

Promoting the Quality of Medicines (PQM) Program

FY 2018 First Quarter Report
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About the Promoting the Quality of Medicines (PQM) Program

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PQM Responsible Staff	Mr. Jude Nwokike, Director

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

As of January 2018, USAID supports PQM's work in 18 countries, 1 regional mission, 1 Cross Bureau program, and 4 core health programs.

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Acronyms

ACT	artemisinin-based combination therapy
ADE	adverse drug event
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CRO	clinical research organization
CRP	Collaborative Registration Procedure
CTD	Common Technical Document
DFDA	Department of Food and Drug Administration [Burma]
DGDA	Directorate General of Drug Administration [Bangladesh]
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
EOI	expression of interest
FPP	finished pharmaceutical product
GCP	good clinical practices
GFDA	Ghana Food and Drug Administration
GLP	good laboratory practices
GPPQCL	good practices for pharmaceutical quality control laboratories
GMP	good manufacturing practices
HPLC	high-performance liquid chromatography
IMC	Inter-Ministerial Committee
LIF	laboratory information file
LMHRA	Liberia Medicines and Health Products Regulatory Authority
MDR-TB	multidrug-resistant tuberculosis
MNCH	maternal, newborn, and child health
MOH	Ministry of Health
MQDB	Medicines Quality Database
MQM	medicines quality monitoring
MRA	medicines regulatory authority
MRIS	medicine registration information system
NAFDAC	National Agency for Food and Drug Administration and Control
NIPRD	National Institute of Pharmaceutical Research and Development
NMCP	National Malaria Control Program
NQCL	national quality control laboratory
NTD	neglected tropical disease
NTP	National Tuberculosis Program
PD	Pharmaceutical Department [Mozambique]
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PMI	U.S. President's Malaria Initiative
PMS	post-marketing surveillance
PQ	prequalification
PQM	Promoting the Quality of Medicines
PV	pharmacovigilance
QA	quality assurance
QC	quality control
QMS	quality management systems
SOP	standard operating procedure
SRA	stringent regulatory authority
TB	tuberculosis
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNIDO	United Nations Industrial Development Organization
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WHO	World Health Organization

Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance in partnering countries to strengthen quality assurance (QA) systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance helps to build the capacity of medicines regulatory authorities (MRAs) and QA systems. PQM supports the manufacture of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH). PQM also provides support to increase the utilization of medical product quality information for decision-making. This report summarizes results achieved during the first quarter of FY 2018, from October 1 to December 31, 2017.

By the end of the first quarter (Q1), 14 out of 20 FY 2018 work plans (70%) had been fully approved, leading to timely implementation of activities. Through increased project management strengthening, PQM continues to see improvement in the timely approval of work plans in comparison to Q1 in previous fiscal years (58% in FY 2017 and 41% in FY 2016).

Quality is paramount to ensuring that the safety and efficacy of medical products are maintained from the moment a product is manufactured, across the entire supply chain, until it reaches the patient. By strengthening systems that help ensure quality—from developing effective and enforceable legislation, policies, and workforce capacity to helping implement regulations, guidelines, and operational procedures—PQM aims to reduce and eliminate substandard and falsified products that pose serious risks to patients' health and undermine global health and development efforts. PQM also supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory actions and are disseminated to all stakeholders.

In Ethiopia, PQM supported the drafting of three guidelines: Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products, and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology. Besides increasing access to new and innovative essential medicines for emerging diseases; this process helped build capacity of the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) on international best practices and the dossier review process. In Mozambique, compendial laboratory testing from an oxytocin post-market surveillance study conducted in Maputo city and Maputo province revealed that 18 samples of oxytocin injection were found to be substandard (manufacturing/storage/distribution practices do not meet required quality standards) and 1 was a falsified product (sample did not contain the active pharmaceutical ingredient of oxytocin), failing both identity and assay tests. The Pharmaceutical Department (PD) and its stakeholders utilized this information for decision making to recall failed product batches and requested PQM's support to expand the oxytocin study country-wide. In Ethiopia, after results from PQM-supported post-marketing surveillance showed the failure of 49 samples of quinine sulfate tablet, EFMHACA recalled the failed sample batches in the market to halt further distribution and protect the public from the consequences associated with these poor-quality products. To help prioritize scarce human and financial resources and plan strategically for product sampling, in Bangladesh, PQM provided support to develop a risk-based testing protocol through several consultative meetings with four National Chemical Laboratory (NCL) core staff members. The draft plan is now under review by NCL senior management and will be implemented once approved by all key stakeholders.

PQM continues to build the capacity of national quality control laboratories to improve laboratory standards through assessments, hands-on training, and proficiency testing. PQM places particular emphasis on strengthening quality management systems to ensure laboratories can comply with internationally recognized standards, such as ISO/IEC 17025:2005 and/or WHO PQ. This quarter in Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) Agulu and Yaba laboratories both maintained their existing ISO 17025:2005 accreditation test methods and also expanded their scope capacity to include microbiology test methods. During the preparation for a third party surveillance audit for scope maintenance and expansion of the laboratories, NAFDAC committed to sustainability and paid for all costs associated with equipment calibration, proficiency tests, and other laboratory supplies with minimal support from PQM.

PQM works with local, national, and international partners to bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, inform decision-making, shape public policies on pharmaceuticals, and support the attainment of public health objectives. In Indonesia, a significant achievement was seen in the first convening of the Ministry of Health (MOH) and public and private pharmaceutical manufacturers to identify public program needs for TB control in the context of the changing guidelines on TB treatment in regulation PMK 67/2016; given the changes in treatment regimens, PQM advocated for this stakeholders meeting to encourage transparency in MOH procurement processes and anticipate upcoming procurements so that manufacturers can meet demand. In Senegal, a major achievement was the establishment of the Inter-Ministerial Committee between the medicines regulatory authority (DPM) and enforcement agencies, which helped DPM to take major regulatory

actions in its fight against the sale of medicines in nonregulated pharmacies and informal markets, including the confiscation of a huge amount of illicit medicines. From Nigeria, NAFDAC's newly appointed Director General, Dr. Moji Adeyeye, visited PQM headquarters for an introduction to the PQM program and USP as she begins her tenure. Separately, a delegation from Burma's Department of Food and Drug Administration, including Director General Dr. Than Htut, met with USP and PQM staff and members of the USAID Agreement Officer's Representative's team.

A continuous supply of quality-assured products—particularly for essential priority medicines for TB, NTDs, and MNCH—is necessary to address national health priorities and plans. PQM works with manufacturers to improve compliance with World Health Organization (WHO) standards, helping them develop and submit dossiers for certification by the WHO Prequalification (PQ) program. PQM also provides technical assistance and guidance to manufacturers for the local production of medicines, which may decrease reliance on international donation and help establish a sustainable local supply with national resources. This quarter in Indonesia, the largest pharmaceutical manufacturer in the region, Kalbe Farma, submitted and received WHO PQ acceptance for its dossier for levofloxacin 500mg tablets, marking the first solid-dosage form product dossier WHO PQ submission from Indonesia. In Bangladesh, PQM collaborated with the National Tuberculosis Program, Director General of Health Services, DGDA, U.S. Agency for International Development (USAID), and other partners to discuss strategies for local production of first-line anti-TB medicines. In Pakistan, chlorhexidine (CHX) 7.1% gel, which PQM provided technical assistance to produce locally, was recently launched in all districts and is now available through the Lady Health Workers program under the Prime Minister's Program for Family Planning and Primary Health Care. In Kazakhstan, PQM continued providing remote assistance to Nobel Almaty Pharmaceutical Factory, which plans to start operations on a new production site in early 2018. For the Core TB program, PQM provided assistance to a kanamycin active pharmaceutical ingredient (API) manufacturer to conduct a cross-contamination assessment and mitigate related risks; this manufacturer also initiated a process study to reduce impurities with a different source of starting material, and PQM will continue to provide assistance for the purification process. PQM also engaged a second API manufacturer and has confirmed a GMP assessment date for February 2018; this manufacturer has received approval from Japan's Pharmaceuticals and Medical Devices Agency for its kanamycin API.

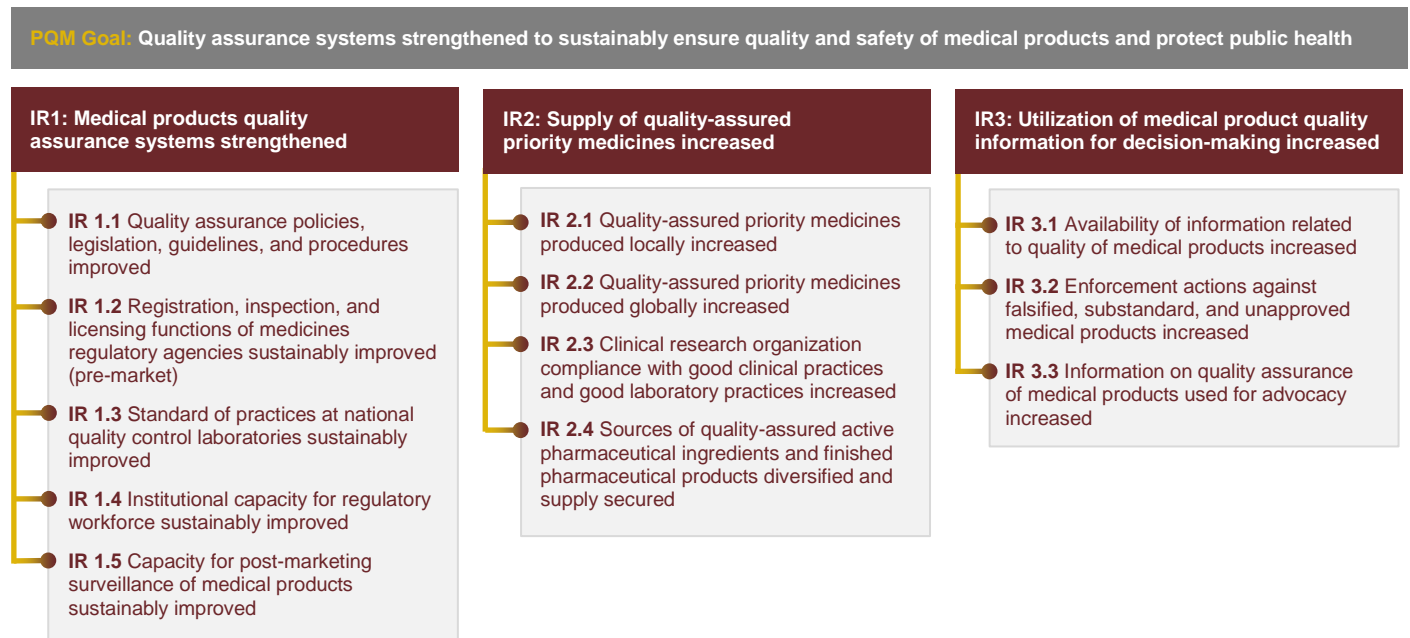
Program Background

The Promoting the Quality of Medicines (PQM) program is a cooperative agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to support low- and middle-income countries in addressing critical issues related to medicines information and quality. The PQM program provides technical assistance to build the capacity of medicines regulatory authorities (MRAs) and quality assurance (QA) systems in countries with weak health systems. PQM also provides technical support to manufacturers of quality-assured priority medicines for malaria, HIV/AIDS, tuberculosis (TB), neglected tropical diseases (NTDs), and maternal, newborn, and child health (MNCH).

During FY 2018, PQM implements projects for 18 USAID country missions, 1 regional mission, 1 Cross Bureau program, and 4 core health programs.

Results Framework

PQM's Results Framework is organized according to three result areas. These complementary areas contribute to PQM's approach of affecting a country's health system as a whole. The globally designed systems-based approach is tailored to fit the needs of individual countries or regions and includes key stakeholders throughout the health system.



This report highlights the results achieved by PQM, organized by result area representing multiple countries where the program works, as well as by country and core portfolio for the October–December 2017 period.

Result Highlights



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

Description of Sub-IRs

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

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

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

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

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

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

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

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

Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved

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

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

structures and processes necessary for effective QMS, PQM builds a sustainable in-country regulatory and QA workforce.

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

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

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

Overview of FY 2018 First Quarter IR1 Achievements

Key Results and Highlights

In Ethiopia during the first quarter, PQM supported the drafting of three guidelines: Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products, and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology. The presence of such guidelines in support of registering specialized products is expected to increase access to new and innovative essential medicines that better address existing and emerging diseases. In addition to their contribution to the alignment of international best practices, these guidelines will also help to comprehensively address the review of dossiers, taking into account the peculiar nature of the stated products. The guidelines were shared with more than 110 local agents for comments. PQM will continue supporting the consultative workshop to finalize the guidelines once existing feedback is incorporated. PQM also provided support in the preparation of a draft Community Pharmacy Audit Manual and standard operating procedures (SOPs) intended to be used by inspectors for the implementation of risk-based inspection of thousands of retail outlets in Ethiopia. The proper implementation of this manual is expected to facilitate detection and prevention of poor-quality medicine in circulation, reduce diversion of products from the public sector, and assist in the proper implementation of good storage and good distribution practices.

Nigeria's regulatory agency, the National Agency for Food and Drug Administration and Control (NAFDAC), made major inroads in advancing sustainability this quarter, as all costs associated with laboratory equipment calibration, proficiency tests, and other laboratory supplies were paid for by the agency. Only minimal technical assistance was required from PQM to prepare for surveillance audits at two NAFDAC laboratories. As a result, NAFDAC's Agulu and Yaba laboratories both maintained their existing test methods and also expanded to microbiology test methods. Official notifications for both laboratories are expected next quarter.

Similarly in Burma, PQM's technical assistance enabled the Department of Food and Drug Administration (DFDA) Nay Pyi Taw Pharmaceutical Chemistry Laboratory to maintain ISO 17025:2005 accreditation for the first year. The laboratory was able to maintain its accreditation on all 10 scopes after the accreditation body, ANAB, conducted a 1-day annual surveillance visit in October 2017. In Ethiopia, an assessment of the quality control laboratory of the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) for reaccreditation and scope expansion was also completed. The assessment was concluded with six minor nonconformities, for which corrective and preventive actions (CAPAs) were prepared and addressed. It also resulted in potential scope expansion to three additional test methods.

Key IR1 Indicators for FY 2018 Q1

Number of individuals trained in QA-/QC-related topics	191
Number of QC laboratories participated in PT/ILT and passed	2 – Nigeria
Number of laboratories with scope expansion	3 – Nigeria, Ethiopia
Number of laboratories accredited or reaccredited	4 – Nigeria, Ethiopia, Burma

IR2: Supply of Quality-Assured Priority Medicines Increased

Description of Sub-IRs

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

Sub-IR 2.1 Quality-assured priority medicines produced locally increased

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

Sub-IR 2.2 Quality-assured priority medicines produced globally increased

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

Sub-IR 2.3 CROs' compliance with good clinical practices and good laboratory practices increased

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

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

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

Overview of FY 2018 First Quarter IR2 Achievements

Key Results and Highlights

A major accomplishment this quarter was Indonesian manufacturer Kalbe Farma, the largest pharmaceutical manufacturer in the Association of Southeast Asian Nations (ASEAN) region, submitting its levofloxacin 500mg tablet product dossier to WHO for prequalification. The subsequent acceptance of this dossier by WHO at the end of Q1

attests that the dossier was complete and ready for review. This is the first oral solid dosage form submission to WHO for PQ in Indonesia, a testament to the hard work and dedication of the PQM and Kalbe Farma teams, with support by Badan Pengawas Obat dan Makanan (BPOM). Following the submission, Kalbe Farma initiated an internal mock audit in anticipation of the upcoming, extensive PQM onsite audit in preparation for a WHO inspection during FY 2018. This marks a major achievement for PQM in Indonesia and represents building Kalbe Farma's overall quality and GMP compliance.

In Pakistan, three manufacturers (Atco Laboratories, Aspin Pharmaceuticals, and Akhai Pharmaceuticals) launched quality-assured chlorhexidine 7.1% gel products in the local market. This locally manufactured quality-assured product has increased the availability of the product for scale-up efforts to launch chlorhexidine 7.1% gel in all districts of Pakistan. In addition, these products are now available for procurement by provincial governments, where they are already included in the list of medicines to be carried in the bags of lady health workers working under the Prime Minister's Program for Family Planning and Primary Care. The manufacturers are also currently looking toward exporting their products to other countries in the region and also to becoming potential suppliers for UNICEF. A fourth manufacturer (Zafa Pharmaceuticals) is expected to start local production by next quarter.

Key IR2 Indicators for FY 2018 Q1

Number of manufacturers supported toward GMP standards	42
Number of dossiers accepted for review	1 – levofloxacin FPP

Number of Manufacturers Provided with Technical Assistance in FY 2018 Q1

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	6	magnesium sulfate FPP, oxytocin dispersible tablet, oxytocin API, and amoxicillin FPP
Core NTD	11	praziquantel API, praziquantel FPP, albendazole API, albendazole FPP, and mebendazole FPP
Core TB	13	clofazimine FPP, cycloserine API, rifapentine API, rifapentine FPP, gatifloxacin API, gatifloxacin FPP, kanamycin API, kanamycin FPP, and rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC)
Ethiopia	1	ethambutol FPP
Indonesia	2	levofloxacin FPP
Kazakhstan	1	levofloxacin FPP and moxifloxacin FPP
Nigeria	3	amoxicillin dispersible tablet FPP, oxytocin FPP, magnesium sulfate FPP, and zinc sulfate FPP
Pakistan	4	chlorhexidine gel FPP
Uzbekistan	1	levofloxacin FPP and moxifloxacin FPP

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

Description of Sub-IRs

The collection, analysis, and use of data on medical products evaluation, inspection, and post-approval surveillance support evidence-based decision-making that is critical for promoting access to quality-assured products and for reducing and eliminating substandard and falsified products. PQM supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory actions and are disseminated to all stakeholders. By working with local, national, and international partners, PQM

helps bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, inform decision-making, shape public policies on pharmaceuticals, and support the attainment of public health objectives.

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

PQM assists national stakeholders with implementing medicines quality monitoring (MQM) to generate data on the quality of pharmaceuticals circulating in country. To sustain such a critically protective public health activity, PQM supports countries to develop or strengthen post-marketing surveillance as a regulatory function. PQM also supports countries to increase the body of knowledge generated on the quality of priority essential medicines used in public health programs, particularly medicines used for MNCH, HIV/AIDS, and TB.

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

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

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

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

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

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

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

Overview of FY 2018 First Quarter IR3 Achievements

Key Results and Highlights

In Senegal this quarter, there was confiscation of a vast amount of poor-quality medicines by the medicines regulatory authority (DPM) and Senegalese law enforcement agencies. In 2014, the Ministry of Health established the Inter-Ministerial Committee (IMC) Act with the main objective of collaboration between the DPM and enforcement agencies to combat the sale and/or import of poor-quality medicines. The establishment of the IMC Act was one of the main outcomes following communication and education campaigns conducted by PQM in 2009 and 2011. With the establishment of this IMC between DPM and enforcement agencies, DPM was able to take regulatory actions in its fight against the sale of medicines in non-regulated pharmacies and informal markets. On November 13, 2017, this joint effort led to the confiscation of two trucks full of poor-quality medicines before they entered Touba City. The confiscated medicines, which included antimalarials, were worth approximately 1,355,160,000 CFA, the equivalent of \$2,419,928 USD.

Also in Q1, EFMHACA took regulatory actions on failed samples following quality testing of products collected during PMS in 2017. Based on EFMHACA's directives, 49 failed samples of quinine sulfate tablet were collected from the market by the importer of the product. Several other products were also collected from the market, including primaquine tablet, zinc sulfate tablet, and artemether injection, on the basis of recall letter issued by EFMHACA following the release of PMS results. Additionally, analysis of product defect reports received through the adverse drug reaction (ADR) reporting system led to the recall of iodine tincture and lidocaine solution for injection, as further investigation on these products confirmed them to be of poor quality. All of these medicines are in high demand in day-to-day clinical practice and could have endangered the lives of many, had they not been detected and withdrawn from the supply chain system in time. This exemplifies one contribution resulting from USAID's investments to strengthen EFMHACA's capacity through building the capacity of the quality control laboratory, establishing PMS systems, and strengthening the pharmacovigilance (PV)/ADR reporting system.

PQM also supported NAFDAC with the facilitation of a dissemination meeting with stakeholders to discuss PMS results of an antimalarial study, which showed that 1.6 percent of sampled products (14 samples) failed QC testing. Key recommendations were made as a result of this meeting, including scheduled plans for removal of failed products from the market and reinforcement of the requirements for storage conditions. NAFDAC continued batch collection of poor-quality oxytocin medicines from all previously identified affected health facilities and markets to ensure the ineffective products could not be accessed and used. This quarter, 10 ampoules of poor-quality oxytocin were collected from various locations in a state of the Federation. The recall exercise is continuous, and a subsequent report is expected from NAFDAC.

Additionally this quarter, in an effort to increase information in the public domain related to the manufacture of quality-assured medicines, PQM finalized and made available the first publication of a product information report (PIR) for amoxicillin. The PIR contains a summary of available literature and expert opinion on the API, analytical methods, toxicology, and formulation and process of the solid dosage form for the product. Information provided includes the chemical structure/formula, International Union of Pure and Applied Chemistry (IUPAC) name, physio-chemical properties, moisture sorption, and solubility-related data. This publication will help manufacturers and MRAs have almost all product information in one place, making it easier for quality-assured amoxicillin to be produced.

Key IR3 Indicators for FY 2018 Q1

Number of samples collected and tested	222
Number of regulatory actions taken	8 – Ethiopia, Nigeria, Senegal

Africa



Benin

I. Quarter 1 Highlights

PQM finalized the review of Benin's national quality control laboratory (LNCQ) draft strategic plan and submitted it to LNCQ management. PQM also submitted the FY 2018 work plan to the USAID Mission for approval.

II. Country Context

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

PQM finalized the review of the LNCQ 5-year strategic plan and submitted a detailed review document to the laboratory's management. Although ambitious, the plan lacks clear steps to achieve strategic objectives. The plan must take into consideration potential changes in the pharmaceutical regulatory system, including reforms by the Directorate of Pharmacy, Medicine, and Diagnostics Exploration and its future transformation into a national pharmaceutical regulatory agency, as well as changes of the regulatory framework that may affect LNCQ's role.

Electrical installation in the laboratory has proven inadequate. LNCQ began and made progress in rewiring the laboratory building. After completing this work and installing a new power generator, LNCQ will be able to function without interruption caused by power surge and shortage, which has damaged several pieces of laboratory equipment in the past. PQM obtained two quotations for a power generator from two local suppliers. The procurement of this equipment will be initiated once the work plan has been approved.

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

Activities under this objective are pending work plan approval and clarification about the process for establishing fixed amount awards (FAAs).

Burkina Faso

I. Quarter 1 Highlights

PQM continues to support the medicines quality control laboratory in strengthening its QMS by developing new SOPs. In a follow-up on PMS activities, the data for testing antimalarials collected in 2017 were finalized after completion of confirmatory testing.

II. Country Context

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

PQM was selected by USAID/Burkina Faso to strengthen the capacity of the country's national MRA, Direction Générale de la Pharmacie, du Médicament et des Laboratoires (DGPML), NQCL, Laboratoire National de Santé

Publique (LNSP), and other major pharmaceutical systems with the primary goal of improving its QA/QC of medicines.

In February 2015, in response to the USAID Mission's request, PQM conducted a rapid assessment of Burkina Faso's QA/QC capabilities and met with key stakeholders involved in the regulation, control, management, and distribution of medicines. The results of the assessment showed that traditional medicines are widely used by patients in Burkina Faso and are included in the Ministry of Health's (MOH) Strategic National Plan. The assessment also revealed an immediate need to strengthen DGPML's capacity and build LNSP's. Strengthening these two pillars of medicines QA is essential to advancing the country from use of unregulated medicines to use of regulated, quality-assured medicines based on international standards. To achieve this goal, it is critical to address the challenges that health programs are facing and to work closely with the Central Medical Store (CAMEG), DGPML, and LNSP to ensure that all medicines procured by USAID and the government are of good quality prior to release into the market and that their quality is maintained throughout the supply chain through to distribution.

III. Quarter 1 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

To prepare NQCL for ISO accreditation, it needs to participate in proficiency testing (PT) for the methods targeted for accreditation. The laboratory is initially using its own resources to perform two PTs. PQM provided NQCL with information about PT providers. Once the laboratory has completed the tests, PQM will review the results and assist NQCL in submitting the results to the PT providers. PQM is planning to facilitate two PTs later in the year (tentatively in Q3 and Q4).

Lab training on UV-Vis initially planned for Q1 has been postponed to March 2018.

Objective 2 – Support sustainable local capacity to monitor the quality of medicine

The medicines quality control laboratory finalized confirmatory testing of 10 samples and updated a data report Excel sheet submitted to PQM. The data show that all of the samples passed screening tests, and samples selected for confirmatory testing also passed. PQM is planning to organize a workshop to share the details of PMS activities with stakeholders in January 2018. This activity will be combined with the introduction of the risk-based approach in implementing PMS and development of a protocol for upcoming PMS activities. The latter will be carried out either through a subaward or direct implementation pending on clarification on the FAA process.

Objective 3 – Support the creation of the National Pharmaceutical Authority

There is nothing to report in this quarter. PQM is waiting for information from the new management of the National Pharmaceutical Regulatory Agency.

Ethiopia

I. Quarter 1 Highlights

During the first quarter, highlights of PQM accomplishments include the following:

1. Supported the drafting of three guidelines: Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products, and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology. The presence of such guidelines in support of registering specialized products is expected to increase access to new and innovative essential medicines that better address existing and emerging diseases. In addition to their contribution to the alignment of international best practices, these guidelines will also help to comprehensively address the review of dossiers, taking into account the peculiar nature of the stated products.
2. PQM also provided support in the preparation of a draft Community Pharmacy Audit Manual and SOPs intended to be used by inspectors for the implementation of risk-based inspection of thousands of retail outlets in Ethiopia. The proper implementation of this manual is expected to facilitate detection and prevention of poor-quality medicine in circulation, reduce diversion of products from the public sector, and assist in the proper implementation of good storage and good distribution practices.

3. Assessment of EFMHACA's quality control laboratory for reaccreditation and scope expansion was completed. The assessment was concluded with six minor nonconformities, for which CAPAs were prepared and addressed. It also resulted in potential scope expansion to three additional test methods and is indicative that the EFMHACA laboratory continues to operate and maintain an internationally acceptable level of compliance.
4. Results from PQM's supported PMS showed the failure of 49 samples of quinine sulfate tablet, 2 samples of primaquine tablet, 2 samples of zinc sulfate tablet, and 2 samples of artemether injection. The failed samples were recalled by EFMHACA to halt further distribution and protect the public from consequences associated with these poor-quality products.
5. PQM continued to provide technical leadership and made presentations at two international-level and one national-level workshops. The workshops and the presentations made by PQM are as follows:
 - Workshop 1: International Workshop on Counterfeit Medicines, Fighting the Illicit Trafficking of Fraudulent Medicines in Africa (September 27–28, 2017), "Tackling the Challenges of Poor Quality Medicines: USP/PQM's Interventions and Results"
 - Workshop 2: Inter-agency Framework of Collaboration for Implementation of NSPA-Pharma Meeting (November 14–15, 2017), "Building Local Manufacturing Capacity: Contributions of USP/PQM Ethiopia"
 - Workshop 3: Continental Forum on Access to Medicines and Health Commodities: Catalyzing Local Production, "Addressing the Scourge of Falsified & Substandard Medicines to Restore Public Confidence: USP/PQM's Experiences and Best Practices"

During the coming quarter, PQM will proceed with refining the draft guidelines and help EFMHACA and regional regulatory bodies to implement risk-based inspection. The results of the assessment of EFMHACA's quality control laboratory are expected to be released during the upcoming quarter both for the renewal of accreditation and scope expansion.

II. Country Context

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

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

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Support to strengthen the medical products quality assurance systems of Ethiopia

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

Guidelines for registration of biological products were developed in FY 17. However, based on request from the management of EFMHACA, this guideline was revised and divided into three separate guidelines namely: Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products (SBPs), and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology. The separation of these guidelines by specific product categories was made considering current international best practices and experiences. The draft guidelines were shared with more than 110 local stakeholders for feedback. PQM will continue supporting the consultative workshop to finalize the guidelines once existing feedback is incorporated.

Following the development and approval of the expedited medicine market authorization strategy during the previous quarter, EFMHACA requested the development of the same strategy for medical devices, and the development of this draft strategy was completed with support from PQM.

PQM has also provided support to continue the revision of the existing/old medicine registration guideline. Revision of the previous guideline was found to be necessary to align it with the changes introduced with the new guideline that takes into account the peculiarity of products. Reasons for initiating revision of the guidelines include the following:

- The existing/old guideline was generic and did not consider the specific nature of some products, such as vaccines and biologicals. With the development of the three new guidelines, there is a need to make the delineation.
- It was found necessary to align the existing guideline with the components on the medicine registration information system.
- Alignment of the guideline with the recently approved expedited marketing authorization strategy was needed.

In the coming quarter, further development/refinement of the registration guideline, finalization, and approval of the draft guidelines, SOPs, and inspection manual are expected to be completed.

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

The development and approval of the GMP inspection manual in FY 2017 and subsequent benefits it offered in streamlining GMP inspection triggered the same need for inspection of medicine retail outlets. As a result, development of this inspection manual progressed during the previous quarter, and the draft was completed in Q1. This inspection manual adopts risk-based inspections as a strategy to improve the effectiveness of inspections conducted by EFMHACA and regional regulatory bodies on medicine distribution channels and retail outlets.

The manual outlines appropriate steps to be followed for auditing medicine retail outlets and distributors with respect to good dispensing, good storage, and good distribution practices. It also requires inspectors to countercheck whether products handled by these establishments align with their respective levels/mandates and are obtained from the right/legal source. This rigorous process of auditing and counterchecking during inspection is expected to boost the capacity of EFMHACA and regional regulators to detect and prevent the circulation of poor-quality medicines, thereby helping to ensure the safety, quality, and effective use of medicines circulating in the market. This manual is expected to be applied during the coming quarter by EFMHACA in partnership with regional regulators. Inspectors will be provided appropriate training and orientation prior to deployment. PQM will continue supporting the efforts of EFMHACA and regional regulatory bodies in the implementation of this manual.

PQM continued to provide ongoing technical support on implementation of the medicine registration information system (MRIS). PQM provided technical support in the orientation of new entrant local stakeholders on MRIS, finalization of pre-import permit track for actual use, evaluation of the limitations of MRIS for new upgrades, preparation/revision of seven checklists, and preparation of five letter of notification formats for incorporation as part of upgrading MRIS.

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

During the first quarter of FY 2018, reassessment of both the medicine and the condom quality control laboratories was conducted from November 13 to 16, 2017. The findings of the assessment showed only six minor nonconformities. Based on the findings, the laboratory prepared and submitted CAPAs. After reviewing the CAPAs, ANAB assessors found all of them to be satisfactory, and the nonconformities were cleared. The assessment of the laboratory in Q1 is expected to expand the scope of accreditation by three additional physio-chemical test methods (Fourier-transform infrared spectroscopy (FTIR), Polarimetry, and Titration).

With the objective of ensuring sustainable laboratory equipment calibration at EFMHACA, PQM continued supporting the national metrology agency (NMI), using resources from USP's supplemental funding. PQM's activities in Q1 included preparing a list of pressure calibration apparatus parts, identifying a supplier, and submitting a purchase order to the vendor. The next step will be delivery of the parts to NMI. In addition, PQM communicated with three potential training centers that can provide hands-on training on calibration of dimension to NMI staff. Quotations were received, and evaluation of the vendors has started.

By using the same USP supplemental funding, PQM is supporting the ISO accreditation of Jimma University's laboratory. In this quarter, procurement of supplies and communication with potential suppliers of the buffers and other reference standards were completed. Communications were also made with Agilent's local agent (Jijie

Laboglass PLC) for a written contract agreement for corrective and preventive maintenance of the laboratory instruments. The local agent made a rapid assessment of the laboratory and reported parts that are needed to conduct corrective and preventive maintenance. It also gave its quotation to conduct the service, which is now under review. Going forward, Jimma University has committed to manage all maintenance related expenditures on its own.

Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved

Training of staff on GMP inspection of sterile product manufacturers was one of the activities rolled over to FY 2018 from FY 2017. The training, which was fully financed and facilitated by PQM, was provided to 31 staff (22 males and 9 females) on October 23–27 in Addis Ababa. This training had been identified as one of EFMHACA's specialized training needs. Building inspectors' capacity on GMP requirements for sterile products will help deter the entrance of poor-quality sterile products, including injectables, infusions, and blood products, into the country. It will also help to speed up inspection of manufacturers that have made applications at EFMHACA.

In FY 2017, PQM provided support in the development of a QMS module for the post-graduate regulatory affairs program of Addis Ababa University (AAU), School of Pharmacy. In Q1 of FY 2018, efforts were made to develop two additional teaching modules, one on "Regulatory Science and Compliance" and the other on "Product Registration and Licensing." PQM initiated processes for in-country development of the modules that also allows participation of experts in Ethiopia, including those from the School of Pharmacy and EFMHACA. These teaching modules will help to build the capacity of School of Pharmacy faculty, who will ultimately use the same module to teach the courses themselves. This will contribute toward sustainability of the post-graduate training program by reducing dependency on experts from overseas.

In line with efforts to build capacity for the local regulatory workforce, PQM continues to partner with AAU to provide technical leadership, experience sharing and professional networking to benefit students at the university. This quarter, PQM participated in a 1-day seminar organized by AAU School of Pharmacy post-graduate students of Regulatory Affairs, Drug-Supply Chain Management, and Social Pharmacy programs. The students made presentations on 11 topics, some of which concentrate on the regulatory systems. Students also prepared 25 posters which they presented during lunch and tea breaks.

Students also made PowerPoint presentations, including on the following topics:

- *Illegal Pharmaceutical Trade, from the perspective of regulation and SCM*
- *Impact of effective regulation for sustainable health supply chain management*
- *The application of PDCA cycle to improve the quality of pharmaceutical distribution*
- *What are the current trends in leadership, management and quality improvements in the SCM industry*
- *End to end data visibility in supply chain*

Participants included USAID, EFMHACA, Pharmaceuticals Fund and Supply Agency, USAID's Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project, AIDSFree, and school administrators. PQM contributed through discussions and feedback on the students' PowerPoint and poster presentations.

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

Results of PMS conducted in 2017 with support from PQM showed the failure of 49 samples of quinine sulfate tablet, 2 samples of primaquine tablet, 2 samples of zinc sulfate tablet, and 2 samples of artemether injection. EFMHACA took immediate action to recall the failed samples, thereby preventing further distribution/circulation and subsequent negative consequences on public health associated with the use of these products. All failed samples of quinine sulfate tablet were found to be from a single Indian manufacturer and imported by one importer. The manufacturer was banned, and EFMHACA plans to collect other types of medicines produced by this manufacturer and imported into the country. The importer of the quinine sulfate was given the responsibility to collect the failed samples from the market. Such commitment by EFMHACA in taking immediate regulatory action following PMS findings is a huge step forward in terms of saving the lives of citizens and safeguarding public safety from the impacts poor-quality medicines.

As part of its contribution to a multi-country study conducted by USP on the quality of RDTs (using USP resources) and based on EFMHACA's needs, PQM provided technical assistance in the development of protocols for collection of rapid diagnostic kits (RDTs) samples from the Ethiopian market. The testing is being conducted on products collected from five countries. Once the test is complete, results will be shared with each country.

PMS on oxytocin is also being conducted in collaboration with Monash University, and testing is currently in progress.

Objective 2 – Support increased supply of quality-assured priority medicines

PQM conducted a follow-up assessment of Cadilla Pharmaceuticals on the status of CAPA after a WHO assessment. On-the-job training was given to staff in selected areas, including change management, risk management, and data integrity. A detailed report is forthcoming.

PQM's participation continued in the implementation of a roadmap and the National Strategy and Plan of Action for Pharmaceuticals Manufacturing Development (NSPA-Pharma). In Q1, manufacturers that were assessed in FY 2017 were categorized into (1) those requiring only technical support and (2) those needing both technical and financial support; this information was submitted to the government. The categorization will help to optimize and strategize the government's support to promote existing local pharmaceutical manufacturing. PQM also played a key role in making a presentation on "Building Local Manufacturing Capacity: Contributions of USP/PQM Ethiopia" and providing feedback at the Inter-Agency Framework of Collaboration for Implementation of NSPA-Pharma Meeting on November 14–15.

As part of the effort to build the Regional Bioequivalence Center's (RBEC) capacity, laboratory equipment procured in FY 2017 was cleared from the customs office and delivered to RBEC. In addition, to address the gap identified during the WHO assessment, PQM contacted the original suppliers of software (SAS and WinNolin) on behalf of RBEC. Activation of the software is expected to happen by next quarter.

Objective 3 – Strengthen utilization of medical product quality information for decision making

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

PQM participated in and presented at an international conference with the theme of Fighting the Illicit Trafficking of Fraudulent Medicines in Africa. The workshop was organized by the Pan African Chamber of Commerce and Industry at the United Nations Economic Commission for Africa Conference Center in Addis Ababa on September 27–28. PQM's Chief of Party presented "Tackling the Challenges of Poor-Quality Medicines: USP/PQM's Interventions and Results."



Continental Forum on Access to Medicines: Catalyzing Local Production, Addis Ababa, December 18–20, 2017

In addition, PQM made a presentation called "Building Local Manufacturing Capacity: Contributions of USP/PQM Ethiopia" at a Continental Forum on Access to Medicines and Health Commodities: Catalyzing Local Production.

PQM also contributed to the preparation of a pharmaceutical traceability strategy by participating in several meetings during the development process. PQM was invited to the antimicrobial resistance (AMR) national advisory committee meeting, which was held in Adama on December 28–29, to contribute to updating the national AMR prevention and containment strategy. PQM contributed to the enrichment of the strategy and also agreed to continue contributing through participation in the subsequent national AMR advisory committee meetings. PQM's recommendation to include "Ensuring Quality of Antimicrobials"

as a key component of the strategy for prevention and containment of AMR was accepted by members of the national advisory body. This forum creates a platform for PQM to continue advocating for medicines quality from manufacture to patient use as part of the efforts to prevent and contain AMR in Ethiopia.

PQM provided technical assistance in the development of four posters as Information Exchange and Communication materials on pharmacovigilance for the public and healthcare providers. The posters are waiting for budget allocation for printing by EFMHACA. Supportive supervision on the Cohort Event Monitoring (CEM) on antiretroviral (ARV) medicines was carried out weekly on 20 health facilities. In addition, three meetings were carried out with ALERT/AHRI on a collaborative activity on the CEM and possible transfer of the cohort. A memorandum of understanding was prepared, the manual was revised, and the activity and allocated budget is now in process to be partially transferred to AHRI.

Activities carried out during the quarter include the following:

- On October 12, PQM facilitated and presented at a workshop attended by 32 participants from 6 hospital pharmacovigilance centers.
- Two meetings were carried out on establishment of a PV center and the support EFMHACA would provide to the selected hospitals. Equipment and reference materials were prioritized and budgeted for each hospital, based on their requests.
- On November 27–30, PQM conducted a workshop on revising the Adverse Event Following Immunization (AEFI) Guideline. The workshop was attended by representatives from the regional health bureau/Expanded Program of Immunization, EFMHACA branches, causality assessment committee, and MOH.
- PQM provided orientation on pharmacovigilance to Gandhi Memorial Hospital for 45 healthcare providers to create awareness on how to recognize, prevent, and report ADRs.
- On October 18–19, PQM provided an orientation on the switch to the next version of Vigiflow data management system. Four EFMHACA staff were trained by two experts from WHO/UMC.
- PQM recorded 125 entries on adverse drug event (ADE) data into the pharmacovigilance data monitoring system and shared 39 ADR reports with WHO.
- Summary report on product defects of diagnostics and medical supplies was shared to the inspection directorate upon request
- PQM provided feedback in the form of acknowledgment letters to 17 healthcare providers.
- PQM briefed the MOH State Minister on the importance and objective of the CEM on ARV to assist him in making a decision regarding possible funding allocation to the activity.

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

EFMHACA took regulatory actions on failed samples following quality testing of products collected during PMS in 2017. Based on EFMHACA's directives, 49 failed samples of quinine sulfate tablet were collected from the market by the importer of the product. Several other products were also collected from the market, including primaquine tablet, zinc sulfate tablet, and artemether injection, on the basis of a recall letter EFMHACA issued following the release of PMS results. Additionally, analysis of product defect reports received through the ADR reporting system led to the recall of iodine tincture and lidocaine solution for injection, as further investigation on these products confirmed them to be of poor quality. All of these medicines are in high demand in day-to-day clinical practice; they could have endangered the lives of many, had they not been detected and withdrawn from the supply chain system in time. This example highlights the contributions of USAID investments made to strengthen the capacity of EFMHACA – in building the capacity of quality control laboratory, establishing PMS systems, and strengthening the PV/ADR reporting system. In addition to saving lives and preventing potential patient harm, this will also contribute to the prevention of AMR, as many of these agents are used in the treatment or prevention of infectious diseases.

Objective 4 – Support office management and strengthen integration of M&E activities within regulatory authority

PQM has provided support to improve and develop the regulatory sector's monitoring and evaluation (M&E) systems by actively being involved in the technical working group established to refine outcome-level indicators set in the health regulatory transformation plan. PQM has provided intensive support in the development of the performance indicators reference sheet (PIRS). Improving EFMHACA's M&E system will help address the existing challenges in measuring achievements at a higher level to make decisions on policy-level changes and appropriately adjust strategies. In addition, EFMHACA has requested PQM's support to develop tools for data collection for key outcome indicators reported by different directorates and branch offices in order to facilitate data collection and consolidation. PQM will continue to support EFMHACA in the completion of the PIRS and in the development of data collection and consolidation tools.

IV. Lessons Learned

PQM's representation on national and international forums, workshops, and meetings has helped in the recognition of the project's role in ensuring the quality of medicines from manufacture to patient use. It is also creating opportunities

for advocacy to recognize product quality as a key priority in all health programs and to call policymakers' attention to building the capacity of regulatory systems.

Ghana

In collaboration with Ghana Food and Drugs Authority (GFDA), PQM finalized the development of the PMS protocol, which was approved by GFDA management for implementation. The focus of this surveillance is to monitor the quality of antimalarial medicines and ascertain their conformity with established specifications as declared in the product label. Sampling began in Q1 and will extend into Q2. Testing is also expected to be completed in Q2. With the implementation of this activity, GFDA will be able to generate data as it seeks to protect the Ghanaian population from substandard and falsified antimalarial medicines, thus contributing to a reduction in mortality due to malaria.

PQM also began the process of working to improve GMP compliance by local manufacturers of artemisinin-based combination therapy (ACT) antimalarial medicines in Ghana. PQM experts, with two GFDA inspectors as observers, visited four local antimalarial medicines manufacturers to perform an assessment of GMP compliance. The assessment involved a review of key pharmaceutical quality management processes and their conformity to GMP using the WHO PQ assessment tool. The assessment allowed PQM to determine the suitability of the manufacturers to receive technical assistance with the goal to improve GMP compliance to internationally acceptable standards and thus be in a position to pursue WHO PQ for the production ACT antimalarial medicines. The four local manufacturers—Entrance Pharmaceuticals, Amponsah Efah Pharmaceuticals, Phyto-Ryker Pharmaceuticals, and Ernest Chemist—are those who responded to the invitation for submission of expression of interest (EOI), jointly issued by GFDA and PQM. In line with PQM's systems-based approach, the assessment also provided an opportunity for GFDA inspectors to participate as observers and gain some expertise in the inspection of GMP facilities.

II. Country Context

Malaria is a leading cause of morbidity and mortality in Ghana. The goal of PMI in Ghana is to reduce malaria deaths and substantially decrease malaria morbidity, toward the long-term goal of elimination. Through PQM, since 2009 USAID has been assisting GFDA to strengthen the medicines quality assurance and quality control systems. Activities have focused on strengthening GFDA's capacity in drug registration, medicines quality control, and PMS. PQM has also recently provided technical assistance to ensure locally manufactured ACTs meet internationally acceptable quality standards.

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

There are several local manufacturers of pharmaceutical products in Ghana. GFDA continues to build capacity for its GMP inspectors to ensure it can adequately inspect facilities and provide guidance to industry to address GMP gaps. This will help to ensure locally produced medicines meet internationally acceptable GMP standards.

III. Quarter 1 Progress by Objective

Objective 1 – Facilitate sustainable implementation of a risk-based approach for PMS of antimalarial and MCH medicines

Activity 1.3: Facilitate PMS for antimalarial products in a sustainable manner using a risk-based approach (continued from FY17)

Preparation for the PMS of antimalarial medicines that began in FY 2017 was protracted for several reasons, primarily the lack of reagents and standards as clearance was delayed by customs at the Ghana airport. The lack of an approved protocol for implementing PMS was also a factor. This PMS activity was thus carried over into the FY 2018 work plan as an activity to be implemented in Q1. In FY 2017 Q4, chemicals and reagents needed for the 2017 antimalarial medicines quality surveillance were purchased and supplied to GFDA for distribution to the various sentinel sites. Minilab™ test kits and consumables at the ports have been cleared. This quarter, in addition to successfully resolving the internal issues related to this activity, including procurement of the needed reagents, standards, and supplies, PQM collaborated with GFDA to finalize the protocol for the implementation of this activity. GFDA promptly approved this protocol. Implementation of the 2017 PMS for antimalarial medicines, including the collection and Minilab™ screening of samples commenced in Q1 and is expected to be completed in Q2.

Activity 1.2: Review PMS protocols using risk-based guidelines

The protocol for this activity was developed, finalized, and approved. The development of the PMS protocol for the 2017 antimalarial surveillance is a major deliverable that has been accomplished. Risk-based components are still being finalized by PQM and are yet to be rolled out. This will be incorporated in the next round of PMS.

Objective 2 – Strengthen Ghana FDA QA/QC system through sustainable laboratory accreditation

No activity to report. Implementation of this activity is planned for Q2.

Objective 3 – Strengthen facility inspection capacity of Ghana FDA

Activity 3.2: Conduct hands-on joint inspection with Ghana FDA inspectors

Ghana FDA inspectors served as observers in the recently conducted assessment of four ACT pharmaceutical manufacturers that responded to the EOI issued by PQM. Two GFDA inspectors participated in each inspection, gaining additional expertise through hands-on observation and contributing to technical questions and discussions in the course of the assessments.

Objective 4 – Increase supply of quality-assured antimalarial products (ACTs) by providing technical assistance to local manufacturers

Activity 4.1: Conduct an assessment of GMP compliance of local manufacturers selected through EOI submission (continued from FY17)

PMI's health system strengthening efforts are tailored to ensure access to quality-assured antimalarial medicines in accordance with national treatment guidelines. In Ghana, a key approach is to ensure accurate diagnosis and prompt treatment with quality-assured ACTs in accordance with national treatment guidelines. In addition to donor-procured ACTs, local manufacturers in Ghana account for nine artemether-lumefantrine (AL) and three artesunate–amodiaquine (AS–AQ) products that were approved by GFDA as of 2017. However, none of these local manufacturers have been assessed by WHO for prequalification of their ACT products. To ensure the locally manufactured ACTs meet internationally acceptable quality standards, PQM will provide technical assistance to local manufacturers of these priority product (AL and AS-AQ) tablets to improve GMP compliance. Local manufacturers, which are able to improve GMP compliance, will have the opportunity to pursue WHO PQ in subsequent years based on the level of compliance.

The manufacturers to benefit from this technical assistance were selected through a transparent EOI submission process. Based on prior experience, PQM recognizes that building capacity to improve GMP compliance is a multiyear activity and therefore applies the limited resources available toward targeted interventions to include a gap assessment, development of CAPAs, and technical assistance to address the gaps.

In Q4, an EOI was issued to identify local manufacturers of ACT medicines that were interested in receiving technical assistance from PQM. Four manufacturers—Entrance Pharmaceuticals, Amponsah Efah Pharmaceuticals, Phyto-Ryker Pharmaceuticals, and Ernerst Chemist—expressed interest. PQM and GFDA inspectors visited the facilities of these four manufacturers on October 29–November 15. Confidential assessment reports detailing the findings from the visits will be shared with the manufacturers and GFDA once completed. The visit afforded PQM the opportunity to implement a joint inspection, thus building the capacity of the GFDA inspection unit. In subsequent months, PQM will provide technical assistance to improve the GMP compliance of the selected manufacturer(s) deemed eligible for assistance.

Guinea

I. Quarter 1 Highlights

As part of building the QC capacity of the Guinea national quality control laboratory (LNCQM), PQM assisted the laboratory director and his staff in conducting an inventory of all laboratory equipment, their respective log books, and needed parts for repair and preventive maintenance.

To move forward with the agenda of the enactment of the pre-project of the pharmaceutical law, PQM initiated the creation of a document titled “Exposé des Motifs” (Explanatory Statement), which includes a summary of all the law documents that have been amended and/or revised by PQM, SIAPS, and the Law Revision National Committee. PQM has contributed greatly to the drafting and finalization of this document, which was presented to the Minister of

Health and his cabinet in December 2017. Additionally, at the request of the USAID Mission, PQM organized meetings with Health Finance and Governance (HFG), a USAID-funded project, and discussed ways to collaborate to assist Guinea's National Assembly during the process of approving the revised law.

II. Country Context

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

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

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

III. Quarter 1 Progress by Objective

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

PQM held meetings with the Inspector General of the MOH and regulatory authority (DNPL) director to follow up on the progress of the Pharmaceutical Law project. The Inspector General met with and presented the Pre-Project Law to the Minister and his cabinet members, who requested an explanatory note highlighting the need for a revision of the law and the major amendments made, along with a corresponding PowerPoint presentation. These will serve as basic documents that will support and facilitate the introduction of the Pre-Project Law by the Minister to the Inter-Ministerial Council, presided by the Prime Minister and the Ministers' Council headed by the President of Guinea. They will also be used during meetings with the Health Commission of the National Assembly, which will play a vital role in the passing and adoption of the law. PQM assisted with drafting the explanatory note and corresponding presentation, which were subsequently validated by the Law Revision National Committee. The President of the Committee is awaiting the next Minister's Cabinet meeting, which is expected to take place in early 2018, to present both documents.

PQM also met with the USAID-funded HFG project, per the USAID/Guinea Mission's recommendation. HFG works closely with the Health Commission members of the National Assembly to build their technical capacity by training them to adequately examine, critique, and defend a law project. The discussions with HFG centered on identifying the appropriate timing and strategy for the National Committee to present the Law Project to the above-mentioned members of the National Assembly. It was determined that before April 2018 would be the best time to arrange an initial meeting.

Objective 2 – Continue strengthening DNPL capacity in product registration

Plans have been made to provide the needed technical assistance for the registration department in Q2–Q3.

Objective 3 – Enable DNPL to assume MQM responsibilities

This activity is ongoing.

Objective 4 – Strengthen QC capacity of LNCQM

PQM continues to provide support to LNCQM in building its QA/QC capacities, as well as GLP through the training of analysts and laboratory staff, provision of laboratory equipment and consumables, and sampling and testing of selected essential medicines. PQM assisted LNCQM staff in conducting an inventory of all existing laboratory equipment; non-functioning equipment were identified and placed in storage. To help improve GLP, information sheets containing equipment specifications were developed, and log books were produced to facilitate information tracking and record keeping. PQM also helped LNCQM staff design a logo for the laboratory. PQM is in the process of procuring laboratory consumables for the Karl Fischer Titrator (delivered to LNCQM in September 2017) and high-performance liquid chromatograph (HPLC), as well as a reference weight set for balance calibration and verification.

Liberia

I. Quarter 1 Highlights

The main activities this quarter included the following:

- Attended and presented PQM activities at the National Malaria Control Program (NMCP)–PMI Implementing Partners' meeting in December.
- With the Liberia Medicines and Health Products Regulatory Authority (LMHRA) and NMCP, planned the remaining FY 2017 activities, including the regional meeting and training on dossier evaluation.
- With NMCP and LMHRA, prepared the implementation plan of FY 2018 activities.
- Discussed with LMHRA the status of the transitional LMHRA QC laboratory.
- Facilitated shipping for medicines collected during the last PMS to the USP laboratory for QC testing.

II. Country Context

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

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

In Liberia, PQM is focused on:

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Rebuilding capacity of LMHRA QC laboratory

The quality control laboratory of LMHRA was gutted by a fire on May 30, 2017. The incident resulted in a loss of about \$600,000 in commodities such as equipment, chemicals, glassware, and other laboratory materials. This figure does not include destruction of the infrastructure.

In order to continue basic screening of medical products, the laboratory has been temporarily housed in a two-room facility that was formerly used to store medicines and chemicals. With this very limited space, the activities conducted are only based on the use of the Minilab™ basic tests.

To ensure the availability of safe and efficacious medicines in Liberia, a new, more spacious facility has been identified for temporary use. PQM is assisting LMHRA during the process of remodeling the new temporary space while waiting to receive Global Fund approval for the construction of a permanent laboratory and offices.

Objective 2 – Continue building the QA/QC capacities of LMHRA in registration and inspection

Plans have been made to provide training on dossier evaluation in Q2.

Objective 3 – Build LMHRA capacity to take appropriate regulatory actions

The FAA was approved by USAID/Washington and the Mission in December 2017. PQM is planning to work with LMHRA during the implementation phase of the FAA.

Objective 4 – Development of integrated PMS in Liberia (via leveraged funding)

PQM worked to facilitate the shipping of medicines collected during the last PMS to the USP laboratory for quality control testing until the temporary laboratory is fully established.

Objective 5 – Expand and improve dissemination efforts to raise awareness about poor-quality medicines

PQM met with the Mission health team, including the director, staff from the U.S. Centers for Disease Control and Prevention (CDC) and PMI, as well as USAID Washington, represented by Christie Hershey. The meeting included the presentation of PQM Liberia FY 2017 activities, accomplishments, and challenges, as well as opportunities for FY 2018. The presentation and discussion were well received by the attendees. The PMI advisor congratulated PQM for the successful achievements of Liberia activities despite the laboratory fire incident of May 2017 and for an excellent presentation made November 28 during an NMCP–PMI meeting.

Mali

I. Quarter 1 Highlights

In order to customize training to meet the needs of the National Laboratory of Health's (LNS) medicines quality control services, PQM conducted an evaluation of laboratory staff members' skills. The evaluation covered GLP and good documentation practices (GDP) compliance, as well as laboratory staff's performance in conducting HPLC, UV-vis, and dissolution tests. PQM also facilitated procurement of PTs for HPLC, UV-Vis, and dissolution. These PTs will provide an independent evaluation of the laboratory's performance. LNS is expected to complete the PTs by the end of January 2018.

Another important activity in Q1 was the implementation of the first phase of antimalarial sample collection, followed by a dissemination workshop to share the results with all stakeholders in health services, including regional health directorates. Following this activity, a report was prepared and submitted to the laboratory directorate for wide dissemination among stakeholders.

II. Country Context

Malaria is the primary cause of morbidity and mortality in Mali. The goal of PMI in Mali is to reduce malaria deaths and substantially decrease malaria morbidity, toward the long-term goal of elimination. Through PQM, since 2008 USAID has been assisting Mali's MOH in strengthening the medicines QA systems. Activities have focused on strengthening the Directorate of Pharmacy and Medicine (DPM) and LNS capacity in pharmacovigilance, drug registration, medicines quality control, and PMS.

The objectives of PQM interventions in Mali are in line with PMI's strategic approach in the area of building capacity and health systems, as described in the PMI 2015–2020 strategic plan. PQM-proposed activities in Mali fall under

PMI's core operating principles that "ensure that all commodities provided to countries are of high quality and that systems are in place to continually improve the quality of services delivered."

III. Quarter 1 Progress by Objective

Objective 1 – Strengthen the capacity of the Directorate of Pharmacy and Medicine

Workshop for dissemination of pharmaceutical QA assessment (and establishment of a committee)

After two inspections and evaluation missions of the pharmaceutical system through DPM, a restitution workshop is necessary to bring together all of the actors in the health sector and share the results of the evaluation through open exchanges. Accordingly, coordination meetings to prepare this workshop were held with DPM and involved the Ministry of Health and Public Hygiene. Despite the progress made during the planning meetings, this activity—initially planned for November—will be carried out in February 2018.

Objective 2 – Strengthen the capacity of the National Laboratory of Health (LNS) to meet international standards

Assist the lab in review and complete required QMS documents

Before the start of this quarter, the LNS manager was replaced. PQM met with the new manager and briefed him on PQM activities, and he expressed his willingness to work closely with PQM.

LNS has not conducted any recent internal audit or evaluation of the work carried out in its medicines quality control laboratory. To assess the progress made by the laboratory since the latest training provided to the analysts, PQM performed an evaluation of staff skills. This evaluation was carried out in the form of a survey, where each staff member estimated his or her level of proficiency in conducting QC tests. Based on these evaluations, the majority of QC staff indicated they needing training on GLP, GDP, use of HPLC, gas chromatography, UV-Vis double beam, and dissolution testing. To obtain an independent evaluation of laboratory staff in conducting these tests, PQM procured PTs. LNS is expected to complete these tests by early Q2. The results of the PTs, along with the survey, will help PQM to customize training to better address the needs of the laboratory.

Similarly, PQM conducted an evaluation of analysts' compliance with GDP. This evaluation consisted of reviewing laboratory notebooks and records generated during a full testing of a single pharmaceutical product from the start of testing until the issuance of a certificate of analysis. It allowed for the identification of some of the most common mistakes made in GDP. For example, many analysts did not record information about the reagents used for the testing and omitted information on the status of laboratory equipment and its calibration status. This evaluation also revealed that the laboratory manager has not been involved in reviewing laboratory work.

To strengthen LNS' QMS, PQM helped in updating two procedures: "Procedure of Procedures" and "Document Control." These two procedures have been finalized and approved by the Director General of LNS. All of the existing SOPs are being updated using the newly approved template.

Two new SOPs on laboratory security and management of chemicals in the laboratory were also written. Additionally, two SOPs on the usage of HPLC Agilent 1260 and 1100 series were drafted.

PQM is updating the microbiology laboratory ISO-17025 Chapter 4 procedures to the newly approved template. These procedures will become LNS' overarching SOPs.

Lastly, PQM is coordinating with the World Bank's Sahel Women Empowerment and Demographic Dividend (SWEDD) project to support LNS in its efforts to achieve ISO 17025 accreditation.

Objective 3 – Strengthen sustainable local capacity to monitor the quality of medicines in the country

Develop sampling plan based on previous round of PMS

To develop a sampling plan using a risk-based approach, PQM analyzed the results from previous PMS activities and identified the areas of focus. The major issue relating to the quality of antimalarial medicines has been the presence of falsified quinine sulfate in the public sector. Although the results indicate that the number of falsified medicines has decreased among the samples collected, there are indications that the issue is persistent and also applies to medicines other than antimalarials, such as antibiotics. The sampling will be focused on public health facilities. PQM identified the health facilities that will be revisited for sample collection. Sample collection in the private sector will be limited to monotherapies, if found.

PQM procured a handheld Raman spectrometer that will be used to detect falsified antimalarials. After training, LNS should be able to use the device for screening medicines other than antimalarials.

PQM drafted a report on the workshop for dissemination of 2017 PMS results. The report has been submitted to and reviewed by LNS management. It will be finalized in early 2018. LNS will submit this report to the Ministry of Health and Public Hygiene for approval of the recommendations of the workshop.

Objective 4 – Facilitate studies on resistance of antimalarial medicines

The activities under this objective will start in May 2018.

IV. Key Challenges

The main challenge this quarter was to have the Directorate of Pharmacy and Medicine agree on a date to hold a workshop for dissemination of the results of the DPM and other institutions involved in quality assurance of pharmaceuticals. The workshop is now planned for the third week of February 2018.

Mozambique

I. Quarter 1 Highlights

PQM continued implementing key FY 2017 carryover activities while waiting for approval of the FY 2018 work plan. The 50 oxytocin samples collected from 27 drug outlets in Maputo province and Maputo city were tested using compendial methods. Based on the compendial laboratory testing, 18 of the samples were found to be substandard (manufacturing/storage/distribution practices do not meet required quality standards) and 1 was a falsified product (sample did not contain the active pharmaceutical ingredient of oxytocin), failing both identity and assay tests. PQM identified two ISO 17025 accredited labs, Vietnam Institute of Drug Quality Control HCMC and USP Ghana, to conduct confirmatory testing of 10 randomly chosen samples. The results from this confirmatory testing by ISO-certified laboratories will allow PQM to build a stronger case to inform decision-makers about the need for further investigation and regulatory actions. PQM also shared preliminary results with the Pharmaceutical Department (PD), national quality control laboratory (LNCQM), and USAID/Mozambique. The PD organized a meeting with the central medical stores (CMAM) to assess the magnitude of the problem. Based on the positive feedback and request from the USAID mission, PQM has started planning for the expansion of the oxytocin study to other provinces.

To assure the quality of the results generated by the laboratory, it is important that the laboratory equipment undergo regular maintenance and calibration by qualified vendors. Following the equipment master list developed by PQM in FY 2017 Q4, LNCQM, with PQM support, identified key equipment that require external vendor calibration; PQM is currently facilitating the contractual process with the vendor for calibration. The activity is planned to take place at the beginning of FY 2018 Q2.

Additionally, based on the LNCQM request, PQM is coordinating procurement of laboratory supplies and reagents to ensure laboratory staff are able to perform their day-to-day activities while utilizing the skills from previous PQM technical training. PQM also obtained a copy of LNCQM's SOP master list to begin identifying critical QMS documents required for LNCQM to apply GLP.

Lastly, the pharmaceutical law was signed by the president, and PD has 180 days to develop key regulations before the law becomes effective. PQM is part of the technical working group developing the key regulations.

II. Country Context

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

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

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

Throughout 2013 and 2014, PQM developed and trained LNCQM technical staff and provided them with day-to-day laboratory consumables, equipment, supplies, and reagents to run the QC laboratory. To date, LNCQM has improved its technical capacity in analytical testing, proficiency, and use of key equipment. Through this PQM training, LNCQM is better able to collaborate with other Portuguese-speaking countries.

The PD and MOH updated the pharmaceutical law of Mozambique in 2016. The law was approved by the parliament in early 2017; in September 2017, it was signed by the President. With more than 90 percent of medicines circulating in Mozambique being imported, the authorities are well aware of the country's vulnerability and exposure to poor-quality medicines. This new legislature offers a great opportunity for PQM and other supporting partners to make long-lasting contributions to the country's efforts to strengthen medicines regulation and work toward eliminating substandard and falsified products in the country.

III. Quarter 1 Progress by Objective

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

Following PQM staff travel to Maputo, Mozambique, in Q4 of FY17, PQM mapped all of the equipment at LNCQM and grouped them into three categories to help the laboratory develop a sustainable approach toward equipment calibration and maintenance. Equipment under category A does not need calibration, category B can be calibrated in house, and category C requires an outside vendor for calibration support. This document will benefit the laboratory by allowing it to plan and track equipment maintenance and calibration to ensure results are consistent, accurate, and reliable. Based on this plan, PQM will support LNCQM in developing essential procedures for in-house equipment calibration. LNCQM and PQM identified 17 pieces of category C equipment that need calibration from an outside vendor. Based on the list shared by the laboratory, PQM obtained quotes from Calibration Consulting Group (CCG), an approved and certified vendor, to provide these services and is currently facilitating the contractual process. The in-country equipment calibration activity is planned for Q2. It is important that the equipment undergo regular maintenance and calibration by qualified vendors. This activity is a GLP requirement, which all laboratories that seek to attain international standards have to maintain.

This quarter LNCQM submitted a procurement list of basic laboratory supplies and reagents to PQM. To support the laboratory's request, PQM identified local vendors and obtained quotes to help reduce delivery time and cost. Most of the consumables requested by the laboratory were nonessential items but were critical for the laboratory to operate. Although PQM agreed to procure these supplies on this occasion, it was communicated to the laboratory to fund procurement of these nonessential consumables on their own going forward. To support LNCQM to procure from reputable vendors, PQM shared the contact information of a PQM-vetted and approved vendor based in Ghana that is able to supply affordable nonessential laboratory supplies within a short timeline. PQM will search for more vendors within the Southern Africa region that meet the same criteria. This is in line with PQM's plan to help the laboratory take more ownership of its activities to promote more sustained outcomes.

PQM obtained a copy of LNCQM's SOP master list to begin identifying critical QMS documents required for LNCQM to apply GLP.

Objective 2 – Support and strengthen post-marketing surveillance

In FY 2017 Q4, PQM conducted an oxytocin study and collected oxytocin injection samples from Maputo city and Maputo province in response to the country's request to assess the quality of oxytocin injection in the local supply chain. A total of 50 samples of oxytocin ampoules from 7 different manufacturers were collected from 27 drug outlets in Maputo province and Maputo city. Out of the seven different manufacturer products imported to Mozambique for sale, only one was registered by PD. Four of the seven products received a waiver by PD to be marketed in the country, while the other two products were neither registered nor approved using a waiver by PD. After compendial laboratory testing, 18 of the samples were found to be substandard (manufacturing/storage/distribution practices do not meet required quality standards), and 1 was a falsified product (sample did not contain the active pharmaceutical ingredient of oxytocin) that failed both identity and assay tests. Of the 19 samples that failed, 7 were not registered with the PD and 12 received waiver approvals by the PD. The breakdown of the samples testing results is in the below table.

Compendial Laboratory Test Results of Oxytocin Injection Samples Analyzed

Sentinel site	Results of Compendia Tests				
	Total number of samples tested	Number of samples passed	% Passed	Number of samples failed	% Failed
Maputo city/Public	24	17	70.8	7	29.2
Maputo city/Private	6	2	33.3	4	66.7
Maputo province/Public	19	12	63.1	7	36.9
Maputo province/Private	1	0	0.0	1	100.0
Total	50	31	62.0%	19	38.0

Although all facilities stored the products according to the manufacturer's recommendation, the storage range observed, 24°C to 27°C, signifies that some facilities were storing the product outside of the recommended manufacturer's range of not more than 25°C. To confirm the compendial test results, PQM contracted two laboratories, USP Ghana and Vietnam Institute of Drug Quality Control HCMC, to perform confirmatory testing of 10 randomly chosen samples. The confirmatory test will provide evidence and assurance from ISO-accredited laboratories for PD in case test results are challenged by the product marketing authorization holder. Although confirmatory tests results are not yet available, PQM informed Mozambique PD, LNCQM, and USAID/Mozambique about the preliminary findings and made recommendations for PD to work with CMAM to assess the magnitude of the problem and take appropriate action, since most of the samples were collected from public sector facilities. In Mozambique, the procurement and distribution of health products to public sector facilities is handled by CMAM. PD's meeting with CMAM was to agree on additional assessment of its stock on hand to guide further decisions.

Following the positive response from the USAID mission on the oxytocin study and requests to expand it to other provinces, PQM is currently planning to expand this activity.

Objective 3 – Provide technical assistance to the Pharmaceutical Department

The pharmaceutical law in Mozambique was signed by the President and officially published in the Boletim da Republica in the country, making the law a legally binding document that will take effect 180 days after its publication. Key regulations have to be developed and ready within the same timeframe. Following the signing of the pharmaceutical law, PQM is working with PD to develop new regulations in line with global and regional standards for ensuring the quality of medical products in the country. PQM is serving on the technical working group for development of new regulations; the current focus is on GMP, registration, and pharmacy licensing.

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

No updates this quarter.

IV. Key Challenges

This quarter the biggest challenge was facilitation of the cold chain shipment of the oxytocin samples from Maputo to USP Ghana and Vietnam Institute of Drug Quality Control HCMC laboratories for confirmatory testing. Finding a vendor that could ship cold chain took over a month of back and forth between LNCQM, PQM, and local shipping vendors, as most shipping companies could not guarantee cold chain shipment to the final destination. This caused delays in getting the samples to the respective laboratories for confirmatory testing. However, through the support of a PQM in-country consultant, a vendor was identified and the oxytocin injection samples were shipped for testing. Test results are expected in Q2.

Nigeria

I. Quarter 1 Highlights

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

Highlights during this quarter included:

- NAFDAC's Agulu and Yaba laboratories both maintained their existing test methods and also expanded to microbiology test methods. Official notifications for both laboratories are expected next quarter.
- NAFDAC committed to sustainability this quarter, as all costs associated with equipment calibration, proficiency tests, and other laboratory supplies were paid by the agency. Minimal technical assistance was provided by PQM during the preparation for surveillance audit by laboratory staff.
- Facilitation of a dissemination meeting by NAFDAC to discuss PMS results of the antimalarial study, which showed that 1.6 percent of sampled products (14 samples) failed QC testing. Key recommendations were made as a result of this meeting, including scheduled plans to remove failed products from the market and reinforce the requirements for storage conditions.

II. Country Context

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

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Increase support to NIPRD laboratory towards attaining international standards of quality and practices

In FY 2017, an extensive gap assessment at NIPRD was completed, and a new roadmap with timelines was developed. Based on the new roadmap, NIPRD commenced the process of equipment procurement, while PQM commenced capacity and skills building of staff on GLP.

In Q1, PQM Nigeria held a meeting with NQA & Conformity Assessment (NQA&CA)—the first ANAB-accredited calibration body in West Africa, located in Lagos, Nigeria—to commence the process of equipment calibration for NIPRD. Working with NQA&CA will eventually eliminate the need to hire foreign consultants, result in cost savings in preventive maintenance and calibration, and help to ensure more sustainable practices for calibration of NIPRD laboratory equipment using local resources. Next steps include conclusion of laboratory hands-on techniques training and commencement of proficiency tests scheduled for next quarter.

Objective 2 – Strengthen the national quality assurance and regulatory system

NAFDAC commits to sustainability

In FY 2017, NAFDAC Zonal Laboratory of Agulu had received official notification of accreditation from ANAB for seven pharmaceutical test methods. Looking ahead, the PQM team organized a roundtable with the Head of NAFDAC, Central Drug Control Laboratory (CDCL) in Yaba and Agulu to discuss preparatory activities toward statutory ISO/IEC 17025:2005 reaccreditation. Further discussions were held on the expansion of scope for both Agulu and Yaba laboratories and their microbiology units. The outcome of the meeting was a well-defined roadmap on the planned scope expansion and the equipment needed for the reaccreditation.

As part of the implementation of the roadmap this quarter, Agulu and Yaba laboratory staff prepared for the mock audit with minimal technical support from PQM staff. PQM conducted a mock audit of the Agulu and Yaba laboratories with the aim of identifying deficiencies and opportunities for improvement in preparation for the ISO/IEC 17025:2005 reaccreditation by the ANSI-ASQ. Findings from the mock audit include two major non-conformances for both laboratories. The team witnessed 8 and 10 compendial testing methods demonstrated by the laboratory staff in Yaba and Agulu, respectively. The PQM team provided technical assistance to the laboratory to address the audit findings. As further support to CDCL Yaba and Agulu toward the ISO 17025 accreditation for microbiology, PQM procured and delivered very minimal complimentary reagents and consumables required for the laboratory demonstrations of the various test scopes to be assessed. NAFDAC has continued to take the lead on sustaining PQM's efforts in the laboratories, as all cost associated with equipment calibration, proficiency tests, and other laboratory supplies were paid by the agency.

NAFDAC Zonal laboratory Agulu passes surveillance audit and expands testing methods

NAFDAC Agulu laboratory in Anambra passed surveillance audits for 7 tests methods and expanded with 9 additional test methods, including 3 microbiology test methods—making a total of 16 test methods. Microbiology tests are required for certain USAID priority MCH commodities. This makes the laboratory the first in Nigeria to have test methods in microbiology. Official notification from ANAB for the successful reaccreditation for ISO 17025:2005 is expected by next quarter. The pharmaceutical testing methods include HPLC, ultraviolet visible spectroscopy, pH measurement, dissolution, loss on drying, Karl Fischer water content determination, uniformity of dosage form (weight variation and content uniformity), melting point, polarimetry, hardness, friability, disintegration, bacteria endotoxin, microbial limit, sterility, and volumetric titration.

NAFDAC Central District Control laboratory Yaba passes surveillance audit and expands testing methods

NAFDAC Yaba laboratory in Lagos passed a surveillance audit for 10 tests methods and expanded with 7 additional test methods, including 3 microbiology test methods—making a total of 17 test methods. Official notification from ANAB for the successful reaccreditation for ISO 17025:2005 is expected by next quarter. The pharmaceutical testing methods include HPLC, ultraviolet visible spectroscopy, pH measurement, dissolution, loss on drying, Karl Fischer water content determination, uniformity of dosage form (weight variation and content uniformity), FTIR, melting point, polarimetry, hardness, friability, disintegration, bacteria endotoxin, microbial limit, sterility, and volumetric titration.

Institutional capacity for regulatory workforce sustainably improved

PQM collaborates with WHO, its regional and country offices, and national health authorities to conduct training courses on a broad spectrum of quality control test procedures and GMP. The courses, held onsite at national drug quality laboratories or at sentinel sites and local laboratories, focus on a wide range of topics related to various facets of medicines quality at the regional, national, and local levels.

In Q1, the PQM team organized a training course on Pharmaceutical Microbiology for 12 participants from the 3 PQM-supported NAFDAC laboratories. This was a requisite training as the laboratories prepared for expansion of test methods in microbiology. Six modules were covered. Pre- and post-tests were conducted to verify participants' understanding; the average score was 75 percent in the post-test, which was a good improvement from the initial average score of 59 percent. Another training was conducted for 45 staff of the Institute of Public Analysts of Nigeria (IPAN) on QMS. Nine modules were covered. Pre- and post-knowledge checks were administered to verify the levels of understanding; the average score was above 80 percent in the post-test, which was a good improvement from the initial average score of 63 percent.

NAFDAC disseminates PMS for antimalarial results

PQM Nigeria focuses on building NAFDAC's capacity to perform PMS as a regulatory function, which is aimed at assessing product quality in the market. This includes monitoring the quality of marketed products throughout the levels of the supply chain.

A dissemination meeting with stakeholders was held this quarter to discuss the outcome of the analysis of antimalarial products sampled in FY 2017 to evaluate product quality in the six geopolitical regions. In attendance

were representatives from the Pharmaceutical Society of Nigeria, National Association of Community Pharmacists of Nigeria, various manufacturers and importers of antimalarial medicines (including CHI Pharmaceuticals, May & Baker, Novartis Pharmaceuticals, and Swiss Pharm Nigeria), Pharmacist Council of Nigeria, and Food and Drug Unit of the Federal MOH. The meeting was also attended by Directors of Pharmaceutical Services from Adamawa and Enugu state, the NAFDAC Director General (represented by the Director of Regulation and Registration), Directors of various NAFDAC directorates, the PQM team, and the Director of the PV/PMS Directorate, as the anchor for the meeting.

Key outcomes of the meeting included:

- NAFDAC Zonal and State Coordinators will follow up on the failed antimalarial samples and ensure the 14 samples of antimalarial medicines that did not conform to quality specifications are removed from circulation.
- NAFDAC Port Inspection Directorate will ensure stringent inspection of imported antimalarial medicines that did not conform to quality specifications.
- Drug Evaluation and Research Directorate should monitor the manufacturers of antimalarial medicines that failed to meet quality specifications to ensure that only quality antimalarial medicines are manufactured, distributed, and used in Nigeria. A next step after the dissemination meeting is commencement of regulatory actions to ensure the ineffective products cannot be accessed by the public.
- Continuation of batch collection of poor-quality oxytocin medicine from all affected health facilities and markets to ensure the ineffective products cannot be accessed and used on pregnant women. This quarter, 10 ampoules of poor-quality oxytocin were collected from various locations in a state of the Federation. The recall exercise is continuous, and a subsequent report is expected from NAFDAC.

PQM Nigeria makes information on oxytocin available to SOGON

PQM Nigeria made a presentation on “Safe Childbirth and Quality Medicines: Results of Oxytocin, Misoprostol, Magnesium Sulfate and Calcium Gluconate Quality Audit” at the 51st annual general meeting and scientific conference of the Society of Gynecology and Obstetrics of Nigeria (SOGON). The theme of this year’s conference was “Maternal and Newborn Health in a Challenging Economy.” The conference attracted over 200 gynecology and obstetrics doctors and dignitaries such as the King of Sokoto and Executive Governors of Sokoto and Yobe State. SOGON expressed its concern about the quality of oxytocin available for use in the country as shown by independent research and corroborated by PQM Nigeria’s survey report on oxytocin.

Objective 3 – Provide technical assistance to selected manufacturers with strong interest and commitments to locally manufacture products of interest (zinc sulfate tablet, oral rehydration salts, chlorhexidine, amoxicillin dispersible tablet, artemether-lumefantrine, oxytocin injection, magnesium sulfate injection, and ready-to-use therapeutic food) to successfully register their products at NAFDAC

As part of building the capacity of local manufacturers, PQM provided technical support to three local manufacturers this quarter. In addition, targeted and product-specific support was provided to one manufacturer toward production of quality-assured sulfadoxine pyrimethamine (SP) (500+25mg) tablet for malaria. This product is used for intermittent preventive treatment of malaria and is recommended for specific high-risk groups such as pregnant women. PQM audited the local manufacturer Emzor Pharmaceuticals to assess its manufacturing practices for SP (500+25mg) tablet. The audit was concluded with a few critical observations, and Emzor Pharmaceuticals is working toward resolving CAPAs identified during the audit. Attaining production of quality-assured SP will be a great step forward in creating local capacity for quality-assured SP available for procurement in Nigeria and the entire Africa region.

Last quarter, Emzor Pharmaceuticals indicated interest in the production of ready-to-use therapeutic foods. PQM commenced technical support in the requisite facility design. This quarter, the team provided technical guidance on equipment selection. Next steps include the initiation process of procurement of selected equipment and construction of the factory.

Other activities carried out under this objective include:

- Continued to provide technical support to Juhel Pharmaceuticals in the stability monitoring of magnesium sulfate injection and oxytocin injection.
- Monitored equipment qualification at Daily Needs Pharmaceuticals.

Objective 4 – Strengthen human capacity of academia

No updates this quarter.

Senegal

I. Quarter 1 Highlights

By far the greatest highlight of this quarter in Senegal was the confiscation of a vast amount of illicit medicines by the national regulatory authority (DPM) and Senegalese law enforcement agencies. The establishment of the IMC between DPM and the enforcement agencies has helped DPM to take major regulatory actions in its fight against the sale of medicines in nonregulated pharmacies and informal markets. On November 13, this joint effort led to the confiscation of two trucks full of clandestine medicines before they entered Touba City. The confiscated medicines, which included the antimalarial artemether, were worth approximately 1,355,160,000 CFA, the equivalent of \$2,419,928 USD.

Other highlights included:

- Attended and participated in the workshop entitled “Validation of the Comprehensive Integrated Strategic Plan” organized by Abt Associates in November. One DPM and national quality control laboratory (LNCM) QA/QC priority highlighted during this workshop has been added to the revised FY 2018 work plan.
- Conducted a follow-up visit in November 2017 to LNCM to review CAPA implementation to address lapses noted during the February 2017 PQM mock audit. PQM provided 2 weeks of technical assistance to assist the laboratory in addressing some challenging findings. The visit included an evaluation of the adequacy of the QMS in place to fulfill ISO/IEC 17025:2005 accreditation requirements and review of the equipment qualification/calibration status based on the scope of accreditation selected by LNCM.
- Assessed laboratory preparedness for ISO 17025 accreditation and updated the roadmap with a timeline to reach ISO 17025 accreditation.
- Established a 1-year contract with LNCM to maintain good functioning of the laboratory equipment.
- Provided technical assistance to DPM to strengthen its registration function, including guidance for the adoption of international standards for submission of registration documents; data specifications and standards for efficient management and transmission of regulatory information; and recommendations on improving registration processes to reduce the lead time in submitting marketing authorization.

II. Country Context

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

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

As part of strengthening LNCM QC capacities, in 2014 PQM performed an audit of the laboratory that revealed the following problems: inadequate QMS; inability of skilled laboratory staff to maintain their roles and responsibilities in the laboratory due to university work commitments; lack of motivation, which led to staff members not fulfilling their assigned duties; insufficient laboratory staff technical capacity to conduct QC testing of medicines according to compendial methods, as part of ISO 17025 and WHO PQ requirements; delays in procuring laboratory equipment;

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

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

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

Objective 1 – To support the LNCM in building its capacity towards ISO 17025 Accreditation

PQM conducted three main activities in Q1 toward addressing Objective 1:

- Conducted a follow-up visit to LNCM in November to review the CAPA implementation to address lapses noted during February 2017 PQM mock audit, and provided 2-week technical assistance to assist the laboratory in addressing some challenging findings. The visit also included an evaluation of the adequacy of the QMS in place to fulfill ISO/IEC 17025:2005 accreditation requirements and review of the equipment qualification/calibration status based on the scope of accreditation selected by LNCM.
- Assessed laboratory preparedness for ISO 17025 accreditation and updated the roadmap with timelines to reach ISO 17025 accreditation.
- Established a 1-year contract with LNCM to maintain good functioning of the laboratory equipment.

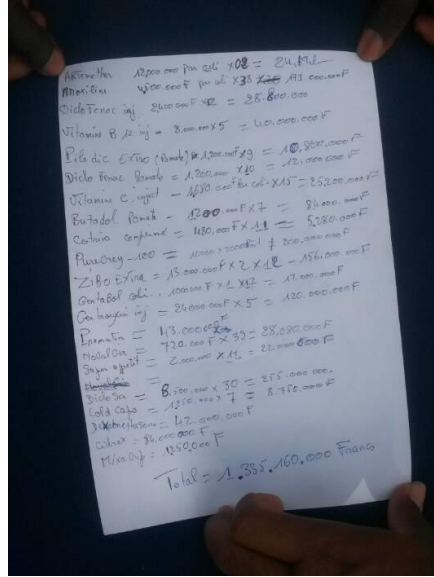
Objective 2 – Adoption of the risk-based PMS system by the LNCM

PQM continued working to finalize the FAA with LNCM with a period of performance of December 1, 2017, through September 30, 2018.

Objective 3 – Support DPM in improving its regulatory functions

A major highlight of this quarter was the confiscation of a huge amount of illicit medicines by DPM and Senegalese law enforcement agencies. The establishment of the IMC between DPM and the enforcement agencies has helped DPM to take major regulatory actions in its fight against the sale of medicines in non-regulated pharmacies and informal markets. On November 13, this joint effort led to the confiscation of two trucks full of clandestine medicines before they entered Touba City. The confiscated medicines, which included antimalarial artemether, were worth approximately 1,355,160,000 CFA, the equivalent of \$2,419,928 USD.

In 2014, the MOH undertook a number of initiatives to ensure the availability of essential medicines and products that are effective, safe, and accessible. These initiatives led to the development of the National Pharmaceutical Policy, National Pharmaceutical Master Plan, and strategic plan of the national pharmaceutical supplier (PNA). In line with these initiatives, in 2017 USAID supported, through Abt Associates, the development of an integrated strategic plan to strengthen the regulatory and control functions of the pharmaceutical institutions (DPM, PNA, and LNCM). To effectively contribute to strengthening the capacities of these entities, PQM attended a workshop titled "Validation of the Comprehensive Integrated Strategic Plan," organized by Abt Associates in November 2017. The workshop activities included organization of thematic groups to reflect on strategic orientations and a logical framework, which is the basis of the integrated strategic plan of pharmacy and medicine. During this workshop, PQM participated in and contributed to the outcomes of the QA/QC working group. One main priority highlighted by the working group was to establish an efficient and integrated regulatory system to ensure that quality-assured essential medicines, including USAID priority medicines, are available for use in Senegal. Activities related to this priority have been included in the revised FY 2018 work plan.



Images from the confiscation of illicit medicines by the DPM and Senegalese law enforcement agencies, including a list of confiscated products and a copy of a local newspaper article about the incident

West Bank and Gaza

I. Quarter 1 Highlights

The FY 2018 work plan was approved by the Mission on October 20. PQM is currently in the process of planning priority activities for Q2 and beyond in concert with USAID.

Angola: The project close-out report was reviewed, approved, and sent to the country mission on December 20, 2017. Following feedback/approval from the mission, the close-out report will be disseminated to country partners and stakeholders.

Kenya: Per a directive from USAID effective May 30, 2017, PQM activities in Kenya remain suspended until further notice.

Asia



Bangladesh

I. Quarter 1 Highlights

PQM's activities during FY 2018 Q1 were focused on the implementation of objectives 1, 2, 3, and 4 in the approved work plan and remaining activities of FY 2017 work plan. The Q1 highlights include the following:

- PQM provided support to the national control laboratory (NCL) to develop its strategic plan through several consultative meetings with four core team laboratory staff members. The draft plan is now under review by NCL senior management.
- PQM provided support to develop a training plan for NCL through a training needs assessment. The draft plan was submitted to the Directorate General of Drug Administration (DGDA) for finalization and incorporation into the DGDA Strategic Training Plan.
- PQM provided support to develop a risk-based testing protocol through several consultative meetings with four NCL core laboratory staff members. The draft plan is now under review by NCL senior management.
- PQM organized an experience sharing workshop on November 6 at the DGDA conference hall. The main objective of this workshop was to raise awareness about assuring the quality of essential priority products (TB, NTD) based on a Bangkok workshop to MRAs and manufacturers of anti-TB and NTD medicines. The workshop was attended by 54 participants, including representatives from 17 manufacturers. The opportunity for using PQM technical assistance to strengthen QA systems was discussed.
- PQM conducted a plenary meeting on November 9 at the Centre for Advance Research in Science (CARS) of Dhaka University to propose a new syllabus to adopt in pharmaceutical science schools that encompasses MRA regulatory functions.
- Members of the PQM team visited Bangladesh on November 13–22. During this visit, the team reviewed QMS documents, oriented laboratory staff on the WHO PQ process, reviewed CAPA implementation progress, checked the status of SOPs, and conducted training on internal audits and management review. The team assessed the vaccine, microbiology, and chemistry laboratories. The team also covered hands-on training on gowning procedure for the microbiology laboratory.
- On December 11, PQM facilitated a DGDA-organized meeting on first-line TB drugs at the DGDA conference hall. This was a long-desired meeting for the National Tuberculosis Program (NTP) in the presence of the Director General of Health Services and Director General of Drug Administration on the issue of procurement and availability of anti-TB medicines in the country. Important stakeholders present at the meeting included WHO, the Bangladesh Association of Pharmaceutical Industries (BAPI), leading pharmaceutical companies, Bangladesh Chemist and Druggist Association (BCDS), DGDA, Directorate General of Health Services (DGHS), NTP, SIAPS, PQM, and USAID. The discussion focused on the availability of quality-assured first-line anti-TB drugs in Bangladesh in a situation where countries should take responsibility for first-line anti-TB medicines.
- PQM facilitated the process to obtain government resources from the Ministry of Finance and the Ministry of Health and Family Welfare to DGDA to incur expenses for VAT, TAX, Customs Duty for Minilab™, and other supports. On July 26, PQM conducted a 1-day workshop on PMS data analysis in which 13 DGDA inspectors participated toward the establishment of PMS for priority medicines in selected geographical locations/districts. In December 2017, district inspectors/DGDA officials completed a survey on risk-based PMS to identify the most critical factors present in different geographical areas, focusing on TB, MNCH, and family planning products, and to select appropriate sites to implement GPHF Minilabs™ as an early detection system of falsified or substandard medicines. Ultimately, Minilabs™ and the risk-based system will help to prioritize sampling and testing based on risk and subsequently save resources because of the reduced number of samples tested and analyzed in the laboratory. Based on the survey, PQM recommended six sentinel sites.
- Training was provided to PQM Bangladesh staff on October 16–18 on PQM processes and procedures, as well as an overview on project management (the planning, organizing, scheduling, leading, communicating, and controlling of work activities to achieve predefined objectives on time and within budget).

II. Country Context

PQM's goal in Bangladesh is to strengthen the institutional capacity for sustainable regulatory and QA/QC systems that meet international standards. To achieve this goal, PQM has developed strategic objectives based on a PQM

gap analysis conducted in April–May 2016 and discussions and consultations with the USAID Bangladesh Mission, DGDA, SIAPS, and other relevant partners/stakeholders.

PQM's overall goal, in collaboration with SIAPS and WHO, is to strengthen selected DGDA regulatory functions based upon extensive discussions among stakeholders. For those areas in Objectives 3 and 4 where SIAPS has been working—including product registration (dossier format and registration software), GMP training, and PMS—PQM will provide technical support to SIAPS, as the lead agency, to provide technical support to DGDA. In consultation with USAID, PQM and SIAPS will continue to work on transitioning these areas of work to PQM before the closeout of the SIAPS program in 2018. For those areas where SIAPS does not have technical knowhow, PQM will provide direct technical assistance to DGDA.

III. Quarter 1 Progress by Objective

Objective 1 – Continue to provide technical assistance to the DGDA laboratory – NCL in Dhaka and DTL in Chittagong towards achieving international ISO/IEC 17025:2005 accreditation or WHO PQ

In terms of laboratory capacity building, PQM has been providing technical guidance/input to NCL to strengthen its QMS toward achieving ISO 17025:2005 accreditation.

PQM worked alongside NCL management and technical staff to follow up on its CAPA progress against the findings from the internal audit and the PQM audit. In Q1, all short-term CAPAs were implemented, with the exception of long-term CAPAs, which are ongoing.

PQM worked closely with NCL to develop and review critical SOPs to improve the traceability of work processes, quality control, and instrument life cycle. With the assistance of PQM technical staff in Bangladesh, an SOP writing team of 8 laboratory analysts was formed to lead the development and review of all laboratory procedures. This serves to encourage NCL staff to take leadership in developing their standard procedures and improve internal processes toward accreditation. Following the establishment of the group, several SOPs have been completed and submitted for review and approval.

Through the training needs assessment, PQM provided support to develop a training plan for NCL. The draft plan has been submitted to DGDA for finalization and incorporation into the DGDA Strategic Training Plan. PQM also provided support to develop a risk-based testing protocol through several consultative meetings with four NCL core laboratory staff members. The draft plan is now under review by NCL senior management. PQM Bangladesh technical staff also conducted training on several topics with NCL staff to enhance their knowledge and capacity towards international standards.

PQM staff visited NCL on November 13–22 and conducted the following activities:

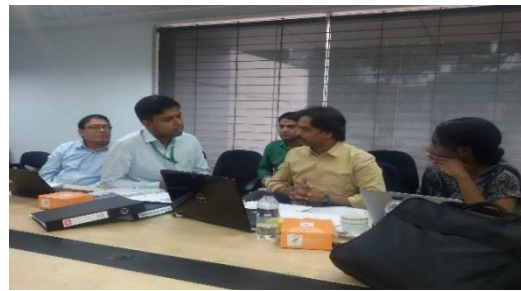
- Reviewed QMS documents, CAPA progress, internal audit findings, management review, strategic plan, organizational chart, decentralizations of roles, and SOPs already generated; provided recommendations to NCL for implementation before the end of Q1.
- Demonstrated the overview and process of ISO 17025 and WHO good pharmaceutical practices to NCL and Chittagong Drug Testing Laboratory (cDTL) staff.
- Reviewed the PT result of microbiology.
- Conducted on-the-job training on internal audit (ISO and WHO requirements) through laboratory inspection/walkthrough. NCL QA led the walk-through, and PQM experts observed while guiding the NCL staff to help them achieve a better understanding of the process.
- Conducted a day-long training on the overview and process of internal auditing and management review overview to all the laboratory staff in Dhaka and three staff from cDTL. A total of 45 staff members joined the training.
- Reviewed the records, forms, and other documentation of the vaccine wing (microbiology and chemistry laboratories) and conducted a walkthrough to identify gaps and limitations. During the walkthrough PQM experts covered both laboratories through a check of the premises, environmental monitoring, cleaning, disinfection and hygiene, sterility test facilities, vaccines and biologics test procedures, cleaning and sanitization, sample handling and waste disposal, equipment calibration and qualification, reagents, labeling, reference standards, and culture media.
- Conducted a hands-on training on the proper gowning process in the sterile facility in the micro laboratory.
- Follow up and guided the laboratory analyst on conducting ILT of sulfamethoxazole and trimethoprim samples. The analyst successfully completed the test on November 21, 2017.



Opening discussion on QMS follow-up visit



Training session on internal auditing and management review process



Gap assessment of vaccine wing (microbiology lab and chemical lab)

Summary of Lab Progress from October 1 to December 31, 2017
PQM staff assisted in developing SOPs, key documents, and CAPA implementation

Items	Number of Items
SOP Review and Development	Approved and implemented SOP: 22
	SOPs drafted, and under review by NCL: 11
CAPA status up to December 24, 2017	
CAPA by PQM (2016) from gap analysis findings (39)	35 CAPA completed (7 CAPA completed in Q1 FY18) Completion of remaining 4 CAPA in process (target timeline within December 30, 2017)
CAPA by PQM (2017) (24)	Completed: 17 (16 completed in Q1 FY18) Completion of remaining 7 CAPA in process (target timeline within December 30, 2017)
CAPA by NCL Internal Audit – June 2017 (26)	Completed: 18 (4 completed in Q1 FY18) Under follow up: 8
CAPA by BAB final Assessment – September 2017 (17)	Completed: 17
Key documents developed during the quarter (4)	<ol style="list-style-type: none"> 1. Draft Laboratory Strategic Plan 2. Draft Risk-based Testing Protocol 3. Draft Training Plan 4. Laboratory Supervision Check List

Objective 2 – Provide technical assistance to local pharmaceutical manufacturers toward WHO PQ for priority MCH/FP and TB products

PQM organized an experience sharing workshop on November 6 at the DGDA conference hall. The main objective of this workshop was to raise awareness about pharmaceutical quality and provide information to MRAs and manufacturers of TB and NTD medicines. It was also an opportunity for regulators and manufacturers to explore and use PQM's technical assistance to strengthen quality systems. Topics discussed at the workshop included PQM technical assistance, the WHO PQ process, current GMP, dossier requirements, and risk assessments. The DGDA Deputy Director, along with other participants who were in a similar workshop held in Bangkok by PQM, shared their experience and lessons learned with the other manufacturers. At the end of the workshop, Incepta Pharmaceuticals Ltd. and Delta Pharma Ltd. expressed their interest in achieving WHO PQ for selected priority products with PQM support.

On December 11 at the DGDA conference hall, PQM facilitated a DGDA-organized meeting on first-line anti-TB drugs. This was a long-desired meeting on NTP in the presence of the Director General of Health Services and Director General of Drug Administration. The meeting was attended by representatives of key stakeholders such as WHO, BAPI, leading pharma companies, BCDS, DGDA, DGHS, NTP, SIAPS, PQM, and USAID. The discussion focused on the availability of quality-assured first-line anti-TB drugs in Bangladesh in a situation where countries should take responsibility for procuring first-line anti-TB medicines.

At the end of the meeting, a core committee was formed to develop a government procurement plan/roadmap toward anti-TB medicines to be procured locally; the plan/roadmap was disseminated to manufacturers for production. DGDA requested PQM to provide technical assistance to manufacturers toward achieving WHO PQ for the products selected by the manufacturers.



Workshop on good laboratory practices and pharmacopeia testing

Objective 3 – In collaboration with SIAPS and WHO, provide technical assistance to strengthen DGDA's regulatory functions

Several activities were implemented to enhance DGDA's regulatory capacity. These include strategic planning, human resources, international standards, and improved post-marketing surveillance.

- PQM worked with SIAPS and WHO to prepare DGDA's FY 2018 training plan based on the DGDA-approved strategic plan and recently developed institutional development plan through WHO's benchmarking tool. PQM actively participated in developing this DGDA draft training plan, in which PQM-focused technical training topics were considered. PQM also indicated areas of training interest in this plan. The draft plan is under review by DGDA and development partners (including PQM).
- PQM participated in the pharmacovigilance meeting on October 22 at the DGDA conference hall, which included the final review of the guideline, and provided input to be incorporated in the guideline.
- PQM's Bangladesh Chief of Party participated in the antimicrobial consumption (AMC) meetings at the DGDA conference hall. The meetings reviewed WHO ongoing support on the AMC Monitoring and Surveillance Study under Banghabondho Sheikh Mujib Medical University.

- On July 26, PQM conducted a 1-day training on PMS data analysis in which 13 DGDA inspectors participated toward the establishment of PMS for priority medicines in selected geographical locations/districts. A survey on risk-based PMS among the district inspectors/DGDA officials was completed in December to identify the most critical factors present in different geographical areas, focusing on TB, MNCH, and family planning products, and to select appropriate sites to implement GPHF Minilabs™ as an early detection system of falsified or substandard medicines. Ultimately, Minilabs™ and the risk-based system will help to prioritize sampling and testing based on risk and subsequently save resources because of the reduced number of samples tested and analyzed in the laboratory. Based on the survey PQM, recommended six sentinel sites.
- PQM conducted a plenary meeting on November 9 at CARS, Dhaka University, to propose a new syllabus for pharmaceutical sciences schools that encompasses MRA regulatory functions.

Objective 4 – Increase visibility and relevance of QA/QC in support to National Health Programs with the primary focus on MNCH, TB and FP programs

PQM initiated discussions on arranging a consultative meeting on a National Policy on Quality Assurance of Medical/Health/Pharmaceutical Products with key health and DGDA stakeholders. The DGDA Director General agreed to convene the meeting in the second half of January 2018. The specific objectives are to provide clear policy directions to public and private health care authorities and professionals regarding quality of medicines and medical products, assist in procurement of quality-assured medicines and medical products, and provide support to the implementation of National Drug Policy 2016 in relation to the medicines quality issues.

IV. Key Challenges

Operational Challenges:

- Safety and security remain a concern in Bangladesh. Since August 2017, half a million Rohingya refugees arrived in the southeast region of Bangladesh, near the border with Myanmar. The current Rohingya refugee crisis may lead to protests and demonstrations in Dhaka, including the Gulshan and Baridhara areas of the city. The focal person is closely working with the Global security director to monitor the security situation.
- Organizational registration process is taking longer than anticipated, hence limiting the visibility of operating the PQM office.
- During the planning process for FY 2018, PQM considered the utilization of Government of Bangladesh resources along with the support provided by USAID. If government resources do not materialize as anticipated, it could hamper the achievement of the overall program objectives.

V. Lessons Learned

Program performance is limited by the scarcity of critical staff with relevant skills and experience at DGDA and NCL/cDTL. The availability of highly motivated, skilled personnel is the key to success.

Motivation of existing NCL and cDTL staff emerged as a concern in different observations. Special attention to identifying and resolving demotivation factors is key to achieving NCL strategic goals.

VI. Sustainability, Partner Contributions, and Ownership

DGDA, NCL, national priority health programs, and the pharmaceutical industries are the prime stakeholders of the PQM program in Bangladesh. PQM has been working closely with these partners. In the process, PQM is providing technical assistance to MRA, NCL, and essential medicines manufacturers to build long-term sustainability toward achieving international standards for the long-term public health benefits.

Burma

I. Quarter 1 Highlights

In FY 2018 Q1, PQM technical assistance enabled the Burmese DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory to maintain ISO 17025:2005 accreditation for the first year. The laboratory maintained its accreditation on all 10 scopes after the accreditation body, ANAB, conducted a 1-day annual surveillance visit in October 2017.

The training-of-trainers approach used by PQM on QMS-related topics has gained momentum, and DFDA trainers proved that they are able to re-train their counterparts following PQM training.

II. Country Context

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

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Support DFDA Burma to revise the current cost structure for quality testing to enable the Nay Pyi Taw laboratory to become self-sustainable

PQM provided technical assistance to DFDA Burma in revising the current cost structure, which is outdated, to reflect the ISO 17025 accreditation status and to cover the actual cost of testing. Priority was given to testing fees of antimalarials, as PQM is coordinating the quality testing of antimalarials being used by the Defeat Malaria Program, a key implementing partner supported by USAID/PMI. Six ACT samples from the Defeat Malaria Program were tested at the DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory, and all of them were found to be conformed to the pharmacopeial specifications.

Objective 2 – Provide technical assistance to Burma's DFDA for ISO re-accreditation and sustainability of the Nay Pyi Taw PC laboratory

The Burmese DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory's ISO 17025:2005 accreditation was achieved in December 2016, and the annual surveillance visit by the accreditation body (ANAB) was due in October 2017. The lead assessor from ANAB conducted the 1-day annual surveillance at the laboratory on December 13, 2017. The lead assessor sat down with DFDA management and the laboratory QA team to review the QMS requirement of ISO 17025:2005 accreditation, and witnessed the demonstration of analytical testing by laboratory personnel. At the end of the visit, the assessor found 3 nonconformities, which were presented to the laboratory. The laboratory corrected all three nonconformities within 2 weeks, and ANAB accepted the corrections. DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory effectively maintained its ISO 17025:2005 accreditation for the first year.

Objective 3 – Provide technical assistance to Burma's DFDA Nay Pyi Taw and Mandalay laboratories on pre- and post-relocations planning and implementation in accordance to ISO 17025 standards

No activities were conducted for this objective in Q1.

Objective 4 – Provide support to DFDA Nay Pyi Taw laboratory’s technical assistance to Mandalay Pharmaceutical Chemistry laboratory for ISO 17025 accreditation preparation

The DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory QA team organized a training workshop on QMS topics on September 30–October 3. PQM had trained the trainers in this workshop on QMS topics back in September 2017 in a “Training of Trainers.” The trainers delivered the trainings on ISO 17025:2005 standards, laboratory safety, GLP, GDP, internal audits, root cause analysis, CAPAs, and management review to 24 laboratory staff from Mandalay, Nay Pyi Taw, and Yangon Pharmaceutical Chemistry Laboratories. This training also provided a refresher on ISO 17025 standards and QMS topics prior to the annual surveillance visit by ANAB.

IV. Lessons Learned

As the training-of-trainers approach on QMS topics clearly showed, PQM should focus on delivering future training to the small group of selected DFDA candidates and intensively build their capacity on the selected topics. PQM should closely observe these trainers delivering the trainings to their counterparts to provide assistance whenever required. In this regard, PQM will be able to develop a sustainable learning system within DFDA as it expands and avoid the need to train on the same topic repeatedly in the future.

V. Sustainability, Partner Contributions, and Ownership

The training-of-trainers approach used by PQM on QMS topics is a good example of creating a sustainable learning environment in a country. The DFDA trainers being trained by PQM successfully delivered the topics they had learned to their counterparts in a professional way, while the participants benefit from the training being conducted in the local language. On the QMS training workshop conducted in October, PQM provided the master training materials, technical guidance, and facilitation apart from the training-of-trainers workshop held a month earlier, while United Nations Office for Project Services (UNOPS)/Regional Artemisinin-resistance Initiative (RAI) provided the venue, accommodation, and meals for the participants. Furthermore, ground transportation was contributed by DFDA, showing a strong partnership in capacity building as part of the efforts to eliminate malaria from Burma.

Indonesia

I. Quarter 1 Highlights

During FY 2018 Q1, PQM Indonesia continued to finalize implementation of the FY 2017 work plan activities with the aim of 90 percent completion by the end of the year. Key successes include the submission to and acceptance for WHO PQ of the Kalbe Farma dossier for levofloxacin 500mg tablets. This marks the first solid-dosage form product dossier submission to WHO for PQ from Indonesia from the largest pharmaceutical manufacturer in the ASEAN region, Kalbe Farma.

The laboratory information file (LIF) submission by the BPOM national quality control laboratory, PTBB, was accepted by WHO as part of its application for PQ of the NQCL. PQM anticipates WHO inspections of both the BPOM laboratory and Kalbe Farma during FY 2018 and will work closely with each partner to achieve positive results.

Sanbe Farma has also targeted submission of its product dossier for levofloxacin 500mg tablets during FY 2018 Q2 following intensive PQM technical assistance.

PQM completed its procurement for the Global Fund project by providing equipment to 11 provincial BPOM laboratories as part of the joint MOH–BPOM sampling exercises meant to generate quality data for government sector medicines, initiated by PQM.

II. Country Context

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

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

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

III. Quarter 1 Progress by Objective

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

PQM Indonesia's Q1 activities included FY 2017 carryover activities toward completion. In November, WHO accepted the LIF submitted by the PTBB Quality Control laboratory of BPOM (submitted in FY 2017 Q4) as part of the application toward PQ. WHO will arrange for the evaluation of the PTBB laboratory for PQ to be conducted in accordance with the terms of the procedures to assess compliance with Good Practices for National Pharmaceutical Control Laboratories at some point during this fiscal year. This is a major accomplishment representing the culmination of the past few years of PQM's technical assistance to the government of Indonesia.

PQM Indonesia began the pilot project to incorporate Minilab™ screening technology to support the national PMS system after consultation, advocacy, and official decree by the Head of BPOM. The pilot project initiated in Jakarta DKI provincial Balai Besar Pengawas Obat dan Makanan (BBPOM) institution, with procurement, supply, and training on the use of Minilab™ to augment compendial testing of medicines collected during PMS activities. Provincial vans are being outfitted with Minilabs™ to enable mobile testing capacity for BPOM at sampling sites and for use in public education.

Following training, PQM worked with BBPOM to conduct field sample collection in five large local medicines markets in Jakarta, followed by screening with Minilab™. Eighty-three anti-TB, ARV, and opportunistic infection medicines samples were collected, and results are pending confirmatory testing during Q2. The result is expected to be included in a pilot study project report to BPOM on cost- and time-effectiveness of incorporating screening technologies within the framework of risk-based PMS. Initial organoleptic and screening results indicate a number of quality issues with medicines, including potential falsified medicines, substandard manufacture, and some public sector medicines being illegally available through private sector outlets. During the remainder of FY 2018, the Minilab™ pilot project will be expanded to the Papua BBPOM in Jayapura. Test results will be disseminated to relevant stakeholders.

The long-term goal for the pilot project to include screening technologies in support of PMS (using compendial analysis) is for BPOM to develop official policy to incorporate screening, and to expand this to all provincial and eventually district BPOM institutions under the government budget. Initial procurement of Minilabs™ for expansion may be sought through support by the Global Fund under the MOH's TB, HIV, and malaria funding.

The Jakarta DKI BBPOM mobile testing van equipped with Minilab™ was featured during a recent national event with the President of the Republic of Indonesia, Head of Police, Minister of Health, and BPOM Head and Delegates during the launch of a national campaign to eradicate illegal medicines and narcotics in Indonesia. PQM's support featured prominently in this highly publicized event, which helped to ensure the visibility of the project and garnered further political support for prioritizing medicines QA as part of the overall strategy to rid the country of illicit, substandard, and falsified medicines.

The second training provided by the pool of experts from PTBB laboratory following from PQM's training of trainers during FY 2017 Q4 was conducted this quarter. The weeklong training on ARV Impurities/Related Substances Testing methods, supported through PEPFAR funding with substantial financial contribution and sponsorship from BPOM itself, was attended by 26 participants from 16 provincial laboratories. This activity was designed as part of an overall strategy for sustainability by building the capacity of the national BPOM staff to conduct training to provincial laboratories using PQM curricula and training standards. Additional support will follow through FY 2018 and FY 2019.

Discussions began on developing protocols in support of the newly procured stability chamber for the national Reference Standards Laboratory (RSL). The national RSL supplies secondary reference standards to the national and 33 provincial BPOM laboratories. However, they have significantly limited capacity for QA, including a lack of equipment and experience with stability testing for their secondary reference standards. PQM will continue to support discussions toward identifying viable strategies to increase quality standards of RSL provided throughout the BPOM

network, with the aim for BPOM to eventually look at financially feasible mechanisms for high-quality procurement and long-term development.

During Q1, PQM Indonesia conducted an advanced analytical training on gas chromatography (GC)/GC–mass spectrometry (MS) for the Jakarta DKI and Jayapura Papua BBPOM institutions, using glycerin impurities as the test subject due to its ubiquitous use in oral preparations and cases of falsification globally. The training was provided to build overall QC capacity for these laboratories in support of their ISO accreditation, and will enable them to conduct analysis on medicinal products for which the monograph requires GC or GC/MS analytical methods.

For the remaining FY 2018 activities, objective 1 will focus primarily on achieving WHO PQ for the PTBB laboratory in Jakarta and the BBPOM laboratory in Denpasar. In addition, capacity-building exercises will focus on strengthening QMS, ensuring ongoing accreditation status is maintained, and providing direct support for testing anti-TB and anti-HIV medicines in Jakarta, Papua, and nationally.

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

The major accomplishment under objective 2 for FY 2018 Q1 was Kalbe Farma's submission of its levofloxacin 500mg table product dossier to WHO for PQ. The subsequent acceptance of this dossier by WHO at the end of Q1 attests to the quality of the completed dossier, which was supported by PQM. This is the first oral solid dosage form submission to WHO for PQ in Indonesia, a testament to the hard work and dedication of the PQM and Kalbe Farma teams, with support from BPOM. Following the submission, Kalbe Farma initiated an internal mock audit in anticipation of the upcoming, extensive PQM onsite audit in preparation for a WHO inspection during FY 2018. This marks a major achievement for PQM in Indonesia and represents building overall quality and GMP compliance for Kalbe Farma, the largest pharmaceutical manufacturer in the ASEAN region.

Extensive follow-up consultations were conducted with Sanbe Farma/Caprifarmindo laboratories to finalize their product dossier for submission to WHO for PQ of levofloxacin 500mg tablets by the end of FY 2018 Q2. Onsite discussions focused on pilot batch study and QC for chemical and physical parameters, with the exception of microbiology testing (TBD). Comparative dissolution results met the requirement of relative standard deviation specifications. Improvements in the QC laboratory following PQM intervention and training were observed, and Sanbe Farma plans to submit the initial 3-month stability data to WHO, pending results of the 6-month study. It is also in the process of submitting a registration variation to BPOM, anticipating that it may need to redo the comparative dissolution study due to changes in the API source. Sanbe Farma is on target to submit its product dossier to WHO by the end of FY 2018 Q2 and has requested additional training on dossier compilation from PQM to address identified gaps in this area.

Dissemination and socialization of the bioequivalence study training (conducted by PQM during FY 2017 Q4) was rolled out to all relevant staff at three CROs that PQM has been supporting: San Clin Eq, Pharma Metric Labs, and Equilab International. PQM supports CROs as an integral component of building QA in Indonesia. Generating reliable bioequivalence data is complex and is a mandatory requirement for product registration by BPOM. Working with CROs to generate quality bioequivalence data will contribute to fulfilling the requirements for registration of generic products in the country. This will further increase the availability of essential products, at a lower cost, to health programs and patients.

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

During Q1, PQM conducted both FY 2017 and FY 2018 work plan activities under objective 3. With new project coordination staff in place, supported by an M&E Specialist, progress is being made both in implementation of activities as well as with overall buy-in and support from government partners, namely MOH and BPOM.

A significant achievement for Q1 was the successful first convening of a stakeholders' consultation among MOH (Farmalkes and National TB Program) and public (BUMN) and private pharmaceutical manufacturers to identify the needs of the public programs for TB control in the context of the changing guidelines on TB treatment outlines in regulation PMK 67/2016. Given the changes in treatment regimens, including adoption of daily dosing 2FDC INH/RIF regimens, as well as increasing dependence on moxifloxacin-based treatments for multidrug-resistant tuberculosis (MDR-TB), PQM advocated for a stakeholders meeting to encourage transparency in MOH procurement processes

via e-catalog, as well as to anticipate upcoming procurements so that manufacturers can meet demand. Stakeholders discussed anticipated procurement sizes and types of products over the next few years with the advent of JKN, budget reliance on domestic funding, and other issues. Manufacturers and partners could then discuss directly with NTP regarding lead times for product research and development, reformulation, and other important considerations. Following this initial consultation, next steps include a more extensive consultation between MOH and BPOM, and including detailed follow-up with manufacturers, requests for potential bidding, evaluation of viable and reasonable sources for products (locally manufactured or imported via Special Access Scheme scenarios), and pricing. PQM will continue this support through FY 2018 and will convene similar stakeholder workshops for the National AIDS Control Program, Farmalkes, BPOM, and manufacturers.

PQM also supported the implementation of the GF-financed joint MOH-BPOM sampling activity in 11 provinces, including an initial evaluation meeting among MOH, PQM, and BPOM. This pilot activity, continuing in FY 2018, was designed to demonstrate practical implementation of PMK 75/2016 and the technical sampling guidelines developed. Testing is currently underway at the provincial BBPOM laboratories, following procurement support by PQM for laboratory equipment and reference materials. Initial organoleptic results indicate quality defects in product labelling, lack of registration for some products, illegal (no registration) parallel imports into the public supply chain, and others. Chemical testing will be completed during Q2, and a joint dissemination workshop will be convened for relevant stakeholders for data sharing and to create an action plan for regulatory enforcement, procurement decisions, and further investigations if necessary. PQM anticipates that data generated during this and subsequent joint sampling and testing activities will be used by JKN as universal health access is scaled up and to ensure that government sector medicines meet quality specifications.

PQM had the opportunity to advocate for medicines quality in national and academic forums during Q1. A presentation on substandard and falsified medicines and storage requirements in pharmaceutical supply chains was given to district-level medicines storage facilities logistics managers through the GF-HSS Supply Chain Management component. Also, the PQM team convened an afternoon symposium on medicines quality-related topics to students and faculty of the Faculty of Pharmacy at the University of Indonesia. This well-attended event initiated cooperation between PQM and the University of Indonesia aimed at ensuring that medicines quality information is included in curricula, and as part of a strategy to engage academics to support medicines QC and bioequivalence study capacity building in partnership with the government.

PQM also worked to support other USAID implementing partners, including Chemonics' GHSC-PSM project at the request of the Mission to help develop components of the national HIV laboratory strategy with the National AIDS Program at MOH. PQM also participated in the dissemination of the revised BPOM Registration Guidelines.

IV. Key Challenges

PQM devoted a large amount of staff time to the annual drafting, approval, and submission process for the BAST document, as required by the Ministry of Finance. The BAST includes financial and activity information for all goods and services handed over to the government of Indonesia from the donor USAID via the PQM project with BPOM. The BAST serves as the annual registration document for the Ministry of Finance, and thus is a sensitive document that takes an extensive amount of staff time to negotiate and finalize. As of the end of Q1, the BAST was finally approved, signed (by BPOM and USAID), and submitted to the Ministry of Finance.

V. Lessons Learned

Perseverance, persistence, and steadfast commitment are the keys to success. The program staff have developed a keen sense of patience coupled with tenacity in order to slowly but dramatically effect change within the government on both policy and practical levels.

VI. Sustainability, Partner Contributions, and Ownership

A key consideration for the PQM Indonesia program is how to sustain activities, competencies, and political will beyond the lifespan of the program. PQM has creatively leveraged large donor funding from the Global Fund to support short-term goals of equipment procurement and establish policies and government procedures (such as joint MOH-BPOM sampling activities for PMS) that will eventually become routinized in the overall government functions (and application of domestic budget support), thus having far-reaching effects beyond the PQM program time period. In addition to the technical aspects of training and technical assistance that PQM provides, PQM is actively engaging with private sector associations, such as the Indonesian Pharmacists' Association, to develop partnerships toward strengthening QA compliance, dissemination of information at a national scale, and garnering of high-level political support. Working together with academia to ensure their long-term buy-in to the concepts and importance of including QA in their pharmacy curricula will help to develop the skills and knowledge of the next generation of private- and government-sector pharmacists. PQM has also established itself, and thereby the project objectives/goals, strongly

within BPOM and has achieved a high degree of positive support and partnership with BPOM. Over the past few years, there has been a dramatic shift in perception, as evidenced by BPOM taking the lead on many PQM-initiated activities, especially partnering with MOH.

Pakistan

I. Quarter 1 Highlights

During FY 2017, PQM provided technical support to four manufacturers of chlorhexidine (CHX) 7.1% gel to improve compliance with current good manufacturing practices (cGMP). As a result, four CHX 7.1% gel products were approved, and after the federal government fixed the price for these products, registration letters were issued to the four manufacturers. PQM followed up with the manufacturers; as a result, three manufacturers (Atco Laboratories, Aspin Pharmaceuticals, and Akhai Pharmaceuticals) launched their products in the market. The fourth manufacturer (Zafa Pharmaceuticals) is expected to start local production by FY 2018 Q2. The availability of locally manufactured quality-assured CHX 7.1% gel has increased the availability of the product for scale-up efforts to launch CHX 7.1% gel in all districts of Pakistan. The manufacturers have made the products available in all provinces and regions of Pakistan for over-the-counter sale to the general public. In addition, these products are now available for procurement by provincial governments, where they are already included in the list of essential medicines for lady health workers working under the Prime Minister's Program for Family Planning and Primary Health Care (this program was launched by the government in 1994). The manufacturers are currently looking toward exporting the product to other countries in the region and also toward becoming potential suppliers for UNICEF. PQM is working with the two manufacturers in preparing the global dossier submissions to UNICEF for Expert Review Panel (ERP).

PQM has also provided support to the Drug Regulatory Authority of Pakistan (DRAP) to strengthen its regulatory system, including developing and conducting training courses on GMP and conducting trainings and holding consultative stakeholders meetings to develop a PMS framework and data-sharing mechanism.

Follow-up activities by PQM will help monitor the success and effectiveness of the trainings conducted. Follow-up helps both in understanding the challenges DRAP faces in implementation of the acquired skills and in establishing the need for future trainings. PQM is working on a strategy to develop a group of master trainers for DRAP. During FY 2017 PQM conducted trainings on different technical aspects, and during FY 2018 PQM will conduct trainings for elected officials in order to develop them as master trainers.

To assess progress in implementing CAPA plans, in FY 2018 Q1 PQM conducted follow-up visits to Aspin Pharmaceuticals and Atco Laboratories, CHX gel manufacturers.

II. Country Context

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

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

III. Quarter 1 Progress by Objective

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

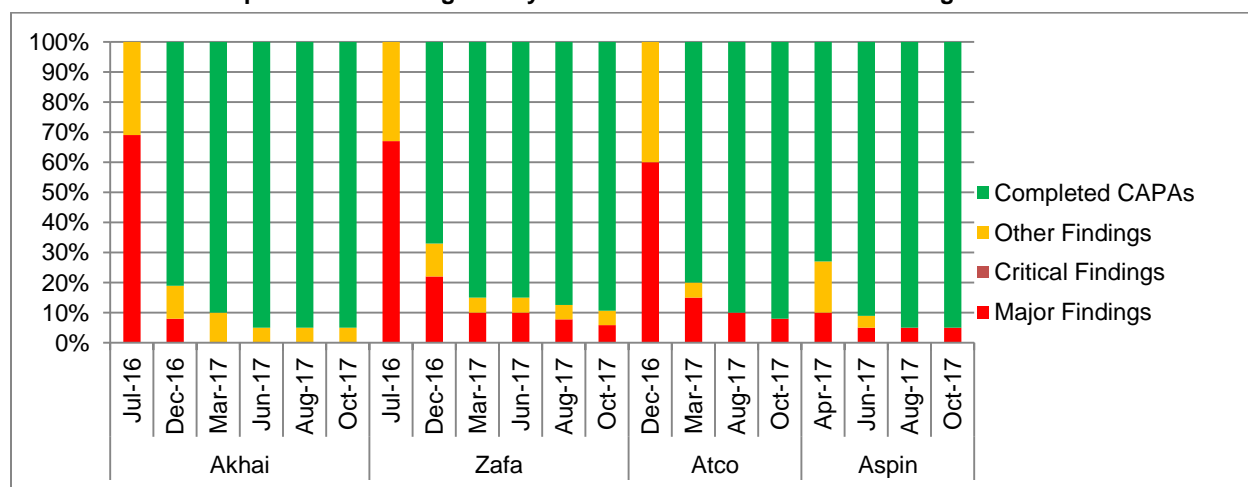
During FY 2018 Q1, PQM continued to work with CHX gel manufacturers to confirm production timelines were maintained and ensure availability for the local market. As a result, three manufacturers (Atco Laboratories, Aspin Pharmaceuticals, and Akhai Pharmaceuticals) have started production to supply the market. In addition, PQM consulted with the USAID Mission in Pakistan to identify other essential medicines with public health impact in the country that may require PQM support. The new medicines identified included oxytocin injection, amoxicillin dispersible tablets (DT), and zinc DT. PQM conducted an assessment of M/s Macter International in Karachi, a potential manufacturer of amoxicillin DT, which is an essential medicine for the treatment of pneumonia. The assessment report was shared with the company’s management, and a CAPA plan was developed.

Oxytocin is a critically required drug for prevention of postpartum hemorrhages and is a life-saving drug. Previously oxytocin was imported into the country, but now the importer has stopped importing this product into Pakistan. Currently, at least one manufacturer is trying to produce the product, but it has not yet been successful in preparing a stable and safe formulation.

Diarrhea remains a leading cause of death globally among children under 5 years of age. Diarrhea contributes to nutritional deficiencies, reduced resistance to infections, and impaired growth and development. Severe diarrhea leads to fluid loss and may be life threatening, particularly in young children and people who are already malnourished or have impaired immunity. Zinc supplementation has been shown to reduce the duration and severity of diarrhea and to prevent subsequent episodes, although the mechanisms by which zinc exerts its anti-diarrheal effect are not fully understood¹. At the present time in Pakistan, zinc DT recommended for children under 5 years of age is not being manufactured. PQM has identified a potential manufacturer and is working to support the manufacturer in development of zinc DT to supply the product locally.

PQM continued its support to the manufacturers of essential products in Pakistan to help increase the supply of locally manufactured quality-assured medicines.

CAPA Implementation Progress by the Four CHX Manufacturers through October 2017



PQM has been working with four manufacturers of CHX 7.1% gel—Zafa Pharmaceuticals, Akhai Pharmaceuticals, Atco Laboratories, and Aspin Pharmaceuticals—to assess the implementation of the recommended CAPA plans and to identify areas where the manufacturers need further PQM support to address the remaining corrective actions. The manufacturers are progressing well in addressing their respective CAPA, as shown in the chart above. Currently PQM is working with two of the four manufacturers to support compliance with international standards on GMP and QMS. With PQM’s technical assistance, three manufacturers (Atco Laboratories, Aspin Pharmaceuticals, and Akhai Pharmaceuticals) have already started production, and the product is now available in the local market. The fourth

¹ http://www.who.int/elena/titles/zinc_diarrhoea/en/

manufacturer (Zafa Pharmaceuticals) could not start production due to a technical issue with the registration letter issued to it by DRAP. However, after this has been addressed, most likely Zafa Pharmaceuticals will be able to start production in FY 2018 Q2. A comprehensive audit of Aspin was conducted in FY 2017 Q1 to ensure implementation of CAPA plans.



Aspin Pharmaceuticals



Akhai Pharmaceuticals



Atco Laboratories

Locally produced CHX gel products from three PQM-supported manufacturers

Pneumonia is the leading cause of mortality in children globally, with an estimated 1.2 million deaths annually, and 60 percent of these deaths occur in just 10 countries, 1 of which is Pakistan.² Amoxicillin is a penicillin-class, broad-spectrum antibiotic that is commonly prescribed to children as first-line treatment of pneumonia. With the help of DRAP's database, PQM identified manufacturers, including Macter International in Karachi, that have a dedicated penicillin manufacturing facility, a requirement for the production of amoxicillin DT. PQM conducted an assessment of the facility in FY 2018 Q1 and prepared a comprehensive assessment report that was shared with the company's management. The manufacturer is now preparing a CAPA plan to address the nonconformities that were noted by the PQM team.

Of every 1,000 Pakistani children born, 89 (nearly 1 in 10) die before their first birthday.³ Pakistan ranks 23rd in the world for under-5 deaths; over half (55%) die in their first month of life. While child mortality has declined slowly since 1990, newborn mortality has actually risen. Most newborn and child deaths can be prevented if trained attendants are present at birth, infants are fully vaccinated and appropriately fed, and avoidable diseases such as pneumonia and diarrhea are prevented.⁴

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

The Pakistan Drug Testing and Research Center (PDTRC) in Lahore is the only ISO 17025:2005-accredited public sector laboratory in the country and has been receiving technical assistance from PQM toward WHO PQ. PDTRC submitted its LIF to WHO for PQ in 2016, which was accepted. Subsequently on December 11–13, the WHO peer audit team visited PDTRC for an audit. Upon WHO's request, PQM accompanied the team during the audit as observers. Some non-critical observations were recorded by the WHO peer audit team. PDTRC management was



Debriefing at PDTRC after peer audit by WHO team



PQM team with WHO auditors and PDTRC Staff

² WHO, *Factsheet: Pneumonia*, WHO, Geneva, April 2012 at <http://www.who.int/mediacentre/factsheets/fs331/en/>.

³ WHO, *Factsheet: Pneumonia*, WHO, Geneva, April 2012 at <http://www.who.int/mediacentre/factsheets/fs331/en/>.

⁴ Pakistan annual Report 2015-UNICEF

debriefed at the end of the assessment, and the detailed report is expected to be available in January 2018. PQM will provide further technical assistance to the laboratory for resolving the nonconformities raised by the audit.

The provincial Drug Testing Laboratory (DTL) in Lahore has submitted an application for ISO 17025:2005 to the Pakistan National Accreditation Council. In December, the PQM team conducted an audit of the facility to assist the laboratory in attaining ISO 17025:2005 accreditation. Per the request of DTL's management, PQM will provide further technical assistance to prepare DTL to attain compliance with WHO PQ requirements. PQM's laboratory assessment report will help the facility to prepare itself for the ISO 17025:2005 audit, as well as serve as a basis for future application for WHO PQ. PQM will provide technical assistance and QMS support to prepare the LIF for submission to WHO PQ.

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

In FY 2018 Q1, PQM continued liaising with DRAP for implementation of the Common Technical Document (CTD) format for registration applications, while also helping to provide suggested resolutions to issues raised by two stakeholders, Pharma Bureau⁵ (PB) and Pakistan Pharmaceutical Manufacturer Association⁶ (PPMA). The issues raised by the industry were:

- Since the import of an API before registration is prohibited by law, it is not possible to conduct developmental studies in accordance with ICH guidelines.
- It is not possible to perform bioequivalence studies because there are no internationally recognized CROs in the country, and conducting those studies abroad is not affordable.
- Since the source of API is to be approved by DRAP in the case of CTD submission, limiting the production of API to a single source will result in the creation of monopolies.
- PB is worried about the data integrity of new research molecules submitted by multinational research-oriented companies.

DRAP held a meeting with both PB and PPMA on December 8 to discuss solutions to the challenges faced by the industry. Since then, DRAP has resolved the challenges, thereby paving the way for implementation of the CTD by the pharmaceutical industry in Pakistan.

A key requirement of registration of a generic product is bioequivalence studies with the originator brand. Due to the absence of internationally recognized CROs in the country, the industry felt that this may not be possible. Therefore, DRAP relaxed the condition of bioequivalence studies on the condition that the applicants conduct comparative dissolution studies with either the innovator or the approved comparator brand and submit the data to DRAP. DRAP also agreed to accept laboratory scale studies as of now (provided a commitment is submitted) and to accept more than one API manufacturing source. Regarding data integrity, DRAP assured that all possible measures will be taken to secure the data submitted by multinational companies.

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

Under the Drugs Act of 1976, both DRAP and provincial governments are responsible for the QA and QC of medicines. DRAP is responsible for compliance with GMP at the manufacturing level, and provinces are to ensure medicines quality in the market, after their registration in the country (post marketing). At present, sharing of QA and QC data between DRAP and provincial health authorities is voluntary. PQM has been working to develop a surveillance framework for sharing data nationally. PQM conducted a stakeholders meeting to discuss a mechanism for sharing medicines' post-marketing quality surveillance data between national and provincial health authorities. This data-sharing system should be accessible to all provincial governments, with the database maintained by DRAP.

During FY 2018 Q1, PQM continued to liaise with the stakeholders to finalize a national framework on PMS to develop an information-sharing mechanism. The guidance document will be presented at the next stakeholders meeting in order to develop consensus on its contents as well as its implementation schedule and logistics.

⁵ Pharma Bureau of Statistics is a subcommittee of the International Chamber of Commerce & Industry in Pakistan and is the representative body of Multinational Pharmaceutical Manufacturers in the Pakistan.

⁶ PPMA is the only association of national manufacturers in Pakistan.

IV. Key Challenges

The non-availability of multiple-entry visas remained a programmatic challenge, hindering the PQM U.S.-based technical team's ability to provide technical assistance in Pakistan. This situation is likely to improve after office registration is granted by the government. With registration status, the government policy allows for 1-year multiple-entry visas for international nongovernmental organization officials traveling for program-related work. In the meantime, the technical gap has been addressed through the inclusion of international ad hoc consultants based in Pakistan. Due to a travel advisory based on security concerns, a visit by PQM U.S.-based technical staff in December 2017 had to be postponed.

PQM has been working collaboratively and strives to maintain open communication with key stakeholders in Pakistan involved in strengthening the regulatory system. Past experience has shown that provincial governments (with the exception of Punjab) are less inclined toward strengthening QA and QC systems, which negatively impacts the performance of many QC laboratories.

At the federal level, the Appellate Laboratory (AL) at the National Institute of Health in Islamabad is pivotal in Pakistan's QC system; however, its equipment is 25 years old, and the building that is housing the laboratory was not built for that purpose. This laboratory requires financial support from the government to procure the equipment and modify the building. With support from Global Fund and other partners, PQM is working to equip and operationalize the AL. Once equipment and staff are in place, PQM will work to build AL's capacity and strengthen its QMS.

Similarly, the Federal Drug Surveillance Laboratory in Islamabad, which is part of DRAP, is facing the challenge of not being able to take its building back from the Medical College (established by the Ministry itself). Thus, expensive equipment is being stored without use and is becoming outdated. PQM has been advocating with the federal government to help the Federal Drug Surveillance Laboratory get the building back.

V. Lessons Learned

PQM works closely with DRAP to strengthen its regulatory capacity. However, a review of provincial health authorities has established that they require more technical assistance, especially in the smaller provinces; this support in the smaller provinces is necessary to protect public health by promoting the standardization of processes and actions country-wide. The technical assistance that the provinces require are in the areas of post-marketing surveillance and strengthening of QA and QC systems for the improvement of the NQCLs under the control of each province.

Learning from visa restrictions and the travel advisory, PQM will maximize the use of locally available international expertise to deliver technical assistance to support the timely implementation of activities in the work plan.

Cambodia: The project close-out report has been completed, reviewed, approved, and sent to the country mission on December 22, 2017. Following feedback/approval from the mission, the close-out report will be disseminated to country partners and stakeholders, in conjunction with reports from key activities implemented during the 2009-2017 period.

Philippines: The following reports on medicines quality monitoring performed during FY17 completed, reviewed, and approved: Medicines Quality Monitoring Program Philippines Report_October 2016–September 2017; CALABARZON DOTS: Sample Collection and Facilities Inspection, and Mindoro Site Visit.

The project close-out report has been completed, reviewed, approved and sent to the country mission on December 26, 2017. Following feedback/approval from the mission, the close-out report will be disseminated to country partners and stakeholders, in conjunction with reports from key activities implemented during the 2009-2017 period.

RDMA: The project close-out report has been completed, reviewed, approved, and sent to the country mission on December 7, 2017. The regional mission provided feedback and concurred with the report.

Eastern Europe & Central Asia



Kazakhstan

I. Quarter 1 Highlights

During Q1, PQM made progress in the implementation of the following FY 2018 work plan activities:

1. PQM prepared confidential reports per results of the assessments of Karaganda, Kostanay, and Astana laboratories.
2. PQM provided remote technical assistance to Karaganda, Kostanay, and Astana laboratories in the implementation of corrective actions resulting from PQM's assessments conducted in June 2017.
3. PQM assisted the Karaganda laboratory in the revision of its LIF in compliance with WHO recommendations.
4. PQM started preparations for a data integrity training to prepare the NQCLs for upcoming WHO PQ; this training will cover one of the critical aspects to be evaluated during WHO inspection.
5. PQM provided further remote technical assistance to Nobel Almaty Pharmaceutical Factory.

PQM provided technical assistance to the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan's (NCEM) three NQCLs to strengthen their QMS in preparation for WHO PQ. As a result of this technical assistance, the laboratories will be better equipped to conduct QC of medicines. Eventually, this will contribute toward ensuring the quality of medicines on the Kazakhstan market. PQM also provided remote assistance to Nobel Almaty Pharmaceutical Factory to facilitate commissioning of operations and ensure GMP compliance of its new site. Compliance with international GMP standards will contribute to the production of quality-assured products.

II. Country Context

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

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

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

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

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

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

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

III. Quarter 1 Progress by Objective

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

PQM prepared confidential reports for assessments of Karaganda, Kostanay, and Astana laboratories. The laboratories began developing corrective action plans, which will be reviewed by PQM. In FY 2017 Q4, NCEM submitted LIFs of Karaganda, Kostanay, and Astana laboratories to WHO. However, WHO strongly advised to proceed with Karaganda laboratory first and, based on the gained experience in the process, NCEM would be in a better position to prepare the two other laboratories for WHO PQ. WHO provided comments to Karaganda LIF, and PQM assisted the laboratory in revising its LIF in compliance with WHO recommendations. PQM will continue support to the laboratory in responding to queries from the WHO PQ team.

One of the weak areas PQM identified in the process of preparation for WHO PQ inspection is understanding of the international requirements for integrity of laboratory data. The staff needs better understanding, documentation, and procedures in this area. PQM decided to provide a data integrity training for the staff of all three laboratories, as well as information technology specialists from NCEM headquarters, which would be held in FY 2018 Q2 in Almaty.

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

In Q1, PQM continued providing remote assistance to Nobel Almaty Pharmaceutical Factory, particularly with reviewing its cleanroom qualification documentation and assisting in the development of the cleaning validation protocol. Nobel plans to start operations on the new production site in January 2018. PQM will conduct a GMP assessment of the new facility in February–March 2018 and discuss next steps in collaboration with Nobel Almaty Pharmaceutical Factory.

Uzbekistan

I. Quarter 1 Highlights

In Q1, PQM worked with Nobel Pharmsanoat, a manufacturer of anti-TB medicines, to provide remote technical assistance in a number of GMP and dossier-related topics. PQM also began preparations for a data integrity training, which is required to prepare the manufacturer for WHO PQ.

This quarter, PQM also began preparations for a GLP training for quality control laboratories of the MRA (Center for Expertise and Standardization of Pharmaceutical Products, Medical Products, and Medical Equipment) and manufacturers.

II. Country Context

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

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

Uzbekistan has an established national MRA: the Directorate of Medicines and Medical Equipment Quality Control (Uzbekistan FDA). Medicines regulation in Uzbekistan is based on numerous legislative and regulatory documents. There is a network of QC laboratories in the country. The central laboratory (State Center of Expert Examination and

Standardization of Drugs) is ISO/IEC 17025 certified and seeking WHO PQ. However regional laboratories are neither ISO 17025 accredited nor WHO prequalified.

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

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

III. Quarter 1 Progress by Objective

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

In Q1, PQM provided remote assistance to Nobel Pharmsanoat in reviewing and providing comments for SOPs. A gap assessment of the new facility will be planned upon completion of commissioning and start-up of operations at the new non-penicillin site.

PQM started arrangements for a data integrity training to prepare the manufacturer for WHO PQ; data integrity is one of the critical aspects to be evaluated during WHO inspection. The training will be held in Q2.

Objective 2 – Strengthen the medicines quality control system

In the fall of 2017, the main PQM partner in Uzbekistan, Uzpharmsanoat (Uzbek State Joint Stock Concern of Pharmaceutical Industry), was liquidated, and a new Agency for Development of Pharmaceutical Industry was formed. PQM continued working with representatives from the new agency on preparation of a committed activity to conduct a GLP training for the staff from manufacturers' quality control laboratories and the State Center for Expertise and Standardization of Pharmaceutical Products, Medical Products, and Medical Equipment under the Agency for Development of Pharmaceutical Industry. The training materials were developed and have been translated into Russian. The training will be conducted in Q2.

Objective 3 – Strengthen GMP inspection system

PQM started discussions with the Agency for Development of Pharmaceutical Industry about the follow-up training for GMP inspectors. The discussions will continue during PQM's visit to the country in January 2018, and an appropriate action plan will be developed.

IV. Key Challenges

The main PQM partner in Uzbekistan—Uzpharmsanoat—was liquidated, and a new Agency for Development of Pharmaceutical Industry was formed. PQM will need to discuss with the Agency their priorities and potentially adjust the work plan.

Core Portfolio



Core MNCH

I. Quarter 1 Highlights

The first PQM publication of the product information report was finalized and made available to the public (manufacturers) on amoxicillin. This product information report contains a summary of available literature and expert opinion on the API, analytical methods, toxicology, and formulation and process of the solid dosage form for the product. Information provided includes the chemical structure/formula, IUPAC name, physio-chemical properties, moisture sorption, and solubility-related data. This publication will help manufacturers and MRAs have almost all product information in one place.

PQM also continued to provide technical assistance to manufacturers to further their progress toward supplying global procurement agencies or WHO PQ.

II. Health Element Context

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

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

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

III. Quarter 1 Progress by Objective

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

During FY 2018 Q1, PQM provided technical assistance to manufacturers of the following MNCH products:

- **Magnesium sulfate FPP:** PQM continued technical assistance on a formulation study to one manufacturer. PQM received CAPAs implemented from a second manufacturer. PQM is in the process of reviewing the CAPAs and providing further comments and guidance to the manufacturer. The manufacturer started working on the dossier for WHO PQ and plans to submit it for PQM’s review in Q2.
- **Oxytocin dispersible tablets:** The manufacturer is in the product development stage with the assistance of PQM. PQM plans to conduct a GMP assessment of the facility in Q2.
- **Oxytocin API:** PQM conducted a GMP assessment of the facility. The manufacturer is currently implementing CAPAs and preparing for the European Directorate for the Quality of Medicines inspection.
- **Amoxicillin FPP:** PQM identified a new manufacturer in FY 2017 Q3. PQM is also working with the manufacturer to identify a new quality-assured source of API. PQM plans to conduct a full GMP assessment in Q2. A second manufacturer is in search of a proper comparator product to conduct a bioequivalence study to be eligible for UNICEF procurement. PQM is providing assistance to identify and obtain the comparator product.

Summary of upcoming activities: The PQM GMP team is continuing to provide technical assistance at various stages to ensure that the manufacturers are making progress toward WHO PQ. This assistance will include a full GMP assessment of the new manufacturer for amoxicillin finished product.

Objective 2 – Provide technical leadership on MNCH medicine quality assurance

PQM participated in the technical consultation meeting on oxytocin quality held in Geneva in October 2017. As result of the meeting, development of an oxytocin quality evidence review paper was initiated. The outline of the paper was developed. PQM will be responsible for development of the selected sections of the paper. PQM is coordinating this work with the various stakeholders involved.

PQM also worked on finalizing the product information report on amoxicillin. This report consolidates much of the needed information for manufacturers to help with producing the quality-assured medicine. The product information report contains a summary of available literature for the API, analytical methods, toxicology, and the formulation and process of the solid dosage form for the product. This report will be made available on the PQM website, among other platforms.

Summary of upcoming activities: PQM plans to work with stakeholders to continue the work on the oxytocin quality evidence review paper. PQM will also participate in the 18th Reproductive Health Supplies Coalition General Membership Meeting that was rescheduled for March 2018 in Brussels, Belgium.

Core NTD

I. Quarter 1 Highlights

PQM has finalized the situation analysis paper “Rapid Assessment of the Neglected Tropical Disease Drug Production and Supply Needs in Five Countries,” and it will be shared with USAID. As a next step, the local manufacturers of NTD medicines will be identified for PQM’s potential support.

PQM has initiated technical assistance to the two selected manufacturers of praziquantel for bioequivalence support in India. The ultimate goal is to support these manufacturers to successfully conduct bioequivalence studies and get prepared for WHO PQ of their product. If they are successful, the global supply of quality-assured praziquantel will increase, contributing to a reduction in the supply gap.

II. Health Element Context

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

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

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

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Increase availability to quality-assured NTD medicines

During Q1, PQM provided technical assistance to manufacturers of the following NTD products:

- **Praziquantel API:** PQM continued to provide technical assistance to manufacturers at various stages toward WHO PQ of praziquantel API. PQM's technical assistance included addressing WHO's queries on dossiers, as well as preparation of submission to WHO PQ.
- **Praziquantel FPP:** PQM continued to provide technical assistance to manufacturers at various stages toward WHO PQ of praziquantel FPP. PQM's technical assistance included conducting GMP assessments of two FPP manufacturing facilities, providing guidance on FPP development, and providing GMP support on CAPA implementation.
- **Albendazole API:** One manufacturer is in the process of implementing the CAPAs from PQM's assessment. PQM's onsite technical assistance visit will be scheduled with the manufacturer. A second manufacturer has completed the product development and is now conducting process validation with PQM's remote technical assistance. PQM plans to make an onsite visit to conduct a GMP assessment in Q2.
- **Albendazole FPP:** One manufacturer is in the product development stage. PQM has been working with the manufacturer and WHO to source the comparator product.
- **Mebendazole FPP:** With PQM assistance, one manufacturer is in the product development stage. PQM is also working with the manufacturer to source the comparator product.

PQM finalized the report on the situation analysis on the availability of quality-assured priority NTD medicines in five high-NTD burden countries (Nigeria, Ethiopia, Tanzania, India, and Indonesia). The final report of the analysis will be shared with USAID for review. Selection of the manufacturers of NTD products in these countries will be made in discussion with USAID.

Summary of upcoming activities: The PQM GMP team continues to provide technical assistance at various stages to ensure that the manufacturers make progress toward WHO PQ. PQM will also select local manufacturers as a result of the situation analysis report and engage them for technical assistance.

Objective 2 – Technical support for bioequivalence study

A thorough evaluation of the applications in response to the EOI for PQM's support of praziquantel bioequivalence studies was conducted in FY 2017 Q4. In FY 2018 Q1, the contracts were finalized for the two manufacturers selected for PQM's technical and financial support. PQM conducted initial GMP assessments for the two manufacturers in December 2017. The assessment reports are being finalized. Once the assessment reports are sent to the manufacturers, next steps will be determined in Q2, and timelines will be set for the bioequivalence studies.

Summary of upcoming activities: Final GMP assessment reports will be sent to the manufacturers, and CAPA plans will be developed. In parallel, PQM will be discussing the timelines for bioequivalence study initiation and design with the manufacturers and their CROs.

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

PQM developed "Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms: Praziquantel" and shared with USAID for comments. The manuscript will be finalized and submitted for publication to the *Journal of Pharmaceutical Sciences* as a "biowaiver monograph." This manuscript will provide very useful information to manufacturers interested in the production of praziquantel.

Core TB

I. Quarter 1 Highlights

One of the priority anti-TB products is clofazimine, which is part of the shorter regimen for treatment of MDR-TB recommended by WHO. PQM has been working with a manufacturer to develop this complicated finished product through the WHO PQ process. The manufacturer and PQM have been working diligently to complete the development process, and the bioequivalence study was initiated in Q1. PQM will continue to work with the manufacturer to conduct due diligence of the CRO in Q2 and provide assistance in compiling the dossier.

II. Health Element Context

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

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

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

III. Quarter 1 Progress by Objective

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

During Q1, PQM provided technical assistance to manufacturers of the following anti-TB products:

- **Clofazimine FPP:** PQM is in the process of translating the CAPAs from the contract manufacturer. Once the translation is complete, the documents will receive a technical review by PQM prior to submission to WHO by the manufacturer. PQM also provided input on the bioequivalence study protocol and design. The study commenced at the end of November.
- **Cycloserine API:** PQM provided remote technical assistance to the manufacturer in solving stability issues. This manufacturer is still in the product development phase.
- **Rifapentine API:** PQM conducted a GMP assessment of one manufacturer in August 2017, and this manufacturer is currently implementing its CAPAs. PQM is providing feedback to a second manufacturer that submitted the API master file for review to PQM. PQM is also working with the starting material and intermediate suppliers to prepare them for WHO's inspection.
- **Rifapentine FPP:** PQM continues to provide assistance in product development.
- **Gatifloxacin API:** PQM is working with the manufacturer to develop the API master file for submission to the WHO PQ team. The API master file is expected to be received for review in Q2. PQM is also working with the manufacturer to develop an analytical method and method validation.
- **Gatifloxacin FPP:** As there is no originator or another comparator product on the market, PQM is providing assistance through communication with the WHO PQ team in sourcing the comparator product. This manufacturer is still in the product development phase.
- **Kanamycin API:** PQM provided assistance to one API manufacturer to conduct cross-contamination assessment and is in the process of implementing PQM's recommendations to mitigate the risks related to potential cross contamination. This manufacturer also initiated a process study to reduce impurity with a different source of starting material, and PQM will continue to provide assistance for the purification process. PQM also engaged a second API manufacturer and has confirmed a GMP assessment date for February

2018. This manufacturer has received approval from Japan's Pharmaceuticals and Medical Devices Agency for its kanamycin API.

- **Kanamycin FPP:** PQM provided input on dossier queries received from WHO PQ on the compatibility study for a plastic filling tube used in the manufacturing process. The company is currently searching for an external laboratory that can conduct this study.
- **Linezolid FPP:** The manufacturer received U.S. FDA inspection in November 2017 and is currently waiting for the final report to be issued. WHO PQ has waived its inspection.
- **Rifampicin/Isoniazid/Ethambutol/Pyrazinamide (4 FDC):** One manufacturer is continuing to implement CAPAs as a result of the GMP assessment in April 2017. The manufacturer completed all of the CAPAs by the end of 2017. The manufacturer plans to initiate the compilation of its dossier to be ready for PQM to review by Q2. A second manufacturer is working on submitting to PQM by Q2 its CAPAs that resulted from the PQM assessment in April 2017. The new facility is complete and has applied for local MRA licensing.

To contribute to ensuring of uninterrupted supply of anti-TB medicines on the U.S. market, PQM advertised a Request for Application (RFA) for rifampicin submission to U.S. FDA. The RFA was advertised for 1 month in August, and six proposals were received. PQM evaluated all of the proposals and has prioritized the top two candidates. A selection memo was sent to the USAID TB team for review and approval. The selection will be finalized in Q2. Bringing new suppliers to the U.S. market will reduce the risk of shortage of the medicine. Increased competition may also have a positive impact on price reduction of the medicine, as U.S. FDA approval makes the medicine eligible for supply through the Stop TB Partnership's Global Drug Facility (GDF). The intervention can potentially increase the number of international quality-assured suppliers, not only in the United States but also on the global public health market, particularly for the countries benefiting from the GDF mechanism.

Summary of upcoming activities: The PQM GMP team will continue to provide technical assistance to the manufacturers. PQM staff will discuss and finalize the selection of the manufacturer for the U.S. FDA submission for rifampin (rifampicin). The candidate will be notified, and award documentation will be initiated in Q2.

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

PQM staff participated in the 48th Union World Conference on Lung Health in Guadalajara, Mexico. PQM participated and contributed to different conference sessions. PQM made a presentation "Supporting TB drugs manufacturers to increase the supply of a life-saving anti-TB medicine: USP Promoting the Quality of Medicines (PQM) technical approach" on the workshop titled, "Accelerated access to new TB medicines, regimens, and diagnostics: the supply management challenges during transitions" along with USAID, GDF, and various country representatives. In the presentation, PQM discussed its technical approaches to strengthening medicines quality assurance systems to ensure the quality of medicines, particularly anti-TB medicines, on the public market. PQM had an opportunity to meet with various stakeholders and partners, including manufacturers of anti-TB medicines.

As Pakistan is graduating from the Global Fund support in supply of anti-TB medicines, PQM has been active in ensuring that there is adequate availability of quality-assured anti-TB medicines on the local market. The Stop-TB Partnership Pakistan organized "National Consultation on Availability of First and Second-Line Anti-tuberculosis Medicine" stakeholder meeting in December 2017. This meeting was organized in collaboration with WHO PQ, GDF, PQM, USAID, DRAP and the government of Pakistan. This meeting was attended by manufacturers that are currently receiving technical assistance from PQM, as well as new potential manufacturers. PQM provided a presentation highlighting PQM technical approaches, including technical assistance to manufacturers of anti-TB medicines. Meeting participants stressed that PQM's technical assistance gives a unique opportunity to ensure that quality-assured anti-TB medicines are sustainably available on the local market after the Global Funds transition.

Summary of upcoming activities: PQM will work with key stakeholders to hold a pharmaceutical quality session at next year's Union meeting. PQM will continue to work with existing manufacturers in Pakistan to ensure full WHO PQ of the first-line medicines.

Cross Bureau

I. Quarter 1 Highlights

This quarter, PQM's Cross Bureau project made progress in developing a web-based version of its tool for developing risk-based sampling plan. Development of this tool version has reached its final stage and will be demonstrated in early 2018.

Another key activity saw progress this quarter as draft country profiles for Bangladesh, Malawi, and Nigeria have been developed and internally reviewed. The draft profiles are now poised for revision to include additional information.

PQM also continued to develop the content for two modules for an e-learning course.

II. Cross Bureau Context

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

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

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

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

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

III. Quarter 1 Progress by Objective

Objective 1 – Increase awareness of the importance of medicines quality

To identify media reports about incidents of poor-quality medicines and analyze compiled information, PQM is working with Cision, a company specialized in conducting media reports analysis. Cision developed a framework and a draft report. PQM reviewed the report and requested that Cision make revisions. The final report covering the period of October 2016 through June 2017 is expected to be available by early Q2.

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

No updates this quarter.

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

PQM continues to develop a web-based version of its tool for developing a risk-based sampling plan. Development of has reached its final stage, and a demonstration of the tool is planned for January 2018.

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

There is nothing to report this quarter, as the tool has already been finalized.

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

PQM continues to develop the content of e-learning courses. The content of module 2 has been developed and was internally reviewed and revised. This module describes the steps involved in medicine development processes. The content of module 1 has been drafted and is undergoing internal review. This module focusses on defining the framework for medicines regulation with emphasis on medicine policy and legislation. It describes the components of a medicine policy.

Objective 6 – Establish regulatory system country profiles

Draft country profiles for Bangladesh, Malawi, and Nigeria have been developed and internally reviewed. The draft documents will be revised to include additional information. Such addition to Bangladesh and Nigeria country profile is easily feasible since PQM has projects and USP offices in these countries.

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

No updates this quarter.

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

No updates this quarter.

<p>Core Malaria: The FY17 Q4 report was submitted to AOR team on November 15, 2017; no feedback has been provided to date. There is no work plan or pipeline for this project for FY18.</p>
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Management Overview

During the first quarter, PQM worked with the USAID missions and core health element teams to obtain approvals for FY 2018 work plans. By the end of the quarter, 14 out of 20 work plans (70%) had been fully approved. Through increased project management strengthening, PQM continues to see improvement in the timely approval of work plans in comparison to previous fiscal years, with FY 2017 and FY 2016 seeing 58 percent and 41 percent of work plans fully approved, respectively, at the end of the first quarter.

In November 2017, PQM released the Annual Performance Report for FY 2017. Covering the period of performance (October 1, 2016–September 30, 2017), the report highlighted PQM's progress and achievements, technical approach, translation of innovation into action, and examples of sustainability and lessons learned. In celebrating the eighth anniversary of the PQM program, Director Jude Nwokike noted in the report that, through USAID's support, PQM has been able to collaborate with committed partners at the global, regional, and local levels toward ensuring that quality-assured medicines are available to those who need them most.

Also in November 2017, Director Nwokike had the opportunity to present at the Fourth Global Forum on Human Resources for Health in Dublin, Ireland, giving an overview of the PQM program and discussing issues related to medicines quality.

Additionally, this quarter the PQM team hosted delegations from the MRAs of Nigeria and Burma. Dr. Moji Adeyeye, newly appointed Director General of Nigeria's NAFDAC, visited in order to be introduced to the PQM program and USP as an organization as she begins her tenure. A delegation from Burma's DFDA, including Director General Dr. Than Htut, met with USP and PQM staff as well as guests from the USAID Agreement Officer's Representative's team. DFDA presented an overview of the agency, plans for expansion, and the technical challenges they face in their PMS. Future areas of collaboration were discussed, and gratitude was afforded for the support Burma has received throughout the years.