate was identified; in process of on boarding.
Operations Manager	1	To advertise/or consider change of responsibility in existing staff consultant – May 2016	To be based in Islamabad.

GMP Specialist/ Consultant	1	Being recruited – on boarding April 2016	Candidate was identified; in process of on boarding.
QC Specialist/ Consultant	1	Being recruited – on boarding April 2016	On target
Finance and Admin Support	1	To advertise May 2016	To be based in Islamabad

PHILIPPINES

Objective 1: Evaluate the efficiency, effectiveness, relevance and impact of the PQM program and particularly the MQM activities in Philippines; provide feedback to PQM Management and USAID Mission to improve the implementation of the program; and ensure accountability for its results.

Activity 1.1: Conduct external evaluation of the PQM program in general and the MQM activities in particular and design a robust M&E system for the program in Philippines.

With the guidance and support from the USAID mission, PQM conducted a 5-year program review of MQM for its approach, implementation, achievement, and contribution that the PQM program has made to the improvement of quality of anti-TB and other essential medicines in support of the Philippines National TB Control program and to safeguard the health of Filipinos.

The objective of this program review was to:

- Identifying the program development and implementation gaps – at objective and activity levels – and how to address them in a timely manner with best practices and solutions;
- Proposing the strategies to program planning and maximize impact of MQM activities; and
- Elucidating and communicating success stories, program highlights, and lessons learned.

The program review started in January 31, 2016 preparing for the analytic protocol/terms of reference with data collection tools. The program review team arrived in Philippines on February 6, 2016 and completed the task on February 19, 2016. The program review team consisted of the following:

- Dr. Abdelkrim Smine (USP consultant), external reviewer
- Feseha Tesema (M&E Manager), internal reviewer
- Yolanda Robles (Professor of Pharmacy), external reviewer.

On February 9, 2016, the finalization of the assessment plan was conducted together with the USAID Mission. From February 10-17, 2016 the team met with all partners and stakeholders for an in-depth interview on the effectiveness and relevance of PQM's technical approach in achieving the program objectives in Philippines. Recommendations were also provided to address the areas of technical focus related to medicine regulation and QA/QC systems strengthening necessary to sustainably achieve desired health outcomes. The team visited four sentinel sites (Bicol, CALABARZON, Davao, and Cebu) as part of the program review.

A debriefing at the US Embassy with the Mission officers took place on February 18, 2016. The draft report was submitted to PQM management and USAID on February 26, 2016. Lastly, on March 21, 2016, a dissemination meeting was conducted in Manila with implementing partners and stakeholders to discuss the result of the program review and hear the feedback on new approaches of PQM to achieve its objectives in the Philippines.

REGIONAL DEVELOPMENT MISSION FOR ASIA (RDMA)

Objective 1: Strengthen the institutional capacity of medicines quality control system for regional impact

Activity 1.1: Continue to support the Chulalongkorn University Faculty of Pharmaceutical Sciences' Pharmaceutical Technology Service Center (PTSC) to reach submission the expression of interest (EOI) and laboratory information files (LIF) with other necessary supporting documents to WHO PQ

The PQM QMS team made an initial assessment on the status of QMS at Chula Pharmaceutical Technology Service Center. The roadmap towards WHO PQ was developed, along with CAPA plan development and implementation. The Quality Manual and 25 major SOPs were translated from Thai into English and were reviewed by the PQM QMS team. The remaining SOPs, about 100 of them, are under adaptation and full revision will be completed by end of July 2016. EOI and LIF submission to WHO PQ is targeted for completion by September 2016.

Activity 1.2: Provide technical assistance to the Laos Food and Drug Quality Control Center to expand its scope of ISO/IEC 17025 accreditation (revised quality manual, SOPs, and other necessary documents, accrediting body (AB) identification) and initial preparation for compilation of necessary laboratory files for submitting the application for re-accreditation with new scope to appropriate accrediting body compilation of necessary laboratory files for submitting the application for re-accreditation with new scope to appropriate accrediting body

PQM QMS team conducted a site visit of Food and Drug Quality Control Center (FDQCC) of Laos to determine the state of the Quality Manual and SOPs for the current ISO/IEC 17025 completed and adjusted the road map for expansion of the scope of method-based accreditation. The Quality Manual was revised and seven chapters (out of 27) of SOPs are under review by the PQM QMS team. FDQCC should be ready for submission of application to an accrediting body outside Laos by the end of September 2017.

EASTERN EUROPE & CENTRAL ASIA

KAZAKHSTAN

Overall Quarter Progress
USAID/Central Asia defined two areas for PQM's technical assistance to Kazakhstan, and the work plan is being developed to provide technical assistance in the following areas:

- Technical assistance to three regional quality control laboratories of Kazakhstani FDA to achieve WHO prequalification;
- Technical assistance to Nobel Almaty Pharmaceutical Factory in reaching the WHO prequalification of TB medicines.

Objective 1: Strengthen quality control laboratories of Kazakhstan FDA
After USAID's approval of the activity, PQM contacted the National Center for Expertise of Medicines, Medical Devices and Medical Equipment (Kazakhstan FDA) to start planning of PQM's technical assistance to three regional laboratories. Kazakhstan FDA defined a focal point for working with PQM. The options for a technical assistance for WHO prequalification or ISO 17025 accreditation were discussed. Kazakhstan FDA decided that their priority is WHO prequalification of the laboratories rather than the ISO accreditation. It was agreed that PQM will provide assistance to three regional laboratories of the FDA towards receiving the WHO prequalification. The ultimate goal of the FDA is to achieve the WHO prequalification of the laboratories by the end of the 2017 calendar year. The laboratories are located in Kostanay, Karaganda, and Pavlodar. PQM requested and received some general information about the laboratories: each of them has three departments, including physic-chemical, microbiological, and toxicological, and the number of staff varies between 15-17.

PQM engaged a consultant to work on this activity. PQM planned the first audit of the laboratories for the end of May or beginning of June. Prior to the trip, PQM will review quality management documents of the laboratories to be submitted by the FDA.

Partner contributions:
Kazakhstan FDA is collaborative and responsive.

Objective 2: Strengthen TB medicines manufacturer's quality assurance system
During the quarter, PQM worked with Nobel Almaty Pharmaceutical Factory to identify the status of implementation of the CAPA plan provided by PQM. Nobel provided the following update: the company is completing construction of a new site, a building that is adjacent to the current facility in Almaty. Nobel is targeting to complete the construction and to have the new production area operational by August 2016. Nobel is working with an engineering firm on all aspects of qualification of critical utilities in the new production area to ensure that they are in compliance with international standards. Due to the size of the construction project, qualification of the control system for the HVAC at the existing production site is scheduled for the summer of 2017. The decision of Nobel's top management, regarding investment into validation of HVAC system at the new site and renovation of the existing building to bring it up to date, is of critical importance as it will allow Nobel to comply with GMP requirements.

Nobel considers completion of construction of the new facility as a top priority, and they are applying the technical recommendations provided earlier by PQM to this new site. Production of Levofloxacin and Moxifloxacin will be transferred to the new site by the end of 2016. However, Nobel will continue to work on implementing CAPAs related to the current site, to ensure that their quality systems are strengthened.

Nobel and PQM have agreed on the action plan to continue PQM's technical assistance. The main agreement is that Nobel should identify a realistic timeline for CAPA implementation and communicate it with PQM. The main focus should be on development of the relevant documentation. PQM will make a decision on the assessment visit to Nobel's new facility, based on Nobel's progress in the CAPAs.

Partner contributions
Nobel is collaborative and is interested in PQM's technical assistance.

UZBEKISTAN

Overall Quarter Progress

PQM has not started active implementation of its activities in Uzbekistan, as the project still has not been approved by the Government of Uzbekistan. Particularly, approval of a memorandum of understanding between USAID/Uzbekistan and the National counterpart, Uzpharmsanoat (Uzbek State Joint-Stock Concern of Pharmaceutical Industry), is still pending. Also according to the local regulations, the "Project Passport," which is the document that describes the activities and provides the project's budget, should be approved by the Government. PQM supported Uzpharmsanoat in development of the "Project Passport" and also in drafting a response after the Ministry of Finance and Ministry of Health provided their comments on the "Passport." The most challenging request from the Ministry of Finance side is to dedicate a certain percentage of the budget for a 'hard component' (i.e. procurement of certain equipment). PQM cannot include procurement of equipment into the work plan and subsequently in the "Project Passport," as no assessment has been done and no information on what equipment is needed to strengthen quality-assurance system of TB medicines manufacturer(s) is available. On the other hand, an assessment cannot be done without approving the project by the Government. Currently PQM is discussing with USAID/Uzbekistan possible solutions for the situation.

LATIN AMERICA & CARIBBEAN

Amazon Malaria Initiative (AMI)

Objective 1: Establish the framework for sustainable south-south collaborations between OMCLs and MRAs in LAC

No activity has been implemented during this quarter.

Objective 2: Establish sustainable in-country capacity to perform QC of medicines in the field

Sub-Objective 2.1: Implement use of Visual and Physical Inspection tools to support QC of medicines in the field (Level 1)

Activity 2.1.1: Develop Country Pilot Databases

Databases containing registration information for antimalarials and other active pharmaceutical principles were finalized for two countries. These databases will be incorporated in the application for computers and mobile devices, currently under development, and will support the pilot studies for the initial assessment of the tool in the field.

Sub-Objective 2.2: Build regional capacity to expand the number of available screening procedures for QC of medicines in the field (Level 2)

Activity 2.2.3: Deliver Method Development

PQM coordinated the collaboration between Peru's OMCL (CNCC) and the GPHF to establish an analytical development program, which will ensure global dissemination of Peru's newly developed and validated methodologies for field analysis of medicines that are not covered in the Minilab™. During this quarter, CNCC finalized the development and validation of a Naproxen field test, whose translation into English is currently being supervised by PQM. GPHF will include this method in coming updated versions of Minilab's™ Manual of Procedures. Additional methods are expected to be finalized in FY16 Q3 and Q4.

Sub-Objective 2.4: Develop database of countries' antimalarial QC activities

Activity 2.4.2: Compile countries information

During this quarter PQM received and compiled the information submitted by several AMI countries, which will be presented and discussed at the Annual AMI partners meeting in Q3 and will help identify countries gaps and needs for sustainable QC programs.