Promoting the Quality of Medicines

Promoting the Quality of Medicines (PQM) Program

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

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Agreement Officer's Representative Team	Mr. Bob Emrey, Lead Health Systems Specialist Ms. Elisabeth Ludeman, Senior Pharmaceutical Management Advisor Ms. Tobey Busch, Senior Pharmaceutical Management Advisor
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The Promoting the Quality of Medicines (PQM) program is a Cooperative Agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to address critical pharmaceutical management challenges in 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
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CHX	chlorhexidine
CRO	clinical research organization
CRP	Collaborative Registration Procedure
DFDA	Department of Food and Drug Administration [Burma]
DGDA	Directorate General of Drug Administration [Bangladesh]
DRAP	Drug Regulatory Authority of Pakistan
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
FPP	finished pharmaceutical product
GFDA	Ghana Food and Drug Administration
GLP	good laboratory practices
GMP	good manufacturing practices
HPLC	high-performance liquid chromatography
LMHRA	Liberia Medicines and Health Products Regulatory Authority
M&E	monitoring and evaluation
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 [Nigeria]
NMCP	National Malaria Control Program
NQCL	national quality control laboratory
NTD	neglected tropical disease
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
QA	quality assurance
QC	quality control
QMS	quality management systems
SOP	standard operating procedure
SRA	stringent regulatory authority
TB	tuberculosis
UNICEF	United Nations Children's Fund
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 second quarter (Q2) of FY 2018, from January 1 to March 31, 2018.

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 (1) the development of guidelines through a collaborative consultative process that involved expert groups, relevant stakeholders, and international organizations; (2) the review of a Recall Directive that will significantly impact the recall process whenever a poor-quality medicine is detected; and (3) the development of a pharmaceutical traceability strategy that will improve supply chain efficiency and transparency. PQM also continued its support to the Ethiopian Food, Medicine and Health Care Administration and Control Authority on inspection of retail outlets via an audit-based inspection that also supports implementation of the community pharmacies' audit manual and peer mentoring. In Guinea, PQM continued to provide support to the Law on Medicines, Other Health Products and Pharmaceutical Exercise, and five presidential decrees supporting the existing pharmaceutical law were developed and submitted for adoption. In Mozambique, PQM contributed to the development of two regulations for good manufacturing practices and medical product registration. In Bangladesh, PQM conducted a gap assessment of the existing pharmacy undergraduate curricula of 21 (out of 39) universities, submitted a draft report with recommendations of curricular changes, and plans further consultation with the Pharmacy Council and relevant stakeholders before getting the universities to adopt and implement the new curricula; the ultimate aim is to ensure future pharmacy graduates are adequately equipped and competent in the regulatory affairs space to meet workplace needs.

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 international standards, helping them develop and submit dossiers for certification by the World Health Organization (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 donations and help establish a sustainable local supply with national resources. In 2016, PQM commenced intense technical assistance to Juhel Pharmaceuticals, a Nigerian manufacturer, for the local production of oxytocin and magnesium sulfate injections. This quarter, the National Agency for Food and Drug Administration and Control (NAFDAC) issued market authorization approval to Juhel for both products, making Juhel Pharmaceuticals the first local manufacturer of oxytocin and magnesium sulfate injections in Africa; increasing the local production and availability of these medicines will contribute to reducing maternal deaths associated with postpartum hemorrhage and preeclampsia in the continent.

With PQM support, in Q2 in Pakistan, local manufacturer Zafa Pharmaceuticals began local production and released its first batches of chlorhexidine (CHX) 7.1% gel. Zafa Pharmaceuticals joins three other local manufacturers that launched CHX 7.1% gel in the previous quarter. It is a success story for PQM Pakistan to facilitate locally manufactured, quality-assured, and safe CHX 7.1% gel by four manufacturers in only two years. The products are now available in all provinces and regions of Pakistan as over-the-counter medicines readily accessible by the general public, are 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), and may soon be available through government tenders. The reach of this success expands as the manufacturers look toward exporting their products to other countries in the region, as well as becoming potential suppliers for UNICEF.

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 Nigeria, PQM continued to provide technical leadership and made presentations at a national-level workshop themed "Oxytocin Injection Quality Audit:

Results from the Clinical Experience Study." The workshop came out of the post-marketing surveillance (PMS) results of critical maternal health products in the country, which revealed that over 70 percent of oxytocin samples analyzed at NAFDAC's ISO accredited laboratories failed quality control (QC) tests. PQM subsequently funded researchers at the Lagos University Teaching Hospital to study whether there is any correlation between the PMS results and clinical experiences of healthcare providers in Lagos state. PQM made presentations at a webinar session titled "Quality Oxytocin: Nigeria" organized by the Maternal Health Supplies Caucus. The combination of these presentations on results from the oxytocin injection quality audit and clinical experience study demonstrated the connection between PMS of medicines and patients' and healthcare providers' experiences.

Through PQM's Cross Bureau project, the "Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries" document was finalized this quarter. These guidelines—which build on WHO guidelines for conducting quality of medicines surveys and medicines testing, as well as more than 15 years of experience in supporting low- and middle-income countries to establish and implement medicines quality monitoring (MQM) activities—aim to help regulatory agencies implement technically sound, cost-effective, and sustainable national PMS programs. Implementation of these risk-based approaches will help countries allocate their limited resources for continuous MQM to ensure the efficacy and safety of medicines when they reach patients, and PQM is already working with selected countries for the prompt use of the guidelines when establishing their national PMS programs.

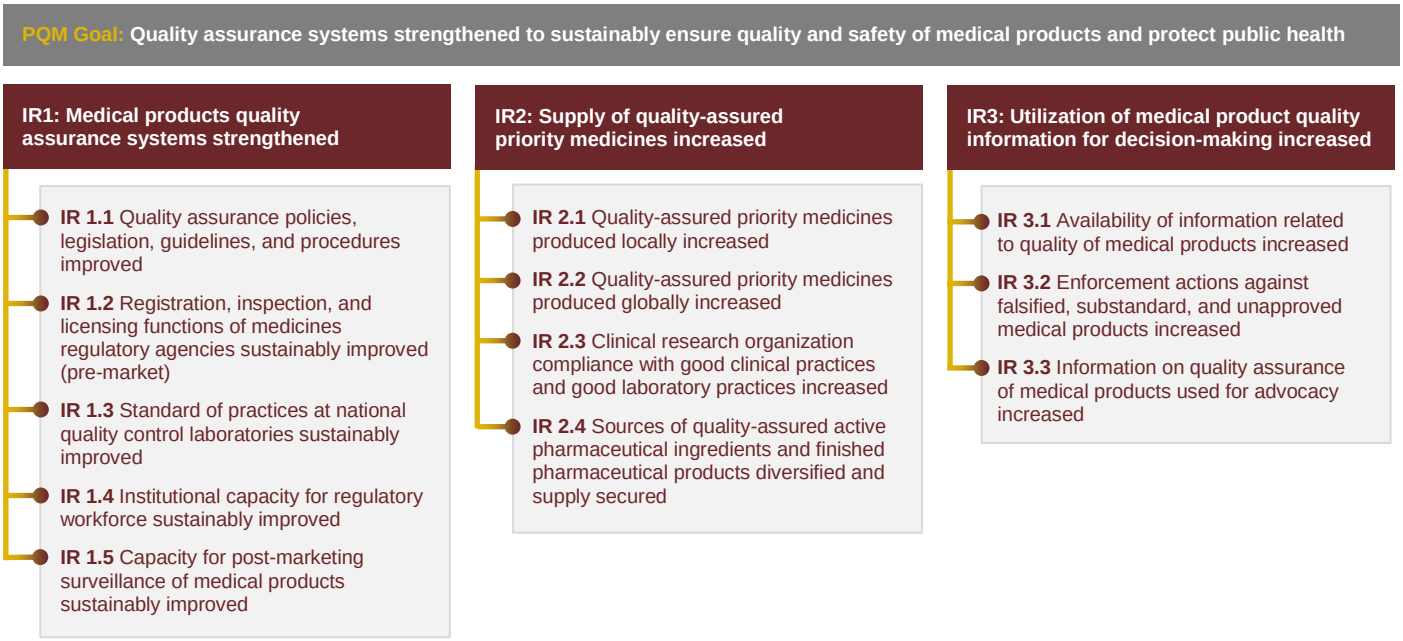
Program Background

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 (LMICs) 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 January–March 2018 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 QA 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 QA topics in preservice 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 preservice 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 Second Quarter IR1 Achievements

Key Results and Highlights

In Ethiopia, PQM continued its support to the regulatory authority, the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA), on inspection of retail outlets. The audit-based inspection (systematic and independent onsite examination and verification of processes, procedures, and/or systems available at retail outlets to ensure compliance) was started by deploying 68 inspectors to retail outlets in Addis Ababa, which is to be followed by selected areas of other regions. The objective of this exercise was to gain information on the practices of community pharmacies and drug stores on the procurement, storage, and dispensing of medicines by auditing past and current transactions on the basis of selected high-risk and/or priority medicines as tracer drugs. PQM provided this support to improve EFMHACA's inspection system and strengthen regional regulatory authorities. Supporting implementation of the community pharmacies' audit manual is also aimed at building the capacity of inspectors from regional regulatory bodies through mentoring and oversight by experienced EFMHACA inspectors. This will help to scale up and sustain future audit-based inspection practices by regional regulatory authorities using the same manual.

In Guinea, PQM continues to provide support to the Law on Medicines, Other Health Products and Pharmaceutical Exercise. As a result of this support, five presidential decrees supporting the existing pharmaceutical law were developed and submitted for adoption. In Mozambique, PQM contributed to the development of two regulations for GMP and medical product registration.

In Bangladesh, PQM successfully conducted a gap assessment of the existing pharmacy undergraduate curricula of 21 out of 39 universities. The purpose of the exercise was to evaluate the coverage of the regulatory functions in the current syllabus. On average, 1.5 out of 55.5 graduate course credits were allocated to regulatory functions. PQM submitted a draft assessment report with recommendations of curricular changes; PQM plans further consultation with the Pharmacy Council and relevant stakeholders before getting the universities to adopt and implement the new curricula. The ultimate aim is to ensure future pharmacy graduates are adequately equipped and competent in the regulatory affairs space to meet workplace needs.

Key IR1 Indicators for FY 2018 Q2

Number of national medicine quality assurance policies, regulations, and legislations developed or updated and submitted for adoption	**2 – Guinea, Mozambique**
Number of individuals completing training in key QA/QC related technical areas	**369**
Number of medical product samples tested	**493**
Percent of tested samples found to be substandard or falsified	**14.4% – Mozambique** **1.9% – Nigeria**
Number of sampling sites added for MQM/PMS activities by the MRA	**12 – Bangladesh, Nigeria**

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 donations 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 medicines to treat TB, malaria, and NTDs. 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 Second Quarter IR2 Achievements

Key Results and Highlights

In 2016, PQM commenced intense technical assistance to Juhel Pharmaceuticals, a Nigerian manufacturer, for the local production of oxytocin and magnesium sulfate injections. This quarter, the medicines regulatory authority, the National Agency for Food and Drug Administration and Control (NAFDAC), issued market authorization approval to

Juhel Pharmaceuticals for both medicine products, making Juhel Pharmaceuticals the first local manufacturer of oxytocin and magnesium sulfate injections in Africa. This achievement will increase the availability of quality-assured oxytocin and magnesium sulfate injections, which will contribute to reducing maternal deaths associated with postpartum hemorrhage and preeclampsia in the continent. Having a local supply closer to the last mile of the supply chain provides potential for improved product quality at the time of administration to patients.

In Pakistan this quarter, a local manufacturer (Zafa Pharmaceuticals) started local production and released its first batches of chlorhexidine (CHX) 7.1% gel with the support of PQM. Zafa Pharmaceuticals joins three other local manufacturers that launched CHX 7.1% gel in the previous quarter. Currently, all four manufacturers have made the products available in all provinces and regions of Pakistan as over-the-counter medicines readily accessible by the general public. The four manufacturers will have a combined production capacity of approximately 24,000,000 tubes per year. These products are also 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. The manufacturers are also working to supply the product through government tenders. It is a success story for PQM Pakistan to facilitate locally manufactured, quality-assured, and safe CHX 7.1% gel by four manufacturers in a short span of only 2 years. The reach of this success expands as the manufacturers look toward exporting their products to other countries in the region, as well as becoming potential suppliers for UNICEF.

Key IR2 Indicators for FY 2018 Q2

Number of priority medicines that achieved local approval with PQM's support	**2 – magnesium sulfate, oxytocin**
Number of manufacturers supported towards WHO PQ, SRA, or local approval	**43**

Number of Manufacturers Provided with Technical Assistance in FY 2018 Q2

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	5	magnesium sulfate FPP, oxytocin API
Core TB	13	rifampicin/isoniazid/ethambutol/pyrazimnamide (4 FDC), linezolid FPP, kanamycin FPP, kanamycin API, gatifloxacin FPP, gatifloxacin API, rifapentine FPP, rifapentine API, clofazimine API, clofazimine FPP
Core NTD	7	praziquantel API, praziquantel FPP, albendazole API, albendazole FPP, mebendazole FPP
Bangladesh	1	chlorhexidine solution FPP
Ethiopia	1	ethambutol FPP
Nigeria	8	oxytocin injection FPP, magnesium sulfate FPP, amoxicillin dispersible tablet (DT) FPP, chlorhexidine FPP, arthemether lumefertrine FPP, zinc sulfate FPP, ready-to-use therapeutic foods (RUTF)
Indonesia	2	levofloxacin FPP
Pakistan	5	chlorhexidine FPP, amoxicillin DT FPP
Uzbekistan	1	levofloxacin 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 PMS 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 Second Quarter IR3 Achievements

Key Results and Highlights

In Nigeria, PQM continued to provide technical leadership and made presentations at a national-level workshop themed "Oxytocin Injection Quality Audit: Results from the Clinical Experience Study." The workshop came out of the PMS results of critical maternal health products in the country, which revealed that over 70 percent of oxytocin samples analyzed at NAFDAC's ISO accredited laboratories failed QC tests. Oxytocin injection is used to begin or improve contractions during labor and reduce bleeding after childbirth. Subsequent to the findings, PQM funded researchers at the Lagos University Teaching Hospital to study whether there is any correlation between the PMS results and clinical experiences of healthcare providers in Lagos state in the use of oxytocin for postpartum hemorrhage treatment. PQM made presentations at a webinar session titled "Quality Oxytocin: Nigeria" organized by the Maternal Health Supplies Caucus. The combination of both presentations on results from the oxytocin injection quality audit and clinical experience study demonstrated the connection between PMS of medicines and patients and healthcare providers' experiences.

Through PQM's Cross Bureau project, the "Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries" document was finalized this quarter. Building on WHO guidelines for conducting quality of medicines surveys and medicines testing, as well as more than 15 years of PQM experience in supporting LMICs to establish and implement MQM activities, these guidelines aim to help regulatory agencies implement technically sound, cost-effective, and sustainable national PMS programs. For this, PQM introduces risk-based elements for both the sampling process (e.g., medicines characteristics, geographical location, types of facilities) as well as for testing (e.g., multilevel testing approach for both field and laboratory QC). Implementation of these risk-based approaches will help countries allocate limited human and financial resources for continuous monitoring of the quality of medicines in the market to ensure their efficacy and safety when they reach patients. PQM is already working with selected countries for the prompt use of these guidelines when establishing their national PMS programs.

Key IR3 Indicator for FY 2018 Q2

Number of regulatory actions made by an MRA	**16 – Nigeria, Ethiopia, Ghana**
Number of publications issued and presentations made on medical products' quality assurance at national or international level	**4 – Risk-based PMS** **10 – Other topics**

Africa

Benin

I. Quarter 2 Highlights

This quarter, Benin's national quality control laboratory (LNCQ) completed electrical rewiring of the laboratory's second floor, a major step toward stabilizing the power in the laboratory. The instability of electrical power previously damaged some sensitive equipment, such as the high-performance liquid chromatography (HPLC), and has impeded the use of other equipment.

Also this quarter, using Minilab™ and handheld Raman spectrometer (NanoRam), LNCQ identified falsified artemether–lumefantrine and sulfadoxine–pyrimethamine among products seized at Cotonou airport. Other activities planned for this quarter have been on hold. This is because procurement and installation of a power generator must be completed before training for laboratory staff on HPLC and dissolution can take place.

II. Country Context

Malaria is the leading cause of morbidity in Benin, which is a high malaria transmission country according to WHO. In 2016, there were 1,324,576 reported and confirmed cases of malaria and 1,646 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 2 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

LNCQ completed electrical rewiring on the second floor of the laboratory. This floor hosts sensitive equipment, such as HPLC and spectrometers. The rewiring was needed in order to keep such equipment from damage due to exposure to high power variations. LNCQ agreed to carry out this work in exchange for PQM providing a power generator. With the generator installed, sensitive instruments can be used to provide continuous medicines QC services to detect substandard and falsified products. Rewiring of other floors is underway. Following the completion of the rewiring of the second floor, PQM finalized the selection of the power generator supplier. A local supplier was selected after considering two other local suppliers and one supplier from Ghana. In anticipation of the procurement and installation of the power generator, PQM plans to provide laboratory training on analytical methods in May 2018.

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

PQM worked with LNCQ to develop a budget for antimalarial PMS activities in anticipation of the establishment of a fixed amount award (FAA) to facilitate PMS activities. In the event that the FAA is delayed, PQM will proceed with direct implementation of these activities.

The laboratory has been using the handheld Raman spectrometer as a screening tool for detection of falsified antimalarials, in addition to Minilab™. Recently, using Minilab™, LNCQ tested medicines seized by Customs at Bernadin Gantin International Airport in Cotonou and detected falsified artemether–lumefantrine (Figure 1). The laboratory also tested suspicious sulfadoxine–pyrimethamine and artemether–lumefantrine samples using the handheld Raman spectrometer and identified falsified products that did not contain any API (Figure 2). Thanks to training and screening tools that PMI provided to LNCQ through the PQM program, the laboratory was able to provide important, timely results to the regulatory authority to protect patients from the falsified medical products. In addition to saving time, LNCQ also saved resources in terms of chemicals and reagents it would have needed if it had used more advance testing methods, illustrating the usefulness of applying a risk-based approach to PMS and QC testing.

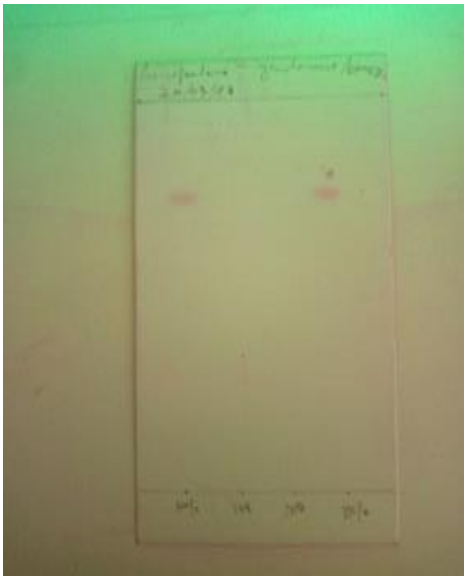


Figure 1: Falsified Coartem detected by LNCQ using Minilab™

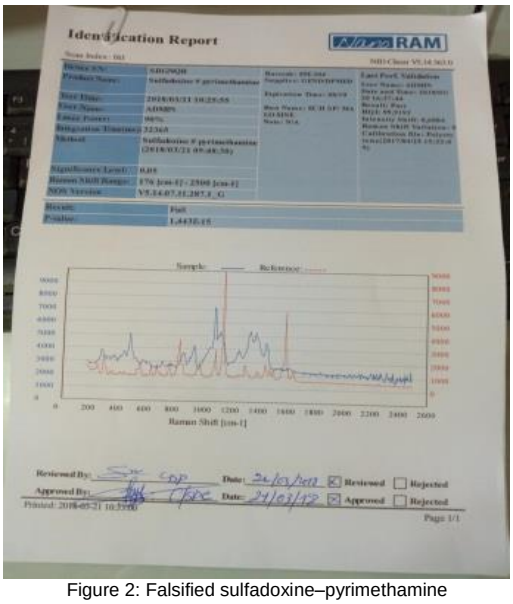


Figure 2: Falsified sulfadoxine–pyrimethamine detected by LNCQ using handheld Raman spectrometer

Burkina Faso

I. Quarter 2 Highlights

PQM continued to support the NQCL in its efforts to attain ISO 17025 accreditation by strengthening its quality management system. In collaboration with the Sahel Women Empowerment and Demographic Dividend (SWEDD) project, PQM assisted the laboratory in developing new QMS documents focused on personnel habilitation and training.

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 (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) National Strategic 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, 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 to distribution.

III. Quarter 2 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

PQM continues to assist the Directorate of Medicine Control (DCM) in strengthening the laboratory's QMS in support of its preparation for ISO 17025:2017 accreditation. Following a request from DCM, PQM participated in a workshop sponsored by the SWEDD project to assist the laboratory in developing QMS documents. The focus of the workshop was on developing new QMS documents relating to human resources, including a staff training guide, staff files, staff competencies form, staff resume, personnel hiring and management, and personnel authorization form.

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

In 2017, PQM facilitated PMS activities. In collaboration with DCM, the regulatory authority collected 172 samples of antimalarial medicines from the public and private sectors. Following screening using Minilab™, 10 samples underwent confirmatory testing. All the samples were found compliant. A workshop for dissemination of FY 2017 PMS activities and presentation of the risk-based approach was planned for January 2018 but has been postponed. It is tentatively planned for the last week of April 2018. The first day of the workshop will be an opportunity for stakeholders to be informed about the activities carried out last year and challenges encountered, and draw lessons learned. The second day will serve to present the risk-based approach to the implementation of PMS and an opportunity for the national pharmaceutical regulatory agency to start developing its own guidance on risk-based PMS.

Objective 3 – Support the creation of the National Pharmaceutical Authority

There is no update for this quarter.

Ethiopia

I. Quarter 2 Highlights

During this quarter, PQM provided technical support to improve the medicine registration system by helping to finalize three new guidelines and complete the revision of one guideline. Support was provided in the incorporation of new tools and testing of the Medicine Registration Information System (MRIS) for newly enhanced features, and feedback was provided to the software developers. PQM provided support in the implementation of audit-based inspection at community pharmacies by EFMHACA, where 68 inspectors were deployed to the field in Addis Ababa. The audit-based inspection is a systematic and independent onsite examination and verification of a process, procedure, or system available at retail outlets to ensure compliance to given requirements. It will also improve the traceability of retail outlets' operations and risk management effectiveness, and improve control and governance processes. This approach is one of the strategies that EFMHACA devised to improve its inspection function and make it more effective at community pharmacies and drug stores. The approach provides the opportunity to promote good distribution and storage practices, as well as good pharmacy practices at the retail outlets level. PQM also helped EFMHACA to organize a workshop to review the Recall Directive, an important enforcement tool that allows for effective recalls at any time when poor-quality medicines are detected after distribution in the country.

The medicines QC laboratory of EFMHACA was ISO 17025 reaccredited for 13 test methods (8 physicochemical and 5 condom test methods) and scope expansion of 3 additional test methods in Q1, and the official certificate was received in Q2. EFMHACA branch laboratories have continued the collection and testing of medicines as part of their routine PMS activity. The laboratories collected 79 samples of medicines during this quarter. Second-round testing of samples from FY 2017 PMS was completed, and findings from the testing revealed that 6 more samples of quinine sulfate tablet failed quality testing. When added to the 49 samples identified in the first round, the total becomes 55 samples of quinine sulfate that failed quality testing. Findings were shared with the USAID mission (PMI) during the monthly update meeting. EFMHACA immediately took regulatory measures by enforcing a recall through the importers of the products. EFMHACA has also supplied laboratory equipment (water purifiers and automatic titrators) worth $94,000 to branch laboratories in which PQM provided technical support to identify the instruments needed and guidance in the overall procurement process. Procurement of the equipment was fully financed by EFMHACA to strengthen the branch laboratories, which demonstrates EFMHACA's commitment, in addition to the routine oversight it provides.

PQM has continued providing technical support to EFMHACA in the implementation of the National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia. This quarter, PQM advised on prioritization and evaluation of technical documents from pharmaceutical industries applying to invest in the sector and occupy space at the industrial park that is under construction. With respect to strengthening the pharmacovigilance systems, PQM conducted supportive supervision of the cohort event monitoring (CEM) on anti-retroviral (ARV) medicines at 20 health facilities on a weekly basis and supported the entry of data for 202 adverse drug events (ADE) into the pharmacovigilance data monitoring system. During the period, 43 product defects were reported through the ADE monitoring system. PQM also provided ongoing support in the development of monitoring and evaluation (M&E) systems for the medicine regulatory sector and automation of the regulatory information flow for decision making. Support provided included development of data collection tools for key performance indicators and high-level outcome indicators reported by different directorates and branch offices. EFMHACA also pursued further enhancement for the M&E system; PQM is providing technical assistance to realize the plan in improvement of the M&E system for better regulatory information flow. Overall, the following key achievements made during the past quarter included the following:

1. EFMHACA deployed 68 inspectors to implement the audit-based inspection of retail outlets in Addis Ababa. The objective is to gain information on the practices of community pharmacies and drug stores on the procurement, storage, and dispensing of medicines by auditing past and current transactions on the basis of selected risky and/or priority medicines as tracer drugs. PQM's role starts from development of the proposal to support in deployment of inspectors. The inspection will also facilitate the mentoring of regional inspectors by experienced EFMHACA inspectors who are co-inspecting using the manual developed with PQM's support.
2. EFMHACA procured and supplied one water distiller and one automatic titrator for each branch laboratory and supported the training of staff. This is one result of the recommendations made through supportive supervision that PQM provided in previous quarters. PQM played a key role by providing technical assistance in the preparation of specifications and guiding EFMHACA in the overall procurement process. The lesson learned from this is that technical assistance needs from PQM still persist, even as EFMHACA uses its own resources in some areas.
3. Based on a request from EFMHACA to coordinate and lead an upcoming large-scale training funded by EFMHACA, PQM developed a full-fledged proposal detailing how the training should be organized at different levels. PQM provided recommendations on training approaches and solicitation of training options, especially for those trainings needing high-level expertise. All the proposals for the trainings have been accepted and are currently being planned for execution.
4. PQM provided technical support in the development of a rapid assessment tool to assess data recording and reporting practices, contexts of M&E systems at different reporting units, available infrastructures, human resources, and budgets to enable implementation of M&E activities. The findings of the rapid assessment will help provide insight on what kinds of approaches need to be used to improve the M&E system and will inform EFMHACA top management about what it takes to implement various options for improvement so that an informed decisions can be made.

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 indicate that, by 2020, the country plans 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 quality-assured, safe, and efficacious, medicines that address the priority health needs of the people of Ethiopia.

III. Quarter 2 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
During Q1, PQM provided support to draft three guidelines and shared with stakeholders for comment. The guidelines were: 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 help to comprehensively address the review of dossiers, taking into account the peculiar nature of the stated products.

In this quarter, 90 percent of the development of these guidelines was completed. The process involved drafting of the guidelines through expert groups, review by relevant stakeholders, and incorporation of comments collected from various stakeholders including international organizations. The guidelines are now awaiting publication on EFMHACA's website. In addition, revision of the Guidelines for the Generic Medicine Registration was 50-percent completed. The process of the revision involved formation of a technical working group, compilation of reference materials, and preparation of the first draft. Currently the guideline is ready for discussion with the EFMHACA medicine registration team. In the same quarter, PQM also provided support for the review of the Recall Directive through a workshop. Workshop participants included experts from associations, manufacturers, importers, wholesalers, hospitals, regional regulatory bodies, and other government organizations. All feedback received from the workshop were incorporated, and the directive was updated and is currently pending approval by EFMHACA management. This directive is the derivative of the Recall Guidelines, which was previously developed with PQM's support. The directive will have significant impact in the effective recall process at any time when poor-quality medicines are detected after distribution for use in the country. The relevance of this directive goes beyond the guidelines, as it is legally binding to be enforced by EFMHACA, which further facilitates the implementation of pharmaceuticals recalls as outlined in the guidelines and help to improve compliance by responsible stakeholders during the removal of poor-quality medicines from the market. The consultative process has also provided a lesson on the value of such process to create opportunities for representatives of ultimate users and regulators to become familiarized on the directive beyond contributing to its enrichment. In the next quarter, finalization of all guidelines stated above is expected to be completed.

PQM also provided technical support in the development of a pharmaceutical traceability strategy. The strategy is approved by the national steering committee and is awaiting publication. The implementation of traceability will help to improve patient safety by making sure patients are not exposed to substandard and falsified medicines and will improve supply chain efficiency and transparency by ensuring the visibility of product movements. Following the strategy, other legal documents are being prepared to outline the details of product visibility by various stakeholders that have a background in making products traceable starting from manufacturing to the public/patient.

Sub-IR 1.2 Registration, inspection, and licensing functions of medicine regulatory agencies sustainably improved (pre-market)
In the past quarter, PQM supported the development of a community pharmacies audit manual and provided technical assistance in the preparation of a proposal for its implementation at retail outlets in Addis Ababa and selected areas in other regions.

During this quarter, PQM continued its support on audit inspection of retail outlets (Addis Ababa, Amhara, Oromia, Tigray, and Benshangul Gumz). Activities performed included completion of the proposal, consecutive discussions with EFMHACA top management on its implementation, and orientation of inspectors on the manual and checklists. Finally, the audit-based inspection of retail outlets was started by deploying 68 inspectors to retail outlets in Addis Ababa, which is to be followed by selected areas in other regions. The objective is to gain information on the practices of community pharmacies and drug stores on the procurement, storage, and dispensing of medicines by auditing past and current transactions on the basis of selected high-risk and/or priority medicines as tracer drugs. Supporting implementation of the manual is also aimed at building the capacity of inspectors from regional regulatory bodies through mentoring and oversight by experienced EFMHACA inspectors. This will help to scale up and sustain future audit-based inspection practices by regional regulatory authorities using the same manual.

PQM also provided technical support in the implementation of good registration practices. As a starting point, an assessment of the Medicine Registration Directorate with respect to good registration practices of existing international recommendations is required. Accordingly, PQM provided technical assistance in the development of a concept note for the assessment of the Medicine Registration Directorate. The assessment will be continued in the

next quarter, and findings from the rapid assessment will help incorporate missing components and correct practices that are not in accordance with international practices, as needed.

PQM has continued providing ongoing technical support on implementation of the MRIS. Testing of the newly upgraded MRIS was done for all tracks, except suspension and cancelation. Following the test, feedback was provided to the software developers of JSI/AIDSFree. Testing of the system included the following functionalities:

- Submitting an application, withdrawing an application, responding to agents' applications, responding to a Further Information Request (FIR).
- Assigning a customer service officer, screening an application, returning an application to an agent, and verification.
- Assigning applications to assessors, application evaluation by assessors, approving application evaluation results, generating a FIR, generating samples, generating rejection letters, and generating market authorization certificates.

PQM has also provided support in providing 2 days of orientation to 43 federal police crime investigators on food, medicine, and health care laws and regulations (March 24–25 at Adama).

In the next quarter, the report on findings of the audit inspection in Addis Ababa will be concluded, and training on Clinical Trial Authorization and Good Clinical Trial Practice GCP Guidelines will be provided to EFMHACA experts who are involved in the oversight of clinical trials and review of clinical protocol and data. The purpose of this technical assistance is to create local capacity in the timely review and approval of clinical trial applications as part of facilitating bioequivalence and related studies that are expected to increase in the near future. This effort will ultimately help in improving the quality of medicines registered for use in Ethiopia by ensuring the availability of evidence-based information and data on their quality, safety, and efficacy. Based on information received from EFMHACA experts, it takes 6 months to 1 year to approve a clinical trial application for a new product, while the cut of time set by EFMHACA states 20 days.

Sub-IR 1.3 Standard of practices at national quality control laboratories sustainably improved
During the past quarter, the NQCL was assessed and the minor nonconformities identified were corrected. The laboratory was waiting for the certificate while the assessment body announced the success.

During this quarter, the EFMHACA QC laboratory received its reaccreditation certificate and scope expansion certificates for three additional test methods. Currently, these new scope expansions increase the total number of accredited test methods to 16 (11 physicochemical and 5 condom test methods). PQM also continued providing technical support for the continuous maintenance of the existing QMS to enable maintenance of the already ISO accredited test methods prior to upcoming annual surveillance of the laboratory. Support provided included the initiation of procurement of proficiency test samples.

In this quarter, as part of strengthening the branch laboratories, EFMHACA procured and supplied one water distiller and one automatic titrator for each branch laboratory and supported staff training. This is one of the results of the recommendations made through supportive supervisions that PQM provided during previous quarters. PQM played a key role by providing technical assistance to identify specifications and guide EFMHACA in the overall procurement process. This experience underlines the relevance of the supportive supervisions made and the responsiveness of EFMHACA to apply routine corrective actions to strengthen the branch laboratories. However, it also shows the continued need for technical assistance from PQM, even in the presence of resources at the regulatory authority.

As part of building local capacity for testing quality of medicines and based on the contract agreement for corrective and preventive maintenance of Jima University made with Agilent, the proposed spare parts were procured for the university's laboratory. The goal of the support, provided through USP funding, is to help the laboratory to become ISO 17025 accredited by replicating the existing experience gained by PQM at the EFMHACA laboratory. The presence of such a qualified laboratory at Jimma University not only enhances the quality of training and research at the university, but also creates an opportunity for the regulatory authority and partners involved in the procurement of drugs to have an alternative avenue for conducting quality testing.

Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved
In the past quarter, PQM initiated processes for in-country development of teaching modules for the regulatory affairs masters' program that involves the participation of in-country experts, including those from the School of Pharmacy and EFMHACA. In Q2, PQM continued working with the School of Pharmacy to prepare two training modules on Product Registration and Inspection and Regulatory Science and Compliance. After approval of the technical and financial proposal, the school will be provided with approval to prepare the module. Accordingly, the school is

currently developing the modules that are intended to be used for the preservice training of the post-graduate program on regulatory affairs.

PQM also participated in a 1-day consultative meeting organized by the Ethiopian Pharmacists Association and Addis Ababa University to discuss and propose on potential curricula for the pharmacy workforce with a special emphasis on preservice training. This curriculum would address the current challenges related to the quality of professionals and respond to the emerging needs of professionals tailored to specific pharmaceutical sectors like the booming pharmaceutical industries in Ethiopia. Participants came from the Pharmaceuticals Fund and Supply Agency, EFMHACA, local manufacturers, universities, the Ministry of Industry, and other government institutions. The meeting concluded with recommendations to generate more evidence on the quality of existing universities, assessment of the current workforce, and articulation of proposed approaches to bring about the desired change.

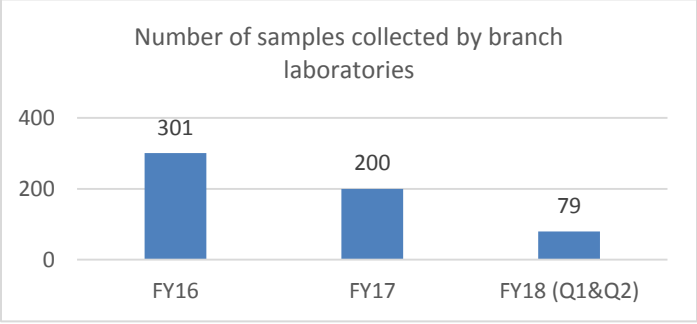
Sub-IR 1.5 Capacity for post-marketing surveillance of medical products sustainably improved
During Q1, results of FY 2017 PMS showed the failure of 49 samples of quinine sulfate tablet, 2 samples of primaquine tablet, and 2 samples of artemether injection. Based on the test results, the products were recalled by EFMHACA.

During Q2, a second round of testing was completed; 6 samples of quinine sulfate tablet were found to be of poor quality, and a regulatory action was taken based on the result. With Q1, the total number of failed quinine sulfate tablets is 55. EFMHACA undertook root cause analysis and found that the problem is related to manufacturing. Accordingly, EFMHACA took measures to recall the products and ban the manufacturer from importing its products to Ethiopia. PQM support provided during this quarter to strengthen the PMS system, both at the federal and branch levels, includes the following:

- PMS protocol revised based on discussions made at two rounds of meetings to conduct the next round of PMS.
- Identification and quantification of reagents and reference standards to conduct testing of FY 2018 PMS samples concluded.
- Minilab™ reference standards for testing of antimalarial medicines procured and supplied to each branch laboratory; branches have started using the reference standards.
- List of laboratory supplies, reagents, and reference standards for conducting testing of PMS samples identified and quantified.

Due to the capacity built at branch laboratories for routine PMS, during Q2, branches collected a total of 79 samples of medicines, 30 of which were antimalarial medicines. The laboratories used both Minilab™ and compendial techniques to conduct the testing. The following table depicts the incorporation of collection and testing of samples by branch laboratories as routine activity since 2016. The branch laboratories are planning the next round of sample collection.

Table 1: Number of Samples Collected by Branch Laboratories



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

In the past quarter, PQM conducted a follow-up assessment of Cadilla Pharmaceuticals on the status of corrective and preventive actions (CAPA) after a WHO assessment. On-the-job training was also given to staff in selected areas. During Q2, PQM provided technical assistance to EFMHACA and the Ministry of Industry to categorize existing manufacturers into (1) those requiring only technical support, and (2) those needing both technical and financial support. The categorization was based on the CAPA made by manufacturers following the findings of a second-round GMP compliance status assessment conducted during the previous year. The GMP assessment result on two rounds (2012 and 2016) showed five of seven companies had increased their overall compliance rate with GMP. Similarly, with respect to the GMP compliance level, five out of nine were at Level II of GMP compliance. Overall, there is a clear increase in the level of compliance with current GMP following implementation of the GMP roadmap, thereby contributing to a lower risk of producing poor-quality medicines. Consequently, the impact on improving public health will increase as the risks of producing poor-quality medicines are reduced.

Based on a request received from the Food, Beverage, and Pharmaceutical Development Institute (FBPDI) of the Ministry of Industry, supportive GMP inspection was conducted at Senseng Phramaceuticals and Humanwell, a new manufacturing facility recently inaugurated. The main objective of the audit was to mentor and train FBPDI staff on GMP supportive audit using the facilities of these new pharmaceutical industries. In addition, the manufacturing facilities will benefit from the audit feedback to make corrective actions in compliance to GMP, if necessary.

During Q2, PQM provided technical assistance through reviewing the status of CAPA implementation by Cadilla Pharmaceuticals with respect to WHO findings. WHO has accepted the CAPA submitted by Cadilla and has requested to set a date for the follow-up inspection. The next step will be completing the CAPA implementation and agreeing on the follow-up inspection date.

Based on a request from EFMHACA to coordinate and lead the upcoming large-scale training funded by EFMHACA, PQM developed a full-fledged proposal detailing how the training should be organized at different levels. PQM provided recommendations on training approaches and solicitation of training options, especially for those trainings needing high-level expertise. The proposal was submitted and approved by EFMHACA. In addition, a concept note was developed and submitted to EFMHACA to help facilitate a request for high-level expertise support from WHO for the training-of-trainers training. The concept note and official letter of request were submitted to WHO through the Ministry of Industry, and a response is expected soon. The demand for this training was triggered by the anticipated expansion of pharmaceutical manufacturing industries in Ethiopia and the existing gaps in capacity of GMP inspectors. EFMHACA has already secured the financial resources to cover all trainings. The categories of identified trainings included:

- Professional certification of selected experts through completion of certified online tests
- Specialized training on selected GMP topics to selected experts
- Training-of-trainers training
- Basic GMP training

PQM also provided technical support to EFMHACA on prioritization and evaluation of technical documents from pharmaceutical industries applying to invest in the sector and occupy space at the industrial park that is under construction. PQM is providing support from the perspective of meeting key QA and regulatory requirements. To date, support was provided to evaluate documents of five companies, and feedback was provided to the prospective companies to fulfill other required documents. While PQM provides the technical support, the ultimate decision in concluding the status of the companies with regard to regulatory compliance is made by EFMHACA management.

In addition, PQM contributed in the preparation of exam questions for the evaluation of GMP experts that are expected to participate in the upcoming GMP inspection. This is in line with the requirements of the GMP directive for selection of inspectors, which was developed and approved by EFMHACA in FY 2017 with support from PQM. The questions have been applied by EFMHACA during this quarter. The purpose of this evaluation is to identify competent GMP inspectors who qualify for auditing manufacturing facilities according to the current GMP requirements.

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

PQM continued its technical support to EFMHACA to strengthen and sustain its pharmacovigilance/medicine safety monitoring system. As a routine support activity, supportive supervision of the cohort event monitoring (CEM) on ARV medicines was carried out weekly at 20 health facilities. Support was given to Armauer Hansen Research Institute (AHRI) to revise the protocol and collect the CVs of all those involved in the CEM to present to the National Ethics Committee. PQM also helped in organizing a workshop at AHRI on March 9, 2018. The objectives of the workshop

were to refresh the data collectors; exchange information, experiences, and best practices; evaluate the quality of data collected so far and take corrective actions; orient new data collectors and new health facilities about the CEM project; introduce AHRI as the new implementer of the activity and its collaboration with EFMHACA; and provide the laboratory facility experts with direction on how to provide laboratory services during the data collection.

During Q2, technical assistance was provided in relation to adverse events following immunization (AEFI) and strengthening the overall pharmacovigilance system. PQM staff attended a meeting with the Ministry of Health State Minister, Director of Medicine Registration, Licensing Director, pharmacovigilance team, and Expanded Program for Immunization (EPI) team at the Ministry of Health regarding AEFI reporting flow. Based on the direction given by the State Minister to translate the reporting form into Amharic, Tigrigna, and Oromiffa, the forms were translated, commented on by regional health bureau EPI experts, and finalized. A letter of enforcement of the implementation was prepared and signed by the State Minister, then sent to all regions, along with the translated and printed report forms.

As a result of PQM's efforts to strengthen EFMHACA's PMS, the government was able to use the results of PMS sampling and testing to take regulatory action. Using FY 2017 PMS data, EFMHACA recalled 11 batches of quinine sulfate that was imported by 1 company in India.

Other supported activities included:

- A concept note was prepared on the long-term and short-term strategies to improve the status of the pharmacovigilance system in the country.
- A summary of a product quality defect report of a local manufacturer (EPHARM) was prepared, and a meeting was carried out between the product quality heads, production manager, EFMHACA Deputy Director, and PQM staff to discuss how to alleviate the various product defect problems received from health facilities with EPHARM products.
- PQM provided orientation to 13 students of Addis Ababa University School of Pharmacy regulatory affairs master's program students on pharmacovigilance.
- PQM supported the entry of 202 ADE data items into the pharmacovigilance data monitoring system. EFMHACA received 43 product defects out of the total 202 ADE received during the period. Regulatory measures were taken on two products after conducting further review and analysis.
- PQM supported the sharing of 10 ADE reports with WHO.
- Feedback in the form of acknowledgment letters was prepared and provided to 62 healthcare providers, together with blank reporting forms and newsletters.
- A letter of further sampling was sent on 15 medicines from reporting health facilities to get more details for the evaluations of the product defect causes.

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

In the previous quarter, PQM provided support to improve and develop the regulatory sector's 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.

Previously, EFMHACA requested the development of tools for data collection on key outcome indicators reported by different directorates and branch offices to facilitate data collection and reporting. In support of this request, in Q2 PQM provided technical support in the development of a rapid assessment tool to assess data recording and reporting practices, contexts of M&E systems at different reporting units, available infrastructures, human resources, and budgets to enable implementation of M&E activities. The findings of the rapid assessment will help provide insight on what kinds of approaches need to be used to improve the system and will inform EFMHACA top management about what it takes to implement various options in automation, allowing for an improved decision-making process. The assessment will be conducted next quarter. In addition, PQM provided support to develop terms of reference (TOR) for the Standardized & Automated Project M&E and Balance Score Card (BSC) Plan and Report System for EFMHACA Programs. The overall objective is to develop and implement the Project M&E and BSC Plan and Report System in EFMHACA so that it is supported by IT programs, tools, and systems.

The next step is mapping of indicators, conducting baseline assessments at facilities reporting to EFMHACA, benchmarking other government institutions using BSC on their M&E systems and automated platforms being used, refining the developed TOR, and developing a complete assessment guide.

IV. Key Challenges

As the government proceeds with the active implementation of the National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia, the demand for technical assistance is growing from the Ministry of Industry, EFMHACA, and manufacturing industries. PQM Ethiopia is unable to cope with the emerging needs using existing resources. For PQM to remain relevant and continue to provide high-quality technical support to the Government of Ethiopia, additional budget allocation would be needed.

V. Lessons Learned

The joint supportive supervision and gap assessment conducted at the branch laboratories along with EFMHACA headquarters staff helped in creating a common understanding and sense of urgency on the challenges associated with the lack of some critical equipment at those laboratories. This allowed EFMHACA headquarters staff to own the responsibility and discuss with decision-makers at the higher level, which ultimately led to procurement and distribution of the critically needed equipment (water purifier/distiller and automatic titrator) to four branch laboratories using EFMHACA's own resources.

Ghana

I. Quarter 2 Highlights

In Q2, PQM continued to support the Ghana Food and Drug Administration (GFDA) in PMS of antimalarial medicines. Following the start of sample collection in December 2017, PQM supported GFDA activities to ensure screening and testing of the samples collected. A total of 422 antimalarial medicines and 75 analgesics was collected, but 4 of the antimalarial samples were chloroquine tablets, an oral monotherapy, which were excluded from testing as the product is banned in the country. A regulatory action by GFDA is being planned to ensure removal of this oral monotherapy from the marketplace. Preliminary results from the level 2 screening of the antimalarials indicate that 20 (N=418) samples did not meet quality specifications. The report on this PMS activity is being finalized by GFDA and will be available in Q3.

In collaboration with GFDA, PQM began preparations for the PMS of uterotonics medicines (oxytocin injection and others) in accordance with the approved work plan. To facilitate this surveillance, PQM is working with GFDA to deploy the use of the newly developed risk-based PMS tool (MedRS) in the planning. This activity is expected to be conducted in Q3.

Following the assessments of four local manufacturers of ACTs in Ghana in Q1, PQM completed the confidential reports, which detailed the finding from the assessments, and shared them with each manufacturer in Q2. Based on the GMP compliance observations and readiness to receive PQM support, PQM identified Entrance Pharmaceuticals Limited as the local ACT manufacturer that will continue to receive technical assistance toward WHO PQ for artemether–lumefantrine tablets. Of the four manufacturers, two manufacturers were at different stages of renovation or construction of their manufacturing facilities and are deemed not ready for the proposed PQM support per the expression of interest (EOI). The fourth had GMP observations that require the manufacturer's management commitment and long-term PQM intervention, which PQM is unable to support at this stage due to period of performance limitations. The GFDA Industry Support Unit is, however, expected to follow up with these manufacturers to ensure progress toward GMP improvements in line with the observation in the confidential reports.

In response to the confidential report, Entrance Pharmaceuticals developed a CAPA plan and submitted it to PQM for review. The CAPA plan is in review, and a timeline of activities and support was also prepared.

PQM also participated and presented some of its accomplishments during the USAID Malaria Operational Plan (MOP) meetings.

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 QA and QC systems. Activities have focused on strengthening GFDA's capacity in drug registration, medicines QC, 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 2 Progress by Objective

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

Advocacy with Ghana FDA for country ownership – Develop a sustainability plan to show increase in country contribution to PMS
In Q2, PQM initiated discussions toward development of a sustainability plan that delineates roles and responsibility with an increase in GFDA's contributions for PMS activities. During a meeting in Rockville, MD, the GFDA Laboratory Services Head of Unit informed PQM that GFDA is in the process of developing an overarching business plan that will include sustainability considerations for GFDA laboratory and PMS activities. To avoid duplication of effort, it was agreed that this planned activity can be amended to include that PQM will provide a technical review for the laboratory and PMS sustainability sections within the business plan document under development by GFDA through the assistance from another donor. GFDA will facilitate the sharing of the draft business plan once it is available for PQM review and comments.

Review PMS protocols using risk-based guidelines
As part of implementing a risk-based approach to sampling for PMS activities, PQM provided training to the six staff of the GFDA PMS team on the newly developed PQM *Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries* and the associated MedRS tool. Two GFDA officials also participated in the African Medicines Quality Forum meeting held in Tanzania, where training on this guidance was also provided by PQM, but with funding support from USP.

Ghana is about to implement medicines quality surveillance for MNCH products and envisions the development of a protocol that incorporates some risk-based considerations as outlined in this new guidance. A budget for the upcoming PMS for MNCH products was presented in Q2 and is currently being reviewed by PQM.

Facilitate PMS for antimalarial products in a sustainable manner using a risk-based approach
Minilab™ screening of samples and confirmatory testing were completed in Q2. A total of 422 antimalarial medicines and 75 analgesics were collected, but 4 of the antimalarial samples were chloroquine tablets, an oral monotherapy, which were excluded from testing as the product is banned in the country. The final report, regulatory actions (if any), and the dissemination of results to stakeholders is expected in Q3.

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

Facilitate ISO 17025 accreditation surveillance and maintenance
Preparations for this activity were initiated in Q2. The GFDA QA manager is taking the lead in the implementation of this activity. As a demonstration of technical sustainability, the GFDA laboratory will internally provide all needed trainings and preparations toward this accreditation. Also, as a demonstration of financial sustainability, GFDA has agreed that PQM will only financially support this accreditation activity by contributing 50 percent of the accreditation cost, and GFDA will cover the other 50 percent out of its annual budget. The GFDA laboratory is concluding arrangements for this activity, and the accreditation visit by ANAB is planned for Q3 in April 2018.

Provide basic reagents or supplies to mitigate urgent shortfall and to ensure laboratory accreditation is maintained
GFDA took delivery of consumables procured by PQM that are used in ultra-performance liquid chromatography (UPLC), laboratory equipment used for analytical testing in the physicochemical laboratory. Analytical testing using HPLC or UPLC is a key laboratory accreditation scope that needs to be maintained.

Objective 3 – Strengthen facility inspection capacity of Ghana FDA

Provide training to strengthen capacity of Ghana FDA to perform inspection of local manufacturing facilities for cGMP compliance and in response to gaps identified through GMP roadmap
GFDA GMP inspectors accompanied PQM in a visit to Entrance Pharmaceuticals to discuss and agree on a draft timeline for PQM interventions. The timelines developed were deemed ambitious, as it proposes to have dossiers submitted by January 2019, with the assumption that there are no unforeseen challenges.

GFDA participation in these technical meetings with manufacturers continues to provide GFDA inspectors from the Industry Support Unit a hands-on approach on how PQM engages and provides technical assistance to supported manufacturers.

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

Facilitate multiple technical assistance visits to manufacturing facilities
In Q1, PQM and GFDA inspectors assessed four local manufacturers (Entrance Pharmaceuticals, Amponsah Efah Pharmaceuticals, Phyto-Riker Pharmaceuticals, and Ernest Chemist) for their GMP compliance toward WHO PQ for the manufacture of ACTs. This quarter, PQM completed the confidential reports for each manufacturer, which were shared with the respective manufacturers. Of the four manufacturers, Entrance Pharmaceuticals was selected to continue receiving technical assistance from PQM, in line with the EOI published in August 2017 and the findings from the GMP compliance inspection conducted from October 29 to November 14, 2017. Technical assistance from PQM will help toward improving Entrance Pharmaceuticals' GMP compliance and submission of a dossier to WHO PQ for artemether–lumefantrine, a first-line ACT in Ghana.

Following the confidential report, Entrance has prepared the required CAPAs and submitted them to PQM for review. A timeline for support toward submission of the dossier for WHO PQ was developed and shared with Entrance. During a PQM visit to participate in the MOP meeting, PQM and GFDA inspectors held meetings with Entrance technical staff and management to discuss and address any concerns regarding the timelines. PQM envisages that the agreed-upon timeline, if implemented accordingly, allows Entrance to submit a dossier for artemether–lumefantrine to WHO PQ in January 2019, ahead of the PQM program period of performance end date.

Guinea

I. Quarter 2 Highlights

The following are highlights of activities implemented in Q2:

- Provided technical assistance to the National Commission to identify and prioritize regulatory provisions for the application of the pharmaceutical law. As a result of PQM's support, five presidential decrees supporting the existing pharmaceutical law were developed and submitted for adoption.
- Reviewed the status of the laboratory and made recommendations to the construction company identified to perform renovations of the laboratory.

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 2 Progress by Objective

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

To help advance the pharmaceutical law with key stakeholders, during Q2, PQM organized a workshop in Kindia, Guinea. PQM supported the legal pharmaceutical framework by:

- Identifying, categorizing, and prioritizing regulatory provisions for the application of the draft law.
- Identifying five presidential decrees that will be provided with the law project to the Council of Ministers. These decrees were deemed as most important and of highest priority, as they must be submitted to the Council of Ministers along with the law project document and the explanatory note
- Finalizing the explanatory note that will be used by the Minister of Health to present the draft law to justify the revision of the 1994 Pharmaceutical Law and highlight the amendments made to it when meeting with the Ministerial Council and the National Assembly.
- Providing reference documents needed to establish pharmaceutical law decrees.
- Participating in the elaboration of two pharmaceutical law decrees: one for the Conseil de l'Ordre (Council of Pharmacists) and one for the PCG (the central medical store in Guinea).

Expected outcomes for the activity included:

- Approval and adoption of the draft pharmaceutical law.
- Application and implementation of the law.
- National Directorate of Pharmaceuticals and Medicines (DNPM) capacity reinforced to ensure its preparedness to serve as national regulatory body.
- NQCL capacity sufficiently reinforced to perform critical analysis and QC of medicines to support and complement DNPM's work.

Next steps are listed below; they reflect DNPM's technical assistance request to PQM and are pending USAID's approval:

1. The PQM consultants will continue to assist in the adoption of the law project by providing comments and recommendations to the commission to help advance it through the Council of Ministers and the National Assembly.
2. PQM will support and guide the commission during the review of the law project by the Minister's cabinet.
3. PQM will assist the commission in developing application and implementation texts in preparation for the adoption of the law by the government and National Assembly.
4. PQM will provide assistance to MOH during the Parliamentary discussions in order to support and defend the different key provisions of the law and secure a solid legal basis for implementation of an effective regulatory framework.
5. Immediately after approval by Parliament, an implementation plan will need to be developed and a series of regulations will be required to implement the new law. PQM can assist in the development of a realistic implementation plan, as well as comprehensive and priority regulations, and in the drafting by DNPM of the decrees and other implementation texts.

Objective 2 – Continue strengthening DNPL capacity in product registration

During a technical assistance trip to Guinea on January 8–18, 2018, PQM continued to help strengthen the capacity of the medicines regulatory authority (DNPM) by meeting with representatives from DNPM, the national drug quality control laboratory (LNCQM), MOH, and other key stakeholders to prepare for the official launch of the first-ever PMS program in Guinea. As part of this strengthening, 25 individuals attended a workshop with the following objectives:

- Define the level of responsibility of all key stakeholders of the PMS exercise.
- Discuss and amend the proposed PMS protocol.
- Draft a list of medications targeted for the current PMS program.
- Identify the levels and sites where samples will be taken from.

Expected outcomes for the activity included:

- Promote and protect the health of the population.
- Provide Guinea with a PMS program protocol that will serve as a guide for PMS activities on the ground.
- Institutionalize ongoing surveillance of the quality of medicines to protect the health of the population.
- Establish a system to monitor the quality of medicines (e.g., anti-TB, ARV, and antimalarial medicines) and contraceptives available on the market in Guinea.
- Strengthen local capacity to monitor the quality of medicines.
- Strengthen the medicines regulatory system.

Next steps include:

- Key health programs and partners will identify a focal point for PMS activities.
- Finalize the PMS protocol and have all stakeholders sign and validate the protocol.
- Plan the first official PMS exercise in Guinea.

Objective 3 – Enable DNPL to assume MQM responsibilities

During a technical assistance trip to Guinea in January 2018, the LNCQM director informed PQM the EU project in Guinea has finally granted the MOH funding to renovate the laboratory. Based on the information provided by the laboratory director, PQM met with the company's representatives and other staff from the MOH and discussed some ways of improving the laboratory renovation plan.

Next steps include:

- Continue building the capacity of the LNCQM through procurement of equipment and technical assistance on QA and QC processes and procedures.
- Provide technical and expert advice through an international consultant to ensure that minimum safety requirements and international standards are incorporated into the renovation plan.
- Continue the dialogue with potential partners to secure more financial and technical assistance to LNCQM.

Objective 4 – Strengthen QC capacity of LNCQM

Currently the laboratory is under renovation with support of the European Union. Laboratory activities will be conducted after completion of the renovation of the laboratory by Q4.

Liberia

I. Quarter 2 Highlights

During Q2, PQM staff visited the remodeled temporary laboratory site and provided guidance in terms of layout and partitioning of the physio-chemistry area.

Also during Q2, at the request of the USAID Mission, PQM gave a presentation to the health team, including the Mission Director. The audience was highly satisfied with PQM's work in Liberia and asked PQM to have the Liberia Medicines and Health Products Regulatory Authority (LMHRA) staff a booth at the embassy fair (April 4, 2018). Additionally, PQM met with LMHRA and discussed ways of communicating under the new LMHRA management. LMHRA agreed to designate a focal point while awaiting the reappointment of the former Managing Director or a new Managing Director.

Additionally, PQM received the signed copy of the FAA and initiated the implementation of PMS activities using risk-based PMS.

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, the National Malaria Control Program (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 2 Progress by Objective

Objective 1 – Rebuilding capacity of LMHRA QC laboratory

LMHRA's Quality Control Laboratory was gutted by a fire on May 30, 2017. To assist LMHRA in acquiring more funds to build a new laboratory, PQM helped LMHRA in drafting a concept note, which LMHRA submitted to the Global Fund. The next step is to get MOH's funding contribution for this project before granting the funds to LMHRA. Securing Global Fund resources will help LMHRA build a permanent laboratory. In the meantime, LMHRA rented a site to be used as a temporary laboratory.

PQM provided guidance on the layout and partitioning of the physio-chemistry area of the laboratory that is undergoing restoration. PQM staff have noticed that the temporary laboratory lacks some safety features and requested LMHRA to inform its local contractor.

After restoration of the temporary laboratory is complete, PQM will assist LMHRA with the installation of laboratory equipment procured through the World Bank, training of staff in laboratory safety and data management, and refresher trainings on compendial testing.

Figure 3: Main laboratory room (before)

Figure 4: Main laboratory room (after)

Figure 5: Instrument room (before)

Figure 6: Instrument room (after)

Also during Q2, at the request of the USAID Mission, PQM gave a presentation to the health team, including the Mission Director. The audience was highly satisfied with PQM's work in Liberia and asked PQM to have LMHRA staff a booth at the embassy fair (April 4, 2018). Additionally, PQM met with LMHRA and discussed ways to communicate under the new LMHRA management. LMHRA agreed to designate a focal point while waiting the reappointment of Mr. Sumo as Managing Director or a new Managing Director.

The training on dossier evaluation, originally scheduled for FY 2017, is now scheduled for April 2018 due to the communication issues that PQM experienced recently following the transition of LMHRA management to Human Resources.

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

Activities pertaining to this objective are planned for Q3 and Q4.

Objective 3 – Build LMHRA capacity to take appropriate regulatory actions

Last year, in collaboration with NMCP and PQM, LMHRA conducted the first recall of monotherapies for malaria treatment in Nimba county. The next recall of monotherapies from another county is planned for Q4, and regulatory activities will follow during the testing of samples that will be collected under the FAA.

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

PQM received the signed copy of the FAA and initiated the implementation of PMS activities using risk-based PMS.

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

For this objective, dissemination meetings with take place after implementation of the PMS round under the FAA.

IV. Key Challenges

Several challenges were reported for this quarter:

- Transition of LMHRA management under the new government.
- Lack of decision-making at the LMHRA level due to the new government's decision to transition the management of all agencies, including LMHRA, to the head of Human Resources.
- Sudden departure of PQM's in-country consultant, which delayed implementation of planned activities.
- Slow progress in remodeling the temporarily laboratory.
- Slow progress in securing funds from the Global Fund for the restoring the laboratory.

Mali

I. Quarter 2 Highlights

In Q2, PQM continued to assist the National Laboratory of Health (LNS) in rebuilding its QMS. Two guidelines and 17 SOPs were developed and submitted for adoption. Other highlights of this quarter include the following:

1. Drafted surveillance protocol with elements of a risk-based approach to sampling and testing.
2. Held a training of trainers on the use of handheld Raman spectrometer for the detection of falsified medicines. Trainers have started training other LNS staff members.
3. Conducted a workshop to disseminate results of the assessment of the medicine regulatory system.

The addition of the handheld Raman spectrometer to existing screening tools will allow testing for falsified antimalarials at the point of care. The device can be used to test medicines other than antimalarials without additional cost.

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 to strengthen 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 2 Progress by Objective

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

In this quarter, PQM completed an activity from FY 2017 that related to this objective. In collaboration with the DPM, PQM organized a workshop on February 15, 2018, to disseminate the results of the assessment of the pharmaceutical regulatory system. DPM chaired the workshop and acted with LNS as rapporteurs. The meeting was attended by 33 participants, many of whom provided feedback on the results presented and contributed to the recommendations/action plan of the workshop. DPM finalized the workshop report and submitted it to the Ministry of Health and Public Hygiene. At a follow-up meeting with DPM, it was agreed that PQM should focus immediate support to DPM to strengthen its QA system by developing procedures for medicine registration activities, as well as assist DPM in developing a code of conduct and guide/procedures for transparency, management of conflict of interest, and confidentiality.

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

To continue strengthening pre- and post-market QC capacity of the LNS, PQM delivered a handheld Raman spectrometer (NanoRam) to the laboratory and trained four laboratory staff on its use in the detection of falsified medicines. The training included an overview of Raman spectroscopy and the NanoRam device, as well as hands-on training. The overview part of the training was also open to two pharmacy students who were receiving training in medicines QC at LNS. PQM provided the hands-on training as training of trainers. It included installation of the device software on a computer that LNS procured for the handheld Raman spectrometer, development and testing of methods for antimalarial medicines, and issuing of testing reports. The trainees drafted procedures and instructions for the installation of the software, development of screening methods, and the use of the device to screen medicines. By the fourth day of training, one trained trainer provided training to one additional laboratory staff member. Trained staff were able to develop methods for screening medicines other than antimalarials, including select antibiotics.

PQM continues to support LNS in developing its QMS to meet international standards. Three procedures (procurement of supplies and service, selection and evaluation of suppliers, and management reviews) have been finalized and are awaiting LNS management approval. PQM helped LNS draft 17 SOPs and 2 guideline documents to strengthen laboratory QMS activities.

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

In collaboration with LNS, PQM drafted a protocol, including a detailed budget, for surveillance of antimalarials. Elements of PQM's risk-based approach were included in the protocol, which is currently under review by LNS and DPM. This includes targeted sampling based on historical data. Most of the sampling in the private sector will focus on monotherapies. PQM will seek the adoption of the protocol by LNS and DPM. Sampling and screening is expected to take place in April through May 2018.

Inclusion of the handheld Raman as an additional screening tool will allow rapid detection of falsified oral solid dosage form antimalarial medicines, such as artemether–lumefantrine, sulfadoxine–pyrimethamine, quinine sulfate, and artesunate–amodiaquine. In addition, the device could be used to detect falsified medicines other than antimalarials. The inclusion of such products in medicines surveillance was decided after review of reports on LNS medicines QC activities (pre- and post-market). Some specific products were identified and included in the surveillance protocol.

Objective 4 – Facilitate studies on resistance of antimalarial medicines

The two current FAAs for the University of Sciences, Technology, and Techniques of Bamako have a 1-year performance period of June 2017–May 2018. In Q2, the Laboratory of Applied Molecular Biology, which is executing the technical work of these FAAs, completed milestone 4 of the study on ACTs' efficacy. Milestone 4 for the seasonal malaria chemoprophylaxis study is expected to be completed soon. The last milestone (5) for both studies is for delivering the final reports and is expected to complete on time.

Mozambique

I. Quarter 2 Highlights

This quarter, PQM continued implementation of approved rolled over FY 2017 activities alongside activities in the current FY 2018 work plan. PQM conducted an assessment of the laboratory (LNCQM) using the ISO/IEC 17025:2005 standard checklist. The purpose of the assessment was to provide information to LNCQM on the gaps it has to address as it prepares for ISO 17025 accreditation. The findings were discussed with LNCQM management and staff, and an action plan was developed with timelines to address and implement corrective actions. The resolution of these nonconformities would help the laboratory to achieve GLP and, potentially, ISO accreditation status. Achieving ISO accreditation would ensure the accuracy and reliability of test results and provide an opportunity for LNCQM to access donor funds, such as from the Global Fund, for medicines sample testing.

PQM facilitated a linkage and established a working relationship between LNCQM and the Instituto Nacional de Normalização e Qualidade (INNOQ). PQM recommended they work out an agreement to support calibration of laboratory equipment. INNOQ is ISO certified to calibrate mass, weight, volume, and temperature equipment. Using INNOQ would save funds and ensure sustainability, since LNCQM instruments would cease to depend on external calibration support. PQM also provided support to LNCQM to review and update laboratory QMS SOPs and build the capacity of LNCQM staff on USP and British Pharmacopeia (BP) compendial testing methods for oxytocin and magnesium sulfate injections. Potential solutions to the current laboratory space constraints were identified, and actions have commenced. PQM solicited support and collaboration from the National TB and Malaria programs, WHO, and Global Fund (in country and Geneva) to support the national pharmacy directorate (DNF) and LNCQM activities and gaps.

The oxytocin injection survey conducted in 2017 was expanded this quarter to seven provinces in Mozambique. Magnesium sulfate injection was added to this expanded PMS survey as an additional MNCH medicine. Preliminary results showed that 21 of the 135 samples of oxytocin injection samples collected failed QC tests, while 4 of the 39 samples of magnesium sulfate injection failed quality tests. Samples of the failed medicines will be sent for confirmatory testing to an external laboratory.

In Q2, PQM continued to provide technical support to DNF on regulation development and provided feedback on the TOR for establishment of a committee that will develop the national medicines policy. Also in Q2, MOH implemented a requirement for pre-shipment inspection for all pharmaceutical products imported from India. PQM supported DNF to achieve this important milestone that will enhance the quality of medicines sent to Mozambique from India.

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 pharmacy department (PD). 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. This law transitioned PD to DNF.

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 antimalarial and anti-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 PQM training, LNCQM is better able to collaborate with other Portuguese-speaking countries.

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 2 Progress by Objective

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

PQM technical staff conducted key informant interviews, witnessed test methods, and reviewed key documents for verification. At the end of the assessment, a nonconformity findings report was generated and discussed with LNCQM management and staff, and an action plan was developed. Subsequently, an ISO 17025 accreditation roadmap was developed. Attaining ISO/IEC 17025 accreditation will provide the opportunity for LNCQM to attain international recognition for accurate and reliable testing and paves the way for new income generation, which is key to sustaining laboratory operations. PQM provided technical support to LNCQM to procure, install, and ensure that state-of-the-art analytical instruments needed are available, functional, and qualified. In pursuance of this goal, the PQM team that visited Mozambique in Q2 identified and established a working relationship with INNOQ, a government-owned calibration institute. PQM facilitated the linkage and established a working relationship between LNCQM and INNOQ. PQM recommended they work out an agreement to support calibration of laboratory equipment. INNOQ is ISO certified to provide mass, weight, volume, and temperature equipment calibration. Using INNOQ would save funds and promote sustainability, since LNCQM would cease to depend on external calibration support for much of its equipment.

PQM brainstormed and identified possible solutions for the LNCQM space constraint. At the end of the meeting, two options were agreed upon to explore (1) reprograming a portion of the LNCQM Global Fund grant for procurement of a container office for laboratory staff and (2) exploring the possibility of making available an unused space that belongs to the maintenance department to LNCQM for expansion. The identified space is adjacent to the laboratory entrance and is where old, unused equipment is currently stored. PQM discussed and supported development of justifications for the reprogramming and building of a new structure for the laboratory.

Five male and five female LNCQM staff were trained on compendial testing of oxytocin and magnesium sulfate injections using USP and BP methods.

Objective 2 – Support and strengthen post-marketing surveillance

In Q2, the results of the confirmatory testing of nine oxytocin injection samples that were collected in the first round of PMS and sent to two external laboratories were released. The nine samples passed sterility tests at both laboratories, but three of the samples sent to the Vietnam Institute of Drug Quality Control HCMC failed the assay test, thus confirming the preliminary results of failure obtained.

PQM supported and strengthened PMS by conducting the expanded survey for PMS for oxytocin injection and added another essential MNCH medicine, magnesium sulfate injection. A total of 174 samples (135 ampoules of oxytocin and 39 ampoules of magnesium sulfate) were collected from public and private sector health facilities and distribution/supply outlets in Niassa, Nampula, Tete, Sofala, Gaza, Inhambane, and Maputo city provinces. The selected provinces represent two provinces each from the central, north, and south regions of Mozambique, in addition to the capital city, Maputo city province. PMS staff from all provinces were trained with DNF and LNCQM staff on the sampling protocol, storage, and cold chain transportation of oxytocin injection.

After compendial laboratory testing, 21 of the 135 tested oxytocin injections and 4 of the 39 tested magnesium sulfate samples failed quality tests; confirmatory tests will be conducted by an external laboratory.

Simultaneously, questionnaires were administered to health care providers at facilities during the PMS activities on the use and effectiveness of oxytocin injections; collected data will be analyzed, and generated information will complement the results of the PMS study.

Objective 3 – Provide technical assistance to the Pharmaceutical Department

This quarter, PQM continued to provide technical support to PD, now called DNF, to develop required regulations suited to the new laws. PQM offered valuable technical advice and technical support and shared best practices with DNF on regulation development, medicine registration, and essentials of an MRA that are aligned to global and regional standards for ensuring the quality of medical products in the country.

PQM reviewed and provided technical inputs to the TOR for the committee on the national medicine policy and the GMP and registration regulations. The PQM team shared best practices on what works well and the content of pharmaceutical regulations in Nigeria and Ethiopia. PQM also advocated for inclusion of QC testing costs in the

registration regulation. Upon request, PQM shared information on TruScan™ handheld Raman quality analyzer specification and contact details with DNF for a planned Global Fund tender.

MOH implemented a requirement for pre-shipment inspection for all pharmaceutical products imported from India. PQM supported DNF to achieve this important milestone that will enhance quality of medicines sent to Mozambique from India.

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

No updates this quarter.

IV. Key Challenges

The main challenges faced by LNCQM are a poor work environment as a result of space constraints, poor motivation of staff, and inability to generate any revenue because the laboratory does not meet international standard requirements for GLP. LNCQM depends on PQM for the supply of reference standards, reagents, and supplies; this is a challenge, since LNCQM currently does not collect fees for services rendered. Although PQM has provided recommendations on multiple strategies to access additional funding for LNCQM, it is still up to the country to implement recommendations. Limited funding is available from the government to support LNCQM operations.

Nigeria

I. Quarter 2 Highlights

The PQM program provides technical assistance in partnering countries to strengthen QA systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance helps to build NAFDAC's capacity and QA systems. PQM supports the manufacture of quality-assured priority essential medicines for malaria and MNCH. PQM also provides support to increase the utilization of medical product quality information for decision-making.

Highlights during this quarter included:

1. The accelerated 6 months' stability study for oxytocin and magnesium sulfate injections concluded. All assessed parameters are within specification.
2. The first ever locally manufactured oxytocin and magnesium sulfate injections in Nigeria were approved by NAFDAC.
3. The comprehensive results of reformulated amoxicillin dispersible tablet (DT) (250 mg and 125 mg) analysis received from USP Rockville laboratory were positive. With this positive result, Daily Need will commence NAFDAC's re-approval process as it makes steady progress in becoming the first local manufacturer of quality-assured amoxicillin DT in Nigeria.
4. To increase information available in the public domain related to the manufacture of quality-assured medicines, PQM finalized and made available the publication on Quality Medicines in Maternal Health: Results of Oxytocin, Misoprostol, Magnesium Sulfate and Calcium Gluconate Quality Audits. This publication will help bring to the fore burning issues surrounding the quality of medicines and maternal health.
5. As a result of technical assistance provided by PQM, Emzor Pharmaceuticals completed process validation for sulfadoxine 500 mg + pyrimethamine 25 mg. All assessed results are within specification, which has further yielded interest for procurement from the Medical Export Group.
6. In the context of its continuous efforts to provide technical leadership, PQM made a presentation at a national-level workshop on clinical experiences with the use of oxytocin Injection by healthcare providers in Lagos, Nigeria.

During the coming quarter, PQM will support a third-party audit of the National Institute of Pharmaceutical Research and Development (NIPRD), and renewal of accreditation and scope expansion of NAFDAC Kaduna laboratory. A press conference with high-level stakeholders in maternal health will be organized by a local manufacturer next quarter for the successful production of oxytocin injection in Nigeria.

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 (FMOH), the Pharmacists Council of Nigeria, NIPRD, and the National Malaria Elimination Program. In addition, there are pharmaceutical and nutraceutical manufacturers and other stakeholders whose activities directly impact the system strengthening of NAFDAC and PQM-supported local manufacturers.

III. Quarter 2 Progress by Objective

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

PQM continues to build the capacity of NQCLs to improve laboratory standards through assessments, hands-on training, and proficiency testing. PQM places particular emphasis on strengthening QMS to ensure laboratories can comply with internationally recognized standards, such as ISO/IEC 17025:2005 and/or WHO PQ. This quarter in Nigeria, selected equipment was calibrated by a local calibration body, NQA&CA. Financially, this has proven to be a step in the right direction, as there was as much as a 20-percent reduction in the cost of equipment calibration. Previously, an international calibration body was engaged for equipment calibration, at a higher cost than the local body.

The PQM team organized a training course on Compendia Technique Dissolution, performance verification testing, HPLC, pH measurement and CAPA program for 25 NIPRD laboratory staff. This was a requisite training as the laboratory prepares for accreditation. Pre- and post-tests of participants' understanding attested to the success of the training, as the average score increased from 31 percent in the pre-training tests to 72 percent in the post-test.

NIPRD submitted to PQM a list of basic laboratory supplies and reagents for procurement; following the request, PQM identified local vendors and obtained quotes that would help reduce delivery time and cost. Most of the consumables requested by the laboratory were items essential for the laboratory to operate. Although PQM agreed to procure these supplies, it was communicated to the laboratory that going forward funding for the procurement of these essential consumables should be the laboratory's responsibility. This is in line with PQM's plan to help the laboratory take more ownership of its activities to promote sustainability of its operations and ensuing outcomes. PQM supported NIPRD with payment for the third-party surveillance audit that is expected next quarter. Next steps include conducting a mock audit and continuous provision of offsite and onsite technical assistance ahead of the third-party surveillance audit.

Other activities carried out this quarter included:

- NIPRD conducted an internal review of its QMS system and developed a CAPA plan to resolved identified nonconformances with remote technical assistance from PQM.
- The QA/QC team provided offsite technical assistance on SOP development for the laboratory.

Objective 2 – Strengthen the national quality assurance and regulatory system

In line with efforts to build the capacity of the local regulatory workforce, PQM continues to partner with NAFDAC to provide technical leadership, experience sharing, and professional networking to benefit non-PQM-supported NAFDAC laboratories. This quarter, NAFDAC's Director General approved a list of 48 laboratory staff members for peer–peer quarterly learning support to other NAFDAC laboratories; the accredited QCL Yaba, Agulu, and Kaduna laboratories will support the other three laboratories in Port Harcourt, Calabar, and Maiduguri, with their own staff,

who will be stationed in these laboratories for a period of time. The personnel stationed at the other laboratories will share their experience and SOPs to standardize processes across all NAFDAC laboratories and build the knowledge and skills of their laboratory colleagues. NAFDAC is financing this effort, as part of its commitment to assume ownership and promote sustainability of its activities and processes. During the coming quarter, PQM will proceed with supportive supervision as quality managers of the ISO accredited laboratories lead the learning sessions.

PQM provided technical assistance to NAFDAC's PMS directorate to develop a risk-based testing protocol for PMS of oxytocin injection, misoprostol tablet, amoxicillin DT, amoxicillin powder for suspension, zinc DT, zinc oral rehydration salts co-pack, oral rehydration salts low and high osmolality, gentamycin injection 40 mg, gentamycin Injection 80 mg, chlorhexidine digluconate gel, dextrose 5% antimalarial, and other MNCH products through several consultative meetings with NAFDAC PMS core staff. The leadership of the directorate working with PQM staff reviewed and approved the protocol. During the coming quarter, NAFDAC will proceed with sample collection following PQM guidelines for the risk-based PMS protocol. The results of the PMS exercise are expected to be released during the upcoming quarters for both antimalarial and MNCH products.

In line with ensuring the sustainability of PQM's assistance in the NAFDAC PMS directorate, the PQM QA/QC team worked with NAFDAC management to identify PMS champions as trainers of trainers (PQM's Collaborative Learning Model) for the directorate, and a sampling training session was conducted for the 14 identified PMS champions. The PMS champions will conduct training sessions for 18 sample collectors who residet in the 6 geopolitical zones, and the sampling exercise will be concluded during the coming quarter. Successful execution will require PQM support to train additional PMS staff in the directorate.

During this quarter, a high-level meeting was held with NAFDAC's Director General to discuss the agency's goals and priorities and how they may be aligned with PQM FY 2018 work plan implementation. Key outcomes of the meeting included:

- NAFDAC's planning and research and statistics (PRS) M&E champions will work with PQM to support the drive to have a pharmaceutical M&E plan that institutes procedural mechanisms for data gathering. The plan will enable the agency to improve reporting of its public health impact in the country.
- PQM will support the Director General's new initiative to train NAFDAC staff by other FDAs in Africa on different regulatory functions.
- The NAFDAC laboratory directorate will work with the PQM QA/QC team to help the non-PQM laboratories harmonize QMS documents and work toward accreditation of NAFDAC's vaccine laboratory.
- With three NAFDAC ISO accredited laboratories being added to the list of Global Fund's testing laboratories, it becomes necessary for NAFDAC leadership to get involved at the decision-making level in the Global Fund's Country Coordinating Mechanism (CCM). The CCM is a central pillar of the Global Fund's architecture to ensure coordinated country-driven, multi-sectoral processes for leveraging additional resources to fight AIDS, TB and Malaria. The NAFDAC Director will meet with the Minister of Health to discuss modalities of NAFDAC's inclusion in the CCM.
- NAFDAC management will establish a system by which information on drug quality and regulatory actions are disseminated to the public at more regular intervals.
- PQM will provide technical assistance as NAFDAC management takes the lead in driving efficiency and effectiveness in the agency through stepwise implementation of ISO 9001 in all NAFDAC spheres, as this is a key requirement for regulatory system strengthening.
- NAFDAC will work with PQM to develop a GMP roadmap for the country, building on the GMP assessment completed by the United Nations Industrial Development Organization through funding from the West African Health Organization.
- The Director General will thoroughly review the organizational structure within the registration and regulatory affairs (R&R) and drug evaluation and research (DER) directorates to clearly define roles and responsibilities on dossier review, in order to avoid overlap of functions.

The meeting with the NAFDAC Director General indicated strong commitment to continue to work with PQM to implement activities using a stepwise approach as outlined in the recommendations of the NAFDAC gap assessment conducted by PQM in FY 2017. In the coming quarter, review of the organizational structures within the R&R and DER directorates, as well as training on dossier review, are expected to be completed.

PQM continued to provide technical leadership and made presentations at a national-level workshop themed "Oxytocin Injection Quality Audit: Results from the Clinical Experience Study." The workshop came out of the PMS results of critical MNCH products in the country, which revealed that more than 70 percent of oxytocin samples

analyzed at NAFDAC's ISO accredited laboratories failed QC tests. Oxytocin injection is used to begin or improve contractions during labor and reduce bleeding after childbirth.

Subsequent to the findings, PQM funded researchers at the Lagos University Teaching Hospital to study whether there is any correlation between the PMS results and clinical experiences of healthcare providers in Lagos state in the use of oxytocin for postpartum hemorrhage treatment.

In line with the dissemination of the findings, different key players gathered in Lagos to discuss the results of the findings. Key participating players included the Commissioner of Health of Lagos state, Dr. Jide Idris, who was represented by the Director of Pharmaceutical Services Ministry of Health Lagos State, Dr. Moyosore Adejumo; Frank Osato Giwa-Osagie, Emeritus and Distinguished Professor of Obstetrics and Gynecology with the Lagos University Teaching Hospital; and Prof. Oluwarotimi Ireti Akinola, representing the Society of Gynecology and Obstetrics of Nigeria. Other attendees included representatives of the National Association of Nigeria Nurses and Midwives, Lagos State Primary Healthcare Board, FMOH, Association of General Private Medical Practitioners of Nigeria, United Nations Population Fund, and Merck Sharp and Dohme Corporation (MSD for Mothers) of Geneva. NAFDAC's Director General, Prof. Mojisola Christianah Adeyeye, commended PQM and USP in the steps they are taking to ensure the distribution of quality medicines across the country. PQM made presentations at a webinar session themed "Quality Oxytocin: Nigeria" organized by the Maternal Health Supplies Caucus. The combination of both presentations on results from the clinical experience study and the clinical experiences of healthcare providers in Lagos state on the use of oxytocin for treatment of postpartum hemorrhage nicely connects the impact of PMS of medicines to the patients and healthcare providers.

Results of PMS conducted during FY 2017 Q4, with PQM support, showed that two samples of quinine sulfate tablet, eight samples of artemether–lumefantrine tablet, one sample of sulfadoxine–pyrimethamine tablet, two samples of other antimalarial brands, and one sample of artemether–amodiaquine tablet failed QC tests. In total, 14 of 741 samples (1.9%) of antimalarial medicines collected from 6 sampling sites failed QC tests. In the coming quarter, NAFDAC is expected to take immediate regulatory action to recall the failed samples, thereby preventing further distribution/circulation and the negative consequences on public health associated with the use of these products. This information will be shared at the pre-malaria operational plan meeting planned for April 2018 in Abuja.

PQM conducted a mock audit of NAFDAC Kaduna laboratory with the aim of identifying deficiencies and opportunities for improvement in preparation for the ISO/IEC 17025:2005 reaccreditation and expansion of test methods. Findings from the mock audit include few minor nonconformances for the laboratory. The team witnessed seven compendia testing methods demonstrated by laboratory staff. The PQM team provided technical assistance to the laboratory to address the audit findings. Next steps after the mock audit include a third-party audit of the laboratory, which is scheduled during the next quarter.

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

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 attain current GMP and improve compliance with WHO standards, helping them to develop and submit dossiers for certification by the WHO PQ program. PQM also provides technical assistance and guidance to manufacturers for the local production of medicines, which may decrease reliance on international donations and help establish a sustainable local supply with national resources. As part of building the capacity of local manufacturers, PQM provided technical support to eight local manufacturers in Q2. Major progress was achieved with the registration of the first locally manufactured oxytocin injection in Nigeria by PQM-supported Juhel Pharmaceuticals, as well as technology transfer to the new facility built by Emzor Pharmaceuticals for the making of quality-assured sulfadoxine–pyrimethamine (500 + 25 mg), whose required accelerated study has been completed.

Last quarter, the PQM GMP team conducted an audit of Emzor Pharmaceuticals' process for manufacturing sulfadoxine–pyrimethamine (500 + 25 mg). A few observations were made during the audit, and technical assistance was provided by the PQM GMP team to institute CAPAs to address the noted observations. This quarter, the GMP team received an updated CAPA report from Emzor Pharmaceuticals. The team conducted a verification visit to ascertain the effectiveness of closed CAPA. The outcome of the verification visit indicated that 95 percent of CAPA were resolved and the Emzor Richfield facility is operating at acceptable current GMP, compliant with WHO GMP standards. The team also provided hands-on support to review and execute the process validation protocol for three consecutive batches of Maldox brand® (sulfadoxine + pyrimethamine 500 + 25 mg) tablets. The process validation was completed, and results were within acceptable criteria.

During Q2, USAID's funded Global Health Supply Chain–Partnership Supply Chain Management (GHSC-PSM) program, implemented by Chemonics International, conducted formative research on the market availability of locally manufactured health commodities, local wholesalers of health commodities, and authorized local distributors of health commodities in Nigeria. PQM facilitated a meeting of PQM-supported local manufacturers and GHSC-PSM with the objective of developing a roadmap to increase local procurement that meets GHSC-PSM procurement requirements. GHSC-PSM shared with PQM-supported local manufacturers an analysis of products prioritized based on programmatic requirements that included impact on morbidity and mortality reduction. PQM-supported local manufacturers expressed their willingness to meet the requirements; however, concerns such as return on investment was shared with GHSC-PSM, as the process involves very large financial investment decisions. GHSC-PSM issued an EOI for the supply of quality-assured priority medicines to May & Baker Nigeria Pharmaceuticals, Emzor Pharmaceuticals, Drugfield Pharmaceuticals, Chi Pharmaceuticals, Tuyil Pharmaceuticals, Daily Need Industries, Pharmatex Industries, Juhel Pharmaceuticals, and Nemel Pharmaceuticals; all of these companies responded with EOI submissions. In the coming quarter, the PQM GMP team will follow up on the results of the EOI submissions and provide technical assistance on identified deficiencies as a result of the EOI submissions. PQM will also continue to collaborate with GHSC-PSM to identify ways in which local procurement of commodities can be further scaled up within the pharmaceutical sector in Nigeria. This activity is in line with PQM Nigeria's strategy to increase the procurement of locally manufactured products.

In 2016, PQM commenced intense technical assistance to Juhel Pharmaceuticals for the local production of oxytocin and magnesium sulfate injections. This quarter, NAFDAC issued market authorization approval to Juhel Pharmaceuticals for locally produced oxytocin injections and magnesium sulfate injections. This makes Juhel Pharmaceuticals the first local manufacturer of oxytocin and magnesium sulfate injections in sub-Saharan Africa, which is a result of technical assistance provided by PQM program. This achievement will increase the availability of quality-assured oxytocin and magnesium sulfate injections, which will have a positive impact on the reduction of maternal deaths related to postpartum hemorrhage and preeclampsia in the continent. In the coming quarter, a local manufacturer—Juhel Pharmaceuticals—will organize a press conference on preventing maternal deaths with quality-assured oxytocin and magnesium sulfate. The aim of the press event is to disseminate widely information about Nigeria's achievement in approving locally produced oxytocin and magnesium sulfate injections, which will increase access to lifesaving medicines for the Nigerian population.

Having a local manufacturer that maintains cold chain for oxytocin down at distribution centers, closer to the last mile of the supply chain, will greatly reduce the risk of degradation due to poor storage and promote better patient outcomes when administered to pregnant women. PQM facilitated a meeting of FMOH's Director of Food and Drug directorate with key members of the Pharmaceutical Manufacturers Group of the Manufacturers Association of Nigeria (PMG-MAN). The objective was to create a forum for the new Director to meet with key PMG-MAN members and discuss opportunities for growth by the pharmaceutical sector in Nigeria. These growth opportunities were hinged on a three-point agenda:

1. Protection of the pharmaceutical industry.
2. Procurement from the industry.
3. Timely payment for procured medicines.

The key outcomes of the meeting included:

- The Director pledged support for the industry and urged PMG-MAN to articulate its position on issues that affect the pharmaceutical manufacturing sector.
- Through the Director of Food and Drug directorate and NAFDAC, PMG-MAN will share with FMOH proposals for policy initiation and implementation in favor of the pharmaceutical sector in Nigeria.

PMG-MAN appreciated PQM Nigeria leadership for creating a platform with the Director of Food and Drug directorate, FMOH remarking that his accessibility was very impressive and signals a new and progressive era for the pharmaceutical industry in Nigeria.

The PQM GMP team conducted a follow-up visit to the management of May & Baker to discuss the status of the public–private partnership with the Federal Government of Nigeria through FMOH on vaccine manufacturing in Nigeria. The CEO made presentations on the extent of completion of the business plan; however, he requested technical assistance in vaccine research and development and on the review of the project plan. In the coming quarter, PQM will develop a roadmap for tailored assistance in research and development.

Other activities carried out this quarter included:

- PQM continued providing technical assistance to Daily Need Industry on reformulated amoxicillin DT 250 and 125 mg. Process validation is expected to commence in the coming quarter.
- PQM reviewed both the stability report and the product development roadmap for chlorhexidine gel by Tuyil Pharmaceuticals. Process validation expected to commence in the coming quarter.
- PQM continued to provide technical assistance to Drugfield Pharmaceuticals on compilation of dossier in compliance with WHO Common Technical Document format.
- PQM followed up with Chi Pharmaceuticals to prepare for the WHO re-inspection visit scheduled for next quarter.
- PQM provided technical assistance to Danadams-Bakai on remodeling of the manufacturing facility, as well as procurement criteria for HVAC and other production equipment.
- PQM provided technical guidance in the review of a memorandum of understanding for technology transfer to a new facility for the production of ready-to-use therapeutic food by Emzor Pharmaceuticals.
- The PQM GMP team held a meeting with the CEO and technical team of Pharmatex Pharmaceuticals. The CEO expressed strong commitment and appreciation for the technical assistance from PQM. He requested for tailored technical assistance in product development of artemether–lumefantrine and laboratory training for analytical method development. Next steps include developing, implementing, and monitoring milestones of tailored technical assistance to the local manufacturer.

Objective 4 – Strengthen human capacity of academia

In FY 2017, PQM provided support in the development of a pharmaceutical quality assurance system (PQS) curriculum for the undergraduate, graduate, and post-graduate studies in QA for faculties of pharmacy in Nigeria. In Q1, PQM initiated processes for pilot-phased implementation of the PQS curriculum through module teaching and tailored mentoring support that also allows the participation of lecturers from Schools of Pharmacy in selected Nigerian universities. These teaching modules will help build the capacity of faculties of Schools of Pharmacy, which will ultimately use the same module to teach the courses themselves. This will contribute toward a sustainable pipeline of skilled professionals for the pharmaceutical sector in Nigeria.

In line with efforts to build a pipeline of capable professionals, PQM commenced a partnership with the Faculty of Pharmacy, Nnamdi Azikwe University Awka, to provide technical leadership, experience sharing, and professional networking to benefit both lecturers and students at the university. This quarter, PQM facilitated a 4-day workshop on the PQS curriculum for 25 academic staff. Topics covered during the workshop included compilation of a dossier in compliance with WHO Common Technical Document format; overview of GMP, including premises, personnel, good practices in production and QC; good documentation practices; PQS–WHO/ICH approach; and the WHO PQ of medicines program. The Dean of the faculty expressed appreciation to PQM Nigeria for the laudable initiative that impacts positively on the country's educational system. Support was requested in the following areas:

- Teaching materials.
- Mentorship for smooth implementation of the new PQS curriculum.
- Experiential learning.
- Reference Standard and USP National Formulary.
- ISO accreditation of the faculty laboratory.

In the coming quarter, PQM Nigeria will provide teaching materials and a current USP National Formulary available within the program, and develop a roadmap for mentoring and experiential learning for the lecturers. PQM Nigeria's Chief of Party made a follow-up visit to the National Universities Commission to discuss the implementation of the PQS curriculum. The outcome of the meeting included a plan to organize a Deans' forum for the purpose of sensitizing all deans of pharmacy schools in Nigeria to adopt the PQS curriculum in their respective schools.

IV. Lessons Learned

PQM's representation at national forums, workshops, and meetings helped promote 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.

Senegal

I. Quarter 2 Highlights

During this quarter, PQM continued to support LNCM in building its capacity toward ISO 17025 accreditation and/or WHO PQ. To that end, PQM contracted with Zef-Sci, a company specializing in qualification, to conduct the following activities: qualification of HPLC systems and detectors (e.g., ultraviolet (UV) fluorescence, electrochemical); qualification of HPLC systems and detectors (operational qualification (OQ)/performance qualification (PQ)); and perform qualification for UV fluorescence, infrared (IR), conductivity, electrochemical, or diode array detector (DAD). The activities took place the last week of March 2018 at LNCM. In parallel to this activity, PQM started the implementation of the laboratory maintenance contract.

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.

III. Quarter 2 Progress by Objective

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

During this quarter, PQM continued to support LNCM in its efforts to attain ISO 17025 accreditation. To that end, PQM contracted Zef-Sci, a company specializing in qualification, to conduct the following activities: qualification of HPLC systems and detectors (e.g., UV fluorescence, electrochemical, etc.); qualification of HPLC systems and detectors (OQ/PV); and qualification for UV fluorescence, IR, conductivity, electrochemical or DAD. These activities were conducted during the last week of March 2018 at LNCM. Zef-Sci will share with PQM and LNCM a detailed technical report in April 2018. In parallel to this activity, PQM started the implementation of the laboratory maintenance contract. A PQM consultant will execute the first work order of this contract in May–June 2018. Additionally, PQM is working on supplies logistics needed to support the calibration of the metrology department. The calibration activities will be conducted by PQM staff during Q3. Having the laboratory equipment operational,

calibrated, and qualified will help the laboratory to conduct tests on the quality of medicines according to international medicines standards and will move forward the agenda of the ISO 17025 accreditation.

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

During Q2, PQM submitted the entire FAA package required for PMS implementation by LNCM to USAID-HQ for review and approval.

Objective 3 – Support DPM in improving its regulatory functions

No updates for this quarter.

West Bank and Gaza

I. Quarter 2 Highlights

To strengthen the capacity of the General Directorate of Pharmacy (GDP) and the Central Public Health Laboratory (CPHL), PQM conducted a 2-week assessment of the GDP using the Global Benchmarking Tool (GBT) and a 2-week assessment of CPHL's QA/QC systems using PQM's stepwise accreditation transaction and training (SATTA) tool. A detailed report on each assessment will be shared with the CPHL and GDP directors by early April. PQM is putting together an action plan to address the findings of both assessments, and trip by four PQM staff members is planned for mid-April 2018.

II. Country Context

PQM has provided technical assistance in the areas of QA and QC, regulatory systems support, and current GMP. In 2015, the PQM program conducted an assessment of manufacturing services in the Palestinian Territory of West Bank and Nablus. However, due to continuing uncertainly in the regional over a period, the PQM program could not undertake additional activities in that area for more than 2 years. In FY 2017, the USAID Mission in Israel, with responsibility for West Bank programming, provided funding for PQM to initiate activities in the West Bank. The focus trip builds on past PQM efforts to provide a comprehensive system approach in building the capacity of the regulatory agency to protect the lives of its people.

III. Quarter 2 Progress by Objective

Objective 1 – Strengthening the General Directorate of Pharmacy's organizational structure and regulatory functions

To strengthen GDP and CPHL capacity, PQM conducted an assessment of the GDP using the GBT and an assessment of CPHL's QA/QC systems using PQM's SATTA tool. The GBT was developed by WHO in collaboration with USP to identify the maturity level of the regulatory authorities globally. The GBT contains 8 sections (from 1 to 8; see below) and PQM added four sections (9 to 12; see below) with a total of 300 questions.

During Q2, PQM used the GBT questionnaire to evaluate GDP activities for each section of the GDP:

- 1 – Regulation System
- 2 – Registration and Market Authorization
- 3 – Vigilance
- 4 – Market Surveillance and Control
- 5 – Licensing Establishments
- 6 – Regulatory Inspection
- 7 – Laboratory Access and Testing
- 8 – Clinical Trials Oversight
- 9 – Control of Drug Promotion and Advertising
- 10 – Control of Narcotics, Psychotropic Substances and Precursors
- 11 – Registration Pharmacy Personnel
- 12 – International Cooperation and Harmonization.

The SATTA was used assess different aspects of the QMS and the technical capacity of CPHL staff according to ISO 17025 accreditation. Attaining this accreditation attests to the laboratory's capacity to assure the quality of medicines reliably and acceptance of the results globally.

During Q2, PQM conducted a 1-week assessment of CPHL using SATTA, which provided detailed information on the processes and technical systems of the laboratory according to ISO 17025 requirements. This assessment entailed the following two steps: (1) assessment of CPHL's existing management and QA system, and (2) evaluation of the laboratory personnel's capacity/skills through method observations and interviews. The 2-week assessment of GDP activities in the Ramallah and Nablus offices was conducted (as mentioned previously) using the GBT questionnaires. The questions were directed to designated responsible staff for each GBT section. The answers are validated at two levels: (1) examination of the related law/guidelines/SOPs, and (2) validation in the field through operators. The main outcomes of the assessment were provided to key stakeholders (e.g., CPHL, GDP, MOH, and USAID).

A detailed report on each assessment will be shared with the CPHL and GDP directors by early April. PQM is putting together an action plan to address the findings of both assessments, and trip by four PQM staff members is planned for mid-April 2018.

Objective 2 – Strengthen the regulatory capacity of the General Directorate of Pharmacy, MOH Palestinian Authority (PA) for improved control and management of pharmaceuticals including but not limited to registration and inspection

Nothing to report this quarter.

Objective 3 – Raise the technical capacity of the General Directorate of Pharmacy, MOH PA to apply to become a member of the regional pharmaceuticals schemes such as the PIC/S and/or to WHO regional initiatives

Nothing to report this quarter.

Objective 4 – Provide direct support to national quality control laboratory (CPHL) toward achieving QMS leading to international ISO/IEC 17025:2005 accreditation and/or WHO PQ of the laboratory

Nothing to report this quarter.

Objective 5 – Provide support to local pharmaceutical manufacturers by supporting compliance with PIC/S

Nothing to report this quarter.

Angola: The project closeout report was submitted to the Mission in Q1, and the Mission acknowledged receipt in Q2.

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

Asia

Bangladesh

I. Quarter 2 Highlights

PQM's activities during FY 2018 Q2 were focused on the implementation of objectives 1, 2, 3, and 4 in the approved work plan and remaining activities of the FY 2017 work plan. Q2 highlights include the following:

- In January, along with WHO and SIAPS, PQM provided support to develop a training plan for the National Control Laboratory (NCL) and the Directorate General of Drug Administration (DGDA) to address the agency's training needs. The plan was approved by the Director General of DGDA and implementation has begun.
- On January 27–31, to strengthen the MRA's PMS system, PQM provided six Global Pharma Health Foundation (GPHF) Minilab™ kits; 13 staff (3 DGDA inspector staff, 7 laboratory staff, and 3 local PQM staff) completed a training of trainers on screening technique through using Minilab™.
- On February 19, DGDA and PQM jointly organized a "Consultative Workshop To Establish National QA/QC Policy for Quality-Assured Medical Products" at the BRAC Center Inn in Dhaka. A core working committee will be formed to develop draft policy document.
- On December 26–27, 2017, PQM conducted a GMP gap assessment at Advanced Chemical Industries Limited (ACI). This was a follow-up assessment at ACI's Narayanganj manufacturing site as part of PQM technical support for CHX gluconate 7.1% solution for umbilical cord care. The purpose of the inspection was to evaluate the manufacturing operations of ACI against the current GMP compliance for CHX gluconate 7.1%. The final assessment and CAPA reports were submitted to ACI on February 13.
- On March 20–22, PQM successfully conducted a 3-day workshop facilitated by PQM Rockville staff, focusing on sampling and testing protocol for strengthening DGDA's risk-based PMS function and capability. As a next step, DGDA agreed to take the lead to develop a risk-based PMS guidance document to establish effective PMS and assure the quality of medicines.
- PQM staff assisted in developing SOPs and key documents and in CAPA implementation. In Q2, 15 SOPs relevant to laboratory processes and instructions for analytical instruments were implemented; 10 CAPAs were closed based on internal and PQM observations by NCL toward achieving compliance with international standards (e.g., ISO 17025:2017).
- NCL staff were trained on five key operational areas of laboratory by Rockville and local experts in four hands-on and theoretical trainings.
- PQM successfully conducted a gap assessment of existing pharmacy undergraduate curricula of 21 of 39 universities. The purpose was to evaluate the coverage of the regulatory functions in the current syllabi. A draft assessment report was submitted by PQM with recommendations for curricular changes. PQM plans to consult with the Pharmacy Council and relevant stakeholders about these recommendations before getting the universities to adopt and implement the new curricula. The ultimate aim is to ensure future pharmacy graduates are adequately equipped and competent in the regulatory affairs space to meet workplace needs.
- During January 21–February 2, PQM arranged a training program on "Strengthening Capacity to Perform QC for Medicines by Developing Calibration, Screening & Compendial Testing Skills." PQM conducted a hands-on training on calibration activities of Karl Fischer titrator, balance, ultraviolet spectrophotometer, disintegration tester, FTIR, and HPLC. After the extensive training, NCL staff were able to perform equipment calibration by themselves.
- PQM Bangladesh staff visited the laboratory eight times this quarter with the laboratory supervision team to identify gaps and noncompliance with standard practices. During these visits, PQM provided support to laboratory staff to instantly resolve gaps and improve their practices.

II. Country Context

PQM's goal in Bangladesh is to strengthen 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 2 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 17025:2017 accreditation or WHO PQ

In terms of laboratory capacity building, PQM has been providing technical guidance to NCL to strengthen its QMS toward achieving ISO 17025:2017 accreditation.

In Q2, NCL management and technical staff worked alongside PQM to follow up on its CAPA from the internal and PQM audits. Ongoing support has been provided to close those CAPA items.

PQM worked closely with NCL to develop and review critical SOPs to improve work processes, QC, and proper instrument usage throughout its life cycle. With the assistance of PQM technical staff in Bangladesh, NCL staff have developed SOPs to strengthen laboratory functions.

In collaboration with WHO, SIAPS, and PQM, DGDA developed its training plan. Through the training needs assessment, PQM provided support to develop the training plan for NCL and DGDA. In January 2018, the plan was approved by DGDA and incorporated into DGDA's 5-year Strategic Training Plan.

PQM Bangladesh technical staff also conducted several trainings with NCL staff to enhance their knowledge and skill toward achieving ISO 17025:2017 accreditation.

PQM HQ staff visited NCL during January 21–February 2, 2018, covering the following activities:

- Shared the overview of general laboratory principles, uniformity of dosage units, and harmonized requirements as described in USP on Weights and Balances, and the proper use of pharmacopeias (e.g., USP, BP, Indian Pharmacopeia) toward achieving ISO 17025:2017 accreditation.
- Strengthened the capacity to perform QC of medicines by developing a calibration and qualification program for laboratory equipment along with appropriate recommendations to NCL for implementing this program. Conducted on-the-job training on good practices for calibration and qualification information <1058> from USP 40.
- Conducted hands-on training on calibration/qualification of the balances, pH, disintegration, HPLC, and FTIR instruments of the laboratory to develop the capacity of NCL staff. In addition, a new metrology team was formed to lead the instrumental support program. PQM staff will continue to work with NCL's new metrology team to sustain their equipment qualification and calibration activities.
- Provided support in the use of dissolution, UV, Karl Fischer, and performance verification testing for QC of medicines to increase the capacity of NCL staff to comply with international standards
- Conducted a training of trainers on screening technique through using the GPHF Minilab™ kit. DGDA inspectors, NCL analysts, and PQM staff successfully completed the training.

Summary of Laboratory Progress from January 1 to March 30, 2018

PQM staff assisted in developing SOPs, key documents, and CAPA implementation

Items	Number of Items completed
Approved and implemented SOPs through PQM review	15
CAPA status in FY 2018 Q2:	
CAPA generated during Q2 (Jan to Mar-2018) based on the observations by PQM audit (46)	Completed: 5 addressed in Q2 Pending: 41 CAPA items to be followed up
Total remaining CAPA up to December-2017:	
CAPA by PQM (2017) (24)	Completed: 19 (2 in Q2) Pending: 5 in process
CAPA by NCL Internal Audit – March 2017 (28)	Completed: 21 (2 in Q2) Pending: 7 to be followed up
CAPA by NCL Internal Audit - June 2017 (26)	Completed: 19 (1 in Q2) Pending: 7 being followed up

Items	Number of Items completed
Key documents developed during Q2 (3)	1. Authorization Letter for performing Calibration 2. Approved Risk-based Testing Protocol 3. Approved Training Plan

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

As part of continuous support, PQM Bangladesh staff conducted a full GMP inspection on December 26–27, 2017, at ACI limited in addition to assessing the implementation of the earlier CAPA plan created by ACI resulting from the PQM inspections held in December 2014 and May 2015. The CAPA plan was generated in relation to manufacturing activities of CHX digluconate 7.1% solution. With PQM's help, ACI appeared to have successfully implemented most of the CAPA plan reported, especially installation of an automated filling line and deployment of a plugging and capping machine instead of a semiauto machine. ACI should be further commended for performing extensive installation qualification (IQ), OQ, and PQ activities with proper documentation for the equipment, including the manufacturing of three validation batches, followed by ongoing stability studies. In addition, some observations regarding the chlorhexidine manufacturing area and manufacturing approach were made in this visit with no critical observations.

On February 25, a meeting was organized by Newborn Health Program & IMCI, Director General of Health Services (DGHS) at the Integrated Management of Childhood Illnesses (IMCI) Conference in EPI Bhaban, Mohakhali, Dhaka. Representatives from the National Neonatal Health Program, UNICEF, USAID, PQM, and Saving Newborn Lives were present. The meeting focused on GMP approval of 7.1% CHX, among other issues. The Deputy Director of Country and Core Programs joined the meeting through Skype and shared valuable information about GMP approval of CHX. ACI expressed its interest and progress in the production of quality-assured CHX; UNICEF is to review the issue of procurement.

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 in strategic planning, human resources, international standards, and improved PMS.

In March, PQM successfully conducted a 3-day workshop on risk-based PMS to develop a sampling and testing protocol for strengthening DGDA's PMS. A PQM Rockville staff member supported the workshop as a resource person. The strengths and weaknesses of current DGDA PMS strategies were identified and mapped for the medicine supply chain in Bangladesh. The group work also identified and prioritized QA risks. An initial draft of a sampling and testing protocol incorporating risk-based approaches was developed. DGDA will take the lead in developing a risk-based PMS guidance document to establish effective PMS and assure the quality of medicines.

PQM completed a gap assessment of the existing pharmacy undergraduate curricula of 21 of 39 universities. The purpose was to assess the presence and status of regulatory functions in the undergraduate syllabi. A draft assessment report is being reviewed and finalized with recommendations for the universities to introduce curricular changes in collaboration with Pharmacy Council, pharmacy and industry associations, DGDA, and universities. This exercise aims to ensure universities will improve their curricula so that future graduates will have the competencies for work in DGDA and relevant pharmaceutical industries. This demands higher attention in Bangladesh because the pharmaceutical sector is growing and pharmacists will bear greater responsibility for supplying quality-assured medicines and medical products.

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

On February 19, Bangladesh DGDA and PQM jointly organized a "Consultative Workshop to Establish a National QA/QC Policy (NQAP) for Quality-Assured Medical Products" at the BRAC Center Inn in Dhaka. The objectives of the workshop were to provide clear policy directions to the public and private health care sectors and professionals regarding quality of medicines and medical products, assist in procurement of quality-assured medicines and medical products, and support implementation of National Drug Policy 2016 in relation to medicines quality issues. The workshop brought together 54 leaders, experts, and participants from various government and nongovernmental agencies, including DGDA, DGHS, Directorate General of Family Planning, Central Medical Stores Depot, NCL,

National TB Program, MNCH, international development partners (e.g., USAID, WHO, UNICEF, Management Sciences for Health, Challenge TB Bangladesh Project, Save the Children, Essential Drugs Company Limited, Consumers Association of Bangladesh, Pharmacy Council of Bangladesh, Pharmacy Department of Dhaka University, Bangabandhu Sheikh Mujib Medical University, Bangladesh Association of Pharmaceutical Industries, Regulatory Society Bangladesh, Bangladesh Chemist & Druggist Samity), and PQM representatives from Dhaka and the United States. Following the workshop, a core working committee has been formed to draft and develop the National QA/QC Policy document.

IV. Key Challenges

Operational Challenges:

- Registration process for local entity has taken longer than anticipated, hence limiting the seamless operations of the PQM field office.
- Transition of key positions (Director General-DGDA, Director-NCL, and Director-National TB Program).
- Parliament election in December 2018 may hamper project implementation to meet the project goals and objectives (e.g., ISO, WHO PQ).
- Acute scarcity of DGDA and NCL staff for effective laboratory operations will affect efforts toward achieving ISO 17025 or WHO PQ.
- During the planning process for FY 2018, PQM considered the utilization of Government of Bangladesh resources along with USAID-provided support. If government resources do not materialize as hoped for, it could have significant negative impact of the project.
- The SIAPS program was officially closed on March 22, 2018. PQM may need discussion with the USAID local mission to review PQM collaborative activities with SIAPS.

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 are 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 the MRA, NCL, and essential medicines manufacturers to ensure sustainability toward achieving international standards for the long-term public health benefits.

Burma

I. Quarter 2 Highlights

In FY 2018 Q2, the Department of Food and Drug Administration (DFDA) laboratory tested samples from external clients such as Defeat Malaria and it was sought to test insecticide-treated nets. To extend the laboratory's capability to test these items, PQM trained 14 laboratory staff on HPLC and gas chromatography methods for testing deltamethrin long-lasting insecticidal nets (LLINs). Fourteen laboratory staff members (all females) received the training. The DFDA laboratory is expected to receive LLINs samples from Vector Works for testing.

PQM was invited to present on the risk-based PMS approach in Yangon and Nay Pyi Taw as part of DFDA activities. At the DFDA, the presentation was mostly given to inspectors. PQM also organized a risk-based PMS workshop. Thirty-six participants from DFDA regional and state offices as well as staff from the DFDA laboratory attended the workshop.

PQM participated the MOP meeting, where data from LLIN training were presented. PQM also reported on the current PQM work plan activities to the Mission.

PQM participated in the Research Paper Reading Sessions and Symposia of the 46th Myanmar Health Research Congress and presented on the role of the national laboratory in the country's PMS.

Lastly, PQM conducted a supportive supervisory visit to the DFDA Mon State Laboratory with DFDA management to identify gaps in infrastructure, technical expertise, and human resources and to provide recommendations for addressing the gaps.

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 fight against 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 and technical assistance to DFDA are timely and 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. DFDA 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 to tailor technical assistance to specific areas of need. PQM's technical assistance to build DFDA's capacity will result in increased availability of quality-assured medicines in the country. This is expected to contribute toward achieving the NMCP's objectives of malaria elimination by 2030.

III. Quarter 2 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 feedback on the proposed new fee structure for DFDA laboratory services. The new proposed fees are currently under review at Burma's DFDA.

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

PQM delivered two capacity-building trainings on deltamethrin LLIN by using HPLC and gas chromatography. The trainees of the Pharmaceutical Chemistry Laboratory, Nay Pyi Taw, DFDA Myanmar received classroom training on:

- HPLC
- Basic principles of gas chromatography

The classroom lectures were followed by hands-on training on:

- Deltamethrin assay by HPLC
- Deltamethrin assay by gas chromatography

The gas chromatography method was a published method and was used only for training purposes. The HPLC method is a Collaborative International Pesticides Analytical Council (CIPAC) method, and it is accepted both by WHO and Vector Works. Indeed, the HPLC method was received from Vector Works for PQM to do the analysis. These two trainings were considered to be unique and specific, since it was the first time the analysis of mosquito nets was carried out in this laboratory. Because it is a new activity for the laboratory, few DFDA analysts were selected to participate in the hands-on part of the HPLC training: 24 participants attended the 1-day theoretical training, and 6 participants completed the training with a 4-day hands-on training. For gas chromatography, 24 participants attended the 1-day classroom theoretical training, and 7 participants completed the 4-day hands-on training. A post-training follow-up visit to the laboratory was conducted in March to review the testing data. This follow-up was only for the HPLC training data. The laboratory scientists performed and analyzed the deltamethrin data, and the results were in agreement with earlier test results from Belgium provided by the PMI team. The

agreement of laboratory results with those conducted in Belgium attests to the capability of the analysts to produce results that are verifiable. The Belgium laboratory whose results were used for comparison is utilized by other PMI implementing partners that work with mosquito nets and assess the quality of deltamethrin active ingredient in the nets.

Training participants were able to apply GLP to their daily laboratory activities, as well as understand the theory and practical applications of USP General Chapter <621> Chromatography and understand the theory and practical applications of both gas chromatography and HPLC to LLIN product analysis. After the training, the Myanmar DFDA Nay Pyi Taw Laboratory followed up with practice tests activities on deltamethrin LLINs assay by HPLC following good documentation practices and data integrity. PQM reviewed testing results and provided additional guidance and feedback on practice test results during the MOP visit in Nay Pyi Taw. The results of the practices—from 1.5 g/kg to 1.6 g/kg—were within the acceptable range of 1.4 g/kg to 1.8 g/kg for the deltamethrin content in newly purchased mosquito nets.

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

The laboratory relocation is slightly delayed due to construction. A request for adjustment to timelines has been made to DFDA.

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

PQM visited the newly built Mandalay laboratory to assess how much work is still needed in order to make decisions on when to implement the activities related to laboratory training.

Objective 5 – Provide technical assistance to DFDA Yangon and Mandalay laboratories on calibration of essential laboratory equipment after the relocation Program Management and Activity Coordination

No update this quarter.

Objective 6 – Strengthen the pharmaceutical quality surveillance system in the country through the introduction of new detection technologies and effective reporting and data management system at the state/regional levels

During Q2, PQM participated in the Research Paper Reading Sessions and Symposia of the 46th Myanmar Health Research Congress held in Yangon and Nay Pyi Taw. PQM was invited to present on risk-based PMS guidelines culminating with a workshop for DFDA Inspectors on PQM's risk-based PMS. The workshop was attended by 36 participants from DFDA, including 24 females and 12 males from DFDA; 22 participants were from DFDA regional and state offices, and the remaining were laboratory staff members.

After presentation of risk-based PMS, the participants identified the elements that should be included in the DFDA PMS program, and initiated drafting the new guidance for PMS. DFDA management expressed their interest in implementing risk-based PMS and requested a follow-up to the workshop.

Indonesia

I. Quarter 2 Highlights

Throughout Q2 FY 2018, PQM Indonesia continued to implement the FY 2017 work plan carryover activities that were completed by end of January 2018. The annual financial and technical assistance handover document (BAST) to the government of Indonesia for 2017 has been drafted, is currently pending internal review within the Badan Pengawas Obat dan Makanan (BPOM) technical units, and was reviewed and approved by the USAID Mission. Following final approvals and signatures by BPOM/USAID, the BAST document will be submitted by BPOM to the Ministry of Finance as per government regulation.

During FY 2018 Q2, activities focused primarily on administrative requirements by the government of Indonesia, as many senior, technical, and structural officers were shifted to other positions. PQM is adapting to the changes in high-

level personnel responsible for program approvals, as well as adjusting roles and responsibilities for implementing activities vis-à-vis responsible technical units. BPOM itself has also undergone significant shifts in the directorate responsible for the national PMS system.

In addition, activities during Q2 focused on preparing BPOM's PTBB national medicines QC laboratory and PT Kalbe Farma for their upcoming WHO inspections for PQ, scheduled for May 2018 (during Q3). Mock audits were conducted for both partners, and they are currently implementing their CAPA plans to address observations and further prepare for the upcoming audits.

PQM also provided onsite technical assistance to Sanbe Farma to help compile its levofloxacin 500 mg tablet product dossier, targeting June 2018 (Q3) for submission of the dossier to WHO for PQ. Progress was made at the provincial Balai Besar Pengawas Obat dan Makanan (BBPOM) laboratory in Denpasar toward completion of its implementation plan for WHO PQ, scheduled for submission by the end of the calendar year 2018.

Two workshops planned for Q2 were delayed until Q3. A data dissemination workshop to share results from Q1 joint MOH–BPOM sampling and testing of anti-TB medicines from government facilities combined with test results from a third-party ARV testing contract were delayed due to extended timelines for laboratory testing and delays in final results. A second workshop on development of a roadmap for procurement on anti-TB medicines for the national TB program, including reformulations, imports, and others to implement new TB regimen changes (for treatment of both TB and multidrug-resistant TB (MDR-TB)) within the public sector was delayed as well. PQM has been facilitating ongoing planning and discussions, including data generation, and assisting with reporting in preparation for both of these important upcoming workshops.

Due to shifts in senior staffing at BPOM, there have been significant delays in setting a formal FY 2018 work plan approval meetings with all technical and administrative units within BPOM. Presidential regulation 80/2017 has restructured BPOM, creating a new Deputy of Prosecution (Deputy IV), and restructuring has shifted a number of key officials. PQM anticipates a work plan approval meeting at the outset of Q3. Although the FY 2018 work plan has already been approved by USAID, further approvals are required by PQM's line ministry BPOM.

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 are 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 to systematically develop robust and reliable QA/QC systems, based on international standards, for medicines in Indonesia.

III. Quarter 2 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

Carryover FY 2017 HIV 1.4

As part of the completion of FY 2017 planned activities (HIV 1.4), PQM rolled out a pilot project incorporating medicines screening with Minilabs™ to support the national PMS system. The current system operates by post-market sampling follow by testing at a full-fledged laboratory using compendial testing, which is costly, time-consuming, and not as efficient as it could be. The total number of samples is limited by the capacity of laboratory analysts to conduct the tests, as well as limitations in equipment, methods/standards, and other constraints. PQM initiated a project to supplement the national PMS system in order to increase cost- and time-efficiency, increase the

total number of samples that can be collected and screened per provincial institution, and address gaps in the national capacity for testing essential medicines as the country implements Universal Health Access by 2019 (under BPJS/JKN programs). During Q2, the pilot project in DKI Jakarta provincial laboratory was completed using the mobile testing laboratories, and data generation and analysis was underway. As a result of the preliminary successes of the pilot program, BPOM has expanded the program of medicines screening with Minilabs™ to eight provincial BBPOM laboratories under the 2018 national sampling strategy (Medan, Serang, DKI Jakarta, Surabaya, Denpasar, Mataram, Kupang, and Jayapura). The planned re-equipping (reagents, reference standards) and training for the expanded eight sites will be done under shared financing by BPOM & USAID (KNCV's Challenge TB and the PQM program). The use of screening technology to supplement the national PMS system was a key output of the PQM program in Indonesia, so this represents a huge achievement and planning success. At the end of Q2, BPOM made a formal request to support rollout of Minilabs™ to all 34 provincial institutions, and PQM will coordinate with the Global Fund in an effort to finance the equipping and training the laboratories during FY 2018.

FY 2018 HIV/TB 1.1

In preparation for the upcoming May 2018 WHO audit of the PTBB NQCL at BPOM, PQM has been providing extensive onsite technical assistance, including conducting an intensive preparatory mock audit of the laboratory during Q2. Four major observations were found, focused mostly on documentation practices. PQM is helping the laboratory to address all observations, including providing a training for 22 people (1 male, 21 female) on CAPA management during the second week of March 2018. Currently in process are revisions to SOPs, training, and other activities to help prepare the laboratory for the May 2018 WHO audit. If successfully qualified by WHO, the PTBB laboratory will be the first QC laboratory in Indonesia to be prequalified by WHO, and one of only four government laboratories in the Association of Southeast Asian Nations (ASEAN) region with WHO PQ recognition.

FY 2018 TB 1.10

During Q2, the PQM program continued its support to the BBPOM Denpasar laboratory toward WHO PQ. This laboratory will be the first provincial/regional QC laboratory in ASEAN to achieve PQ, if successfully audited. During this quarter, PQM provided training and technical assistance on:

- New ISO 17025:2017 requirements and executing implementation plans.
- Training for 10 people on WHO GPPQCL TRS 957, 2010, Annex 1 (international requirements for laboratories).
- Developed 11 internal quality procedures designed to be in compliance with WHO standards.
- Revision of the Quality Manual and Level 2 Documents to comply with the new current version of ISO/IEC 17025:2017.
- Supported the initial training on the newly-upgraded software for the laboratory's analytical equipment.

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

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FY 2018 TB 2.3

During Q2, PQM conducted an intensive mock audit of the Kalbe Farma facilities in preparation for a WHO audit in May 2018 to evaluate the production of levofloxacin 500 mg tablets for PQ. Following the submission of a confidential audit report to Kalbe Farma, the PQM team is endeavoring to assist in addressing all observations prior to May 2018 when WHO will conduct the formal audit for PQ. If successful, this will be the first prequalified solid dosage form medicine, and the first anti-TB product prequalified in Indonesia.

Carryover FY 2017 TB 2.5

A 3-day training workshop for BPOM regulators/inspectors and pharmaceutical industry partners was conducted on CAPA management during Q2. The 32 participants included staff from Kalbe Farma, Sanbe Farma/ Caprifarmindo, Phapros Kimia Farma, Indofarma, Biofarma, Imedco and Zenith Pharmaceuticals. Following this initial training, as required by PQM, a "dissemination" training was conducted onsite for relevant Kalbe Farma staff to socialize and disseminate the information to an additional 27 staff. A similar internal training was conducted by Sanbe Farma in Bandung for an additional 40 onsite staff. By requiring "dissemination trainings" to internal staff, PQM effectively transmits the contents of training materials which is cost-effective and increases the total number of staff trained.

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

FY 2018 3.8

During Q2, the PQM team presented a lecture for 200 pharmacy students and professors at the University of Indonesia as part of awareness raising activities for the professional community. The topic for Q2 was *Anti-microbial resistance and medicines quality: global overview and national action plans for Indonesia*. This is part of an ongoing effort to increase pharmacy students' exposure to important public health issues for Indonesia related to medicines QA to supplement their routine academic curriculum.

FY 2018 3.10

During Q2, PQM finalized the draft BAST financial and technical assistance handover document with BPOM and USAID. This document is especially complicated based on the assignment of BPOM technical units for signature approval, financial reporting, and ensuring adequate handover for any commodities. Once finalized by PQM, the document will be reviewed and approved by USAID and then finally approved and signed by each technical unit within BPOM on an annual basis. The BAST document is used as the financial and training donor support provided under the umbrella agreements as per registration with the government of Indonesia between the U.S. and Indonesian governments' bilateral agreements. PQM also convened a technical discussion with the new technical Directorate in BPOM responsible for the national PMS program: Directorate for Safety, Quality, and Export Import of Drugs, Narcotics, Psychotropics, Precursors, and Addictive Substances. Based on overall agreement with previous and proposed PQM-initiated activities, the Director also requested additional support to equip, train, and roll out the implementation of Minilabs™ for screening medicines in support of the national PQM program. A formal request is forthcoming, and PQM is convening discussions with the national TB and HIV programs on feasibility of reprogramming funds to accommodate this request. Initial support would be for 24 additional Minilabs™, followed by potentially more to equip the new district-level BPOM depots under development. This represents a major opportunity for PQM to provide technical assistance on building the national PMS program to support risk-based planning and execution using the three-level structure developed by PQM. A key aspect of this is that BPOM will be in the position to report to the President that it has the capacity to test all the important JKN-provided essential medicines within the public sector, a major achievement that PQM is directly supporting.

IV. Key Challenges

The main challenges for implementation of the PQM program during Q2 were delays in important planned workshops to support data dissemination and collaboration between MOH and BPOM for government sector medicines sampled and tested beginning in Q1. In addition, structural and functional changes in BPOM staffing have led to delays in the 2017 BAST document being finally signed, approved, and submitted to the Ministry of Finance, as well as leading to delays in important planning, approval, and coordination meetings with BPOM technical units for the FY 2018 USAID-approved work plan.

V. Lessons Learned

PQM has learned that the majority of the technical implementation of activities and assistance must be built on a solid foundation of administrative and logistic approvals and support. PQM has major responsibilities with the government for reporting, handover, government approvals, and an administrative/legal framework within which to work. When these structures are not clear or set and agreed upon prior to implementation of technical activities, there are inevitable delays and internal issues created within the government.

Pakistan

I. Quarter 2 Highlights

During FY 2018 Q1, with PQM's support, three local manufacturers (Atco Laboratories, Aspin Pharmaceuticals, and Akhai Pharmaceuticals) launched CHX 7.1% gel. The fourth manufacturer (Zafa Pharmaceuticals) started local production during Q1, and its first batches were launched in Q2. All four manufacturers have made the products available in all provinces and regions of Pakistan as over-the-counter medicines, readily accessible by the general public. It is a success story for PQM Pakistan to facilitate locally manufactured, quality-assured and safe CHX 7.1% gel by four PQM-supported manufacturers in the short span of 2 years. Additionally, 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). All the manufacturers are now working to supply the product through government tenders. Atco Laboratories and Aspin Pharmaceuticals are currently looking toward exporting the product to other countries in the region, as well as becoming potential suppliers for UNICEF. Both manufacturers have submitted their EOIs to UNICEF. Aspin Pharmaceuticals has also submitted its dossier to UNICEF, and it is expecting a facility inspection by the UNICEF team in the near future. PQM is working with Atco Laboratories in preparing the global dossier submission to UNICEF. In order to assess progress in implementing CAPA plans, PQM conducted follow-up visits to Aspin Pharmaceuticals and Atco Laboratories in FY 2018 Q2.

In addition, PQM continued providing support to the Drug Regulatory Authority of Pakistan (DRAP) to strengthen its regulatory system, especially development of QMS for regulatory functions, and prepare its institutional development plan to address the second self-assessment that was conducted in FY 2017 with PQM support. As part of its support to DRAP, during FY 2018 Q2, PQM held a training of trainers on the use of Minilabs™ as a screening tool for assuring the quality of medicines in the supply chain.

II. Country Context

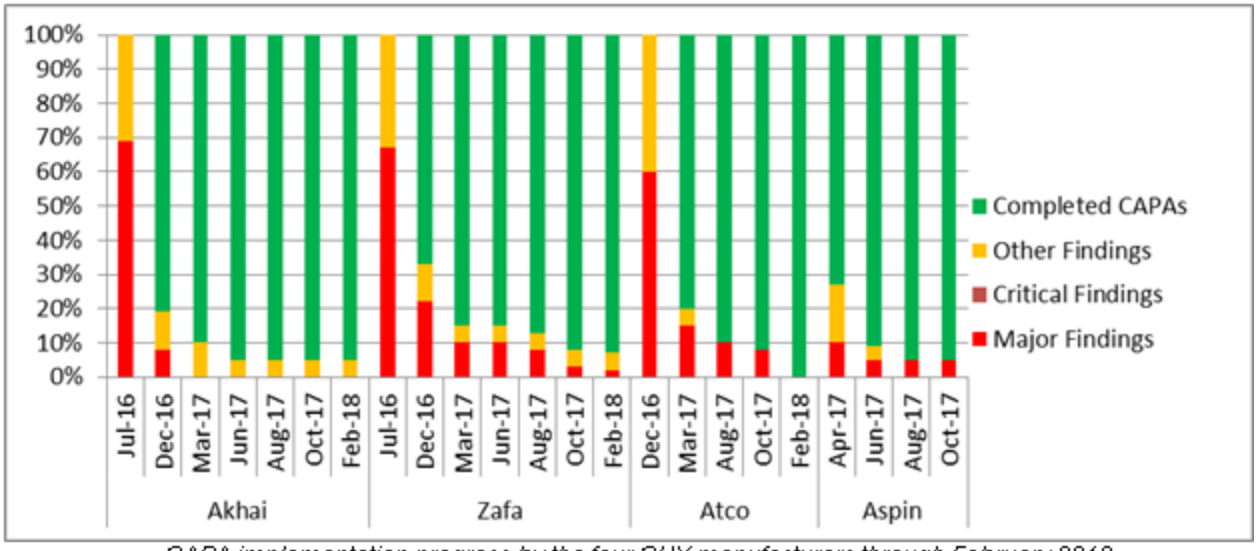
Chlorhexidine has been included in the ongoing U.N. Commission on Life-Saving Commodities for Women and Children. PQM is called to work alongside other implementation partners to help USAID achieve the objective of introducing quality-assured CHX in Pakistan. The collective effort would contribute to the Pakistani Government's effort to reduce the mortality (currently at 200,000 deaths/year, about 22 cases/hour) of newborns caused by cord infections, mainly due to the lack of availability of quality CHX gels.

PQM is tasked with providing technical assistance to potential manufacturers of CHX gel in improving their manufacturing quality standards. In addition, PQM will help strengthen DRAP's capacity, improving medicines registration processes, PMS, and other key functions, including enabling the QC laboratories toward international standards and practices. To effectively safeguard the quality of essential medicines, including CHX, a systematic approach to pharmaceutical regulation and management must be implemented throughout the country. PQM's initiative to improving quality standards of medicines covers all key components of medicines QA; it must also be complemented by adequate legislation and a regulatory framework. Such coordinated efforts, encompassing the pre- and post-market activities to render other oversights in monitoring, evaluation, documentation, tracking, and surveillance, are necessary to deliver needed improvements to the quality of medicines for public health.

III. Quarter 2 Progress by Objective

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

PQM 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 identify areas where the manufacturers need further PQM support to address the remaining corrective actions. The progress of manufacturers on CAPA implementation is shown in the chart below. With PQM's technical assistance, all four manufacturers have already started production, and the product is now available in the local market. During FY 2018 Q2, PQM continued to work with CHX gel manufacturers, with the objective to help these manufacturers close the remaining noncompliances as determined by PQM's comprehensive assessment of the manufacturers. As a result, two manufacturers (Atco Laboratories and Aspin Pharmaceuticals) have progressed steadily. Atco Laboratories has successfully closed its CAPA by addressing all noncompliances from PQM's assessment. Aspin Pharmaceuticals has also made good progress in addressing its CAPAs and is expected to close its CAPA in FY 2018 Q3. In addition, PQM is working with Atco Laboratories and Aspin Pharmaceuticals to support compliance with international standards on GMP and QMS. Aspin Pharmaceuticals submitted its dossier to UNICEF's Expert Review Panel (ERP). The PQM team is working with Aspin to close all noncompliances to meet international GMP compliance. PQM is also working with Atco Laboratories in preparation of its dossier for UNICEF ERP. Atco Laboratories' dossier will be ready for submission to UNICEF in FY 2018 Q3.



CAPA implementation progress by the four CHX manufacturers through February 2018

PQM has consulted with the USAID/ Pakistan to identify other essential MNCH medicines with public health impact needing PQM support; these products include amoxicillin DT, oxytocin injection, zinc DT, and zinc DT/oral rehydration salts co-pack. Amoxicillin is an effective broad-spectrum antibiotic, especially for the treatment of bacterial pneumonia in children. Its availability and use as a first-line treatment for pneumonia in countries with a high burden caseload remains limited, despite higher effectiveness than existing alternative treatments.

The use of uterotonics (oxytocin alone as the first choice) plays a central role in the treatment of postpartum hemorrhage. Uterine massage is recommended for the treatment of postpartum hemorrhage as soon as it is diagnosed, and initial fluid resuscitation with isotonic crystalloids is recommended. Previously, oxytocin was imported into the country, but unfortunately now this has stopped; the increasing value of the U.S. dollar against the Pakistan rupee has made the importation of oxytocin not viable for the pharmaceutical companies.

Diarrhea remains a leading cause of death globally among children under 5 years of age. Zinc supplementation has been shown to reduce the duration and severity of diarrhea and to prevent subsequent episodes. At the present time in Pakistan, zinc DT (recommended for children under 5 years of age) is not being manufactured locally.

PQM has identified the following manufacturers as potential suppliers of the mentioned products:

1. Amoxicillin dispersible tablets: Macter International (Karachi) and CSH Pharmaceuticals (Lahore).
2. Oxytocin (postpartum hemorrhage): Indus Pharma (Indus has started manufacturing the much needed oxytocin injection; however, its compliance with GMP requires improvements in order to be acceptable at an international level. PQM has started discussions with Indus Pharma management concerning the technical assistance that PQM can provide.)
3. Zinc DT: Pharmevo, Aspin Pharmaceuticals, and Atco Laboratories (PQM has discussed with the management of these manufacturers the technical assistance that PQM can provide in the development of zinc DT to make the product available locally.)
4. Zinc DT/oral rehydration salts co-pack: Atco Laboratories.

PQM conducted a baseline assessment of Macter International's penicillin manufacturing in FY 2018 Q1 and prepared a comprehensive assessment report that was shared with the company's management. The manufacturer prepared the CAPA based on the PQM assessment report. Macter International developed and shared the draft CAPA plan with PQM, and the PQM team is reviewing it. Once the CAPA plan is prepared and approved by PQM, assistance will be provided to the manufacturer in closing its noncompliances in a short time so the manufacturer can receive early approval from DRAP to produce the product. However, considering the importance of the product and its need, PQM has identified CSH Pharmaceuticals as another potential manufacturer of amoxicillin DT; CSH Pharmaceuticals has submitted an EOI, and its GMP assessment will take place in FY 2018 Q3.

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

PQM continued working with three laboratories in FY 2018 Q2 to improve their QMS standards: CDL Karachi, DTL Lahore, and Pakistan Drugs Testing and Research Center (PDTRC) Lahore. Below are updates of the status of the three laboratories:

CDL Karachi: PQM continued to provide technical assistance to CDL Karachi for the development of QMS and required SOPs. The drafts for 21 SOPs prepared by laboratory management were reviewed, and appropriate improvements were made to them. PQM also drafted eight new essential SOPs that will be required for WHO PQ. PQM is continuing to review the remaining SOPs (already prepared) and will work with CDL Karachi management to finalize all SOPs required for WHO PQ. Required trainings on all SOPs will be conducted for CDL Karachi staff, utilizing PQM experts to provide these trainings. The laboratory information file was also reviewed, and CDL Karachi is working to improve the document to be resubmitted to WHO PQ. When PQM started to provide its technical assistance to CDL Karachi, the activities remained focused on the training of technical staff and review of documentation to help prepare the laboratory for WHO PQ. However, in working with the laboratory, PQM realized that the laboratory is in dire need of infrastructure development, new equipment, and more staff. Through persistent advocacy, PQM convinced DRAP management to invest in infrastructure, procurement of new equipment, and additional staff. As a result, DRAP management has committed U.S. $ 2.8 million in infrastructure development and procurement of new equipment. CDL Lahore has been understaffed and unable to perform its assigned functions properly. This issue has been highlighted with DRAP management on different occasions. Thus, the strength and capacity of CDL Karachi analysts has been enhanced by adding five new Assistant Directors as analysts. PQM has also provided technical support to CDL Karachi for its laboratory design layout and recommendations on equipment and specifications that will meet international standards.

DTL Lahore: As a follow-up to the preliminary assessment of DTL Lahore in December 2017, a comprehensive assessment was made during January 2018. The objective of the January 2018 assessment was to make a detailed gap analysis and prepare a comprehensive report on QMS and required improvement in the overall standard to meet GLP. During the assessment process, it was apparent that there was a need for immediate training on data integrity, change control management, deviation handling, and risk assessment. These trainings were conducted right away for all technical staff of DTL Lahore over 2 days. The objective of the trainings were to ensure the newly inducted laboratory technical staff will be well-versed in the latest developments in GLP. This training included 4 modules; 43 persons (26 males, 17 females) completed the training.

PDTRC Lahore: PDTRC received the WHO Peer Audit Report in February 2018 and has prepared a response to the observations reported during the peer audit in December 2017. The CAPA plan was prepared by PDTRC Lahore, and the PQM team in Pakistan is reviewing the plan for completeness. Once finalized, the CAPA plan will be submitted back to WHO by April 2018, within the stipulated 2 months' response time.

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

During FY 2018 Q2, PQM continued liaising with DRAP's Division of Pharmaceutical Evaluation & Registration to help resolve the challenges faced by the division for implementation of the Common Technical Document format for registration applications. PQM also provided guidance in compilation of a drugs database; this database was uploaded on DRAP's website to support transparency and knowledge for all stakeholders.

In addition, PQM convinced DRAP to start work on its own organizational QMS (global benchmarking), after a second assessment by PQM using the WHO GBT that was completed in January/February 2018. DRAP agreed to follow up on the assessment with PQM support by identifying an internal audit team, who will be trained in the first week of April. DRAP also identified an internal audit team for preparing an "institutional development plan," which will contribute to achieving Maturity Level 3 as defined by the Global Benchmarking Tool. DRAP signed on as a member of the collaborating registration program with WHO in Geneva. This program allows for DRAP to expedite the registration of WHO prequalified medicines, thus removing barriers to register quality medicines. PQM support for this activity will continue in the next quarters as well.

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

During FY 2018 Q2, PQM continued to liaise with stakeholders to finalize a national framework/policy on PMS to develop an information-sharing mechanism. The draft 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. To achieve the objective of establishing a robust risk-based PMS and to train the regulators on the three-level approach, PQM conducted a 3-day training workshop at CDL Karachi on "Utilization of GPHF Minilab™ as a Screening Method for Risk-Based Post-Market Surveillance." The training was facilitated by PQM local technical resources and a Rockville-based expert through WebEx. One inspector from each province and an analyst from the provincial Drug Testing Laboratory (DTL) participated in the training (including DRAP's regional and headquarters QA officers). In total, 21 persons (18 males, 3 females) were trained. The objective of the training workshop was to train participants as master trainers to ensure the sustainability of risk-based PMS. The training consisted of both interactive presentations and hands-on use of the Minilab™. The participants were also given the task to propose a guideline for use of the Minilab™ in the field. The Director of CDL Karachi was included in this task and presented on his work on risk-based PMS for his laboratory. The participants took part in interactive sessions and came up with recommendations; for example, the legal framework was discussed during a brain-storming session, and recommended changes were suggested. The working group tasked with developing a legal framework came up with a broader outline of the framework, which was presented to the participants for their additional input. The next PMS consultative meeting will use this draft framework for developing the guideline for the use of the Minilab™ in the field in Pakistan.

IV. Key Challenges

The non-availability of multiple-entry visas and the existence of a travel advisory remained a programmatic challenge, hindering the PQM U.S.-based technical team's ability to provide technical assistance in Pakistan. The registration of USP has been recommended by the scrutiny committee of Ministry of Interior, and the memorandum of understanding is likely to be signed by April 2018. 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 PQM international consultants who are 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 regulatory strengthening stakeholders in Pakistan. Past experience has shown that provincial governments (with the exception of Punjab) are less inclined toward strengthening of QA and QC systems, which negatively impacts the performance of many QC laboratories.

At the federal level, the Appellate Laboratory 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 is not adequate based on current international standards. This laboratory requires financial support from the government to procure equipment and renovate the building. Due to PQM's advocacy, as well as support from Global Fund and other partners, PQM is working to equip and operationalize the Appellate Laboratory. Once equipment and staff are in place, PQM will then begin to build and strengthen the Appellate Laboratory's QMS capacity.

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 countrywide. The technical assistance that the provinces require is in the area of PMS and strengthening of the provincial QC laboratories. Therefore, PQM's assistance at the provincial level through DRAP-centered activities will help strengthen the regulatory system.

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

Cambodia: Following feedback from the Mission, the revised closeout report was submitted and approved.

Philippines: Following feedback from the Mission, a revised version was submitted on February 8, 2018. The mission communicated on March 12, 2018, that further comments were being consolidated, but to date they have not been received.

Eastern Europe & Central Asia

Kazakhstan

I. Quarter 2 Highlights

During Q2, PQM:

1. 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.
2. PQM conducted a data integrity training for 17 NCQL staff in preparation for WHO PQ; this training covered one of the critical aspects to be evaluated during WHO inspection.
3. PQM visited Nobel Almaty Pharmaceutical Factory for GMP assessment of the new site.

PQM provides technical assistance to three NQCLs of the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM) 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 in the Kazakhstan market. PQM also visited Nobel Almaty Pharmaceutical Factory to perform a GMP gap assessment of the new site and prepare the manufacturer for future WHO inspection. 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 2 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 continued remote technical assistance to laboratories in Karaganda, Kostanay, and Astana. The Karaganda laboratory developed a corrective action plan, which was reviewed by PQM. PQM also reviewed some revised and newly developed QMS documents from the Karaganda laboratory and provided comments and recommendations.

In addition to remote technical assistance in FY 2018 Q2, PQM provided training to 17 representatives from regional QC laboratories in Karaganda, Astana, Kostanay, Ust Kamenogorsk, and Almaty Testing Center on the fundamental principles of data integrity as it relates to medicines QC testing laboratories. The overall expectation of participants was to gain better understanding of data integrity and enhance their knowledge base. as well as application of the principles. Based on the results from the training evaluation feedback, most of the participants strongly agreed that training expectations were met. The training enhanced the laboratory's ability to identify data integrity issues and perform self-assessment of its quality and technical operations. The interactive sessions allowed participants to ask questions and share their laboratory experiences.

It was agreed that participants would disseminate knowledge gained to other members of their laboratories; the laboratories would review their SOPs related to data integrity and revise them, as applicable. It was recommended that all territorial branches of NCEM laboratories should harmonize the relevant procedures to ensure consistency in application.

PQM will continue to provide technical assistance to the Karaganda laboratory in the form of document review. A PQM consultant will serve as an observer during the Karaganda WHO PQ inspection and provide assistance to resolve inspection observations.

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 January 2018, Nobel Almaty Pharmaceutical Factory started operations on the new production site. In February 2018, PQM conducted a 3-day GMP gap assessment of the new facility and identified observations that would need correction before a WHO PQ audit is requested. Strengthening the quality systems at the manufacturing site will lead to better understanding and enhance documentation needed to improve the quality of the dossier for WHO PQ submission. Nobel Almaty Pharmaceutical Factory has the capacity and resources to implement all the corrective actions resulting from the GMP assessment. The manufacturer should have all corrective action completed before the series of validation batches can be used for the biowaiver tests.

PQM will continue to provide remote assistance to Nobel Almaty Pharmaceutical Factory. PQM will provide the manufacturer a confidential assessment report with detailed observations. PQM will also review the process validation documentation, bio waiver studies and Common Technical Document dossier for levofloxacin when provided by Nobel Almaty Pharmaceutical Factory.

Uzbekistan

I. Quarter 2 Highlights

In Q2, PQM:

1. Conducted a data integrity training for 22 individuals to ensure compliance with international standards to representatives of Nobel Pharmsanoat.
2. Visited Nobel Pharmsanoat for an initial GMP assessment of the new site.
3. Provided an "Implementation of Good Laboratory Practices (GLP) in Quality Control Laboratories" training to 19 representatives of QC laboratories of the Agency for Development of Pharmaceutical Industry of the Ministry of Health, the Republic of Uzbekistan.

This quarter, PQM began preparations for a Pharmaceutical Inspection Co-operation Scheme (PIC/S) and GMP training for the GMP inspectorate of Uzbek MRA (State Center for Expertise and Standardization of Pharmaceutical

Products, Medical Products, and Medical Equipment). PQM also started preparations for training on the new ISO 17025:2017 for staff of QC laboratories of the Agency for Development of Pharmaceutical Industry. In addition, PQM will visit the Tashkent QC laboratory for an assessment of its QMS for compliance with the new ISO 17025:2017 standards. PQM started the process of equipment procurement for the QC laboratory of the Agency for Development of Pharmaceutical Industry.

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 small 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 2 Progress by Objective

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

In January 2018, PQM conducted a data integrity training to strengthen quality management system to ensure compliance with international standards to representatives of Nobel Pharmsanoat. Data integrity is one of the critical aspects to be evaluated during WHO PQ inspection. Training was provided to 22 participants representing Nobel Pharmsanoat and Nobel Almaty Pharmaceutical Factory from Kazakhstan. The training aimed to enhance the ability of the staff to identify data integrity issues and perform self-assessment of its quality and technical operations. Discussions throughout the sessions provided participants with opportunities to ask questions and share their experiences.

Nobel Pharmsanoat is in the process of completing construction of the new site where the product selected for WHO PQ will be manufactured. In February 2018, PQM conducted a 3-day initial GMP assessment of the new facility. PQM identified observations that need corrective actions. During the assessment debrief, recommendations for corrective actions were shared with staff of the company.

PQM will continue providing assistance to Nobel Pharmsanoat. Nobel Pharmsanoat still needs to make a decision on the specific product (levofloxacin or moxifloxacin) to put forward for WHO PQ. PQM will develop a confidential assessment report with detailed observations; Nobel Pharmsanoat will prepare a CAPA plan as a response to PQM confidential report. PQM will assist Nobel Pharmsanoat in implementation of the corrective actions.

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 to move forward with implementing the committed activity, GLP training for staff from the manufacturers' QC laboratories and the Agency for Development of Pharmaceutical Industry. In January 2018, a GLP training to strengthen the national medicines QC system was conducted. Training was provided to 19 participants representing 7 pharmaceutical manufacturers and the Agency for Development of Pharmaceutical Industry.

The GLP training was focused on providing participants with an overview of WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL/WHO) and basic principles on how to implement QMS in QC laboratories within the pharmaceutical industry.

As the new Agency for Development of Pharmaceutical Industry became a legal successor of the liquidated Uzpharmsanoat, it was agreed with USAID/Uzbekistan and the management of the Agency that further assistance in strengthening the medicines QC system would be provided to QC laboratories of the Agency for Development of Pharmaceutical Industry. PQM started preparations for the training on the new ISO 17025:2017 for staff of QC laboratories of the Agency. PQM will also visit the Tashkent QC laboratory for an assessment of its QMS to assess compliance with the new ISO 17025:2017. The ISO training and assessment visit will be held in FY 2018 Q3.

PQM started the process of equipment procurement for the Uzbek MRA's QC laboratory.

Objective 3 – Strengthen GMP inspection system

In Q2, PQM began preparations for PIC/S and GMP training for the GMP inspectorate of the State Center for Expertise and Standardization of Pharmaceutical Products, Medical Products, and Medical Equipment, which will be held in FY 2018 Q3.

Core Portfolio

Core MNCH

I. Quarter 2 Highlights

In Q2, PQM staff attended and participated in the reproductive, maternal, newborn, child and adolescent health (RMNCAH) Quality Assurance Meeting (ISG) on March 8, 2018, at the World Bank. PQM made a presentation on "Elements of a Harmonized Quality Assurance Framework for Procurement of Quality-Assured MNCH Products Using Donor Funds."

As a follow-up to the oxytocin consultation meeting held in Geneva, Switzerland, in Q1, PQM completed and submitted its contribution to an article on oxytocin quality issues. The scope of the article centers around the quality issues associated with the medicine and will provide recommendations to ensure quality. The article is a collaborative engagement with members of the USAID Maternal Health team, GHSC-PSM project, Monash University, and Concept Foundation.

PQM will continue to provide technical assistance to manufacturers to advance their progress toward supplying to 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 2 Progress by Objective

Objective 1 – Increase the availability of quality-assured MNCH products

During Q2, PQM provided technical assistance to manufacturers of the following MNCH products:

- **Magnesium sulfate FPP**: One manufacturer is in the process of purchasing the API to conduct development and validation batches. A second manufacturer completed the dossier compilation in March 2018. PQM will work with the manufacturer to review the full dossier prior to submission to the WHO PQ team.
- **Oxytocin FPP**: The manufacturer has made a management decision not to move forward on development of this product. This is due to the temperature requirements for manufacturing and storage of the product.
- **Oxytocin API**: PQM provided assistance to an API manufacturer by preparing the new facility to receive Certificate of Suitability to the European Pharmacopeia recertification. No further assistance is needed for this manufacturer.
- **Amoxicillin FPP**: PQM identified a new manufacturer in March 2018. PQM plans to send the questionnaire for completion by the manufacturer and fully engage in Q3. A second manufacturer in China has been inactive, and PQM will no longer engage this company in receiving technical assistance.

PQM's Manufacturing Services Group continues to provide technical assistance at various stages to ensure that the manufacturers are making progress toward WHO PQ or for global procurement eligibility. This assistance will include a full GMP assessment of the new manufacturer for amoxicillin finished product and dossier review for magnesium sulfate for WHO PQ submission. PQM will continue to search for and identify a potential gentamycin manufacturer.

Objective 2 – Help to increase access to quality-assured MNCH products

Data are being collected on the registration status of oxytocin and magnesium sulfate injections in USAID's priority countries. The data and subsequent analysis will help identify the barriers faced by manufacturers. PQM has also engaged in discussion with the WHO Collaborative Registration Procedure (CRP) to conduct a workshop for MRAs in southeast Asia to introduce the WHO CRP and engage at least one MRA to participate.

A consultant will be identified and engaged in Q3 to conduct registration status analysis of oxytocin and magnesium sulfate in USAID's priority countries. The consultant will initiate work with oversight from PQM staff, as well as review information collected from various stakeholders (in form of a questionnaire) and databases. PQM will continue to actively engage WHO CRP team to collaborate in the workshop.

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

PQM has actively collaborated with the RMNCAH group (including The Concept Foundation and USAID) to develop and harmonize a QA policy for procurement of MNCH commodities by countries using donor funds. PQM provided technical leadership by indicating and explaining the critical elements of a QA policy as it pertains to finished pharmaceutical products. In addition to the policy proposal, PQM staff attended and participated in the RMNCAH Quality Assurance Meeting (ISG) on March 8 at the World Bank. PQM staff presented on "Elements of a Harmonized Quality Assurance Framework for Procurement of Quality-Assured MNCH Products Using Donor Funds," which described in detail the proposed QA policy and its elements. PQM also completed work with the University of Minnesota on a detailed systematic literature review and meta-analysis of the quality of oxytocin supply globally, specifically as it relates to the shelf life and stability. The report is under internal PQM review and will be disseminated widely in Q3. Lastly, PQM's technical input was requested by USAID in the review of draft guidelines on the procurement of MNCH medicines.

Core NTD

I. Quarter 2 Highlights

PQM has finalized the situation analysis paper, "Rapid Assessment of the Neglected Tropical Disease Drug Production and Supply Needs in Five Countries," and has shared with USAID for review.

PQM has also initiated technical assistance to two selected manufacturers for bioequivalence support in India.

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 treatment. 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 PQ of anti-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 2 Progress by Objective

Objective 1 – Increase availability to quality-assured NTD medicines

During Q2, PQM provided technical assistance to manufacturers of the following NTD products:

- **Praziquantel API**: PQM continued to provide technical assistance to three manufacturers at various stages toward WHO PQ of praziquantel API. Two API facilities have been inspected by WHO PQ: one is still expecting the inspection report, and the other has been accepted by WHO PQ for review. PQM's technical assistance also included addressing WHO's queries on dossiers.
- **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 a GMP assessment of two FPP manufacturing facilities and providing guidance on FPP process validation.
- **Albendazole API**: One manufacturer is in the process of re-engagement, and a second manufacturer is implementing the CAPA plan resulting from PQM's audit.
- **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**: PQM staff traveled to China in Q2 and met with the manufacturer to discuss the pipeline of products and their status. The management of the manufacturer has decided to move forward on another NTD product (albendazole) and is no longer interested in moving forward on WHO PQ for mebendazole.

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 was shared with USAID for review, and comments were received. PQM incorporated and addressed the comments and questions from USAID. The revised report was resubmitted to USAID for review. The decision on selection of the manufacturers of NTD products in these countries will be made in discussion with USAID.

Objective 2 – Technical support for bioequivalence study

PQM developed audit reports of two manufacturers of praziquantel FPP selected for assistance in conducting bioequivalence studies. The reports were sent to the manufacturers and based on the findings; CAPA plans have been developed by the manufacturers and submitted for PQM's review. The PQM team is reviewing the CAPAs and setting timelines to initiate audit of the CROs and review of the bioequivalence protocols. Timelines for bioequivalence study, CAPA implementation, and dossier compilation will be set with the manufacturer and PQM team.

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

This activity is not yet approved for FY 2018.

Core TB

I. Quarter 2 Highlights

Clofazimine is one of the highest priority products for USAID. PQM continued its technical assistance to the manufacturer of clofazimine FPP and audited the CRO conducting a bioequivalence study. Based on the audit results, the CRO developed a CAPA plan. Approval of the manufacturer selected for U.S. FDA submission of

rifampicin was received from USAID. PQM has been working diligently with the manufacturer to collect the required documents to execute the subaward contract according to USAID regulations.

Due to absence of a gatifloxacin comparator product on the market, PQM developed a concept note with recommendations for a solution. The concept note was submitted to the WHO TB team, who will use it to advocate for a solution with various WHO teams on a path forward to ensure the availability of quality-assured gatifloxacin finished product.

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 2 Progress by Objective

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

During Q2, PQM provided technical assistance to manufacturers of the following TB products:

- **Clofazimine FPP**: PQM audited the CRO conducting the bioequivalence study on clofazimine FPP in January 2018. Based on the audit, the CAPA plan has been developed by the CRO and is currently being reviewed by PQM. The bioequivalence study for the clofazimine FPP was initiated in November 2017. The semi-replicate design required three dosings with a 2-month washout period in between the dosings. The last dosing of subjects for the bioequivalence study is scheduled to occur in the last week of March and first week of April.
- **Clofazimine API**: The manufacturer submitted the API master file (MF) to WHO PQ in February 2017. It received the first query and worked continuously with the starting material manufacturer to address the deficiencies. The manufacturer submitted responses to WHO on February 28. PQM provided remote assistance to the manufacture in response to WHO PQ.
- **Rifapentine API**: One PQM-supported manufacturer is in the process of renovating its facility and awaiting local regulatory approval. In the meantime, the manufacturer is continuing to implement CAPAs. PQM also provided feedback to a second manufacturer that submitted its API MF for review. PQM is waiting to receive the revised API MF in Q3 to review, prior to submission to WHO PQ.
- **Rifapentine FPP**: PQM is continuing to provide assistance in product development for one manufacturer. PQM engaged a second manufacturer in March 2018 who expressed interest in developing the formulation. PQM will continue to work with the manufacturer and conduct an initial GMP assessment in Q3.
- **Gatifloxacin API**: PQM reviewed and provided comments for the API MF; the manufacturer is incorporating the comments and will resend the updated API MF for review.
- **Gatifloxacin FPP**: In order to establish the quality and efficacy of their product, product sponsors are required to demonstrate interchangeability of the product through bioequivalence studies. However, to demonstrate interchangeability, the comparator product (against which the product for submission needs to be characterized for quality and efficacy) has to be properly sourced. For gatifloxacin, there is no comparator product from well-regulated markets, which becomes a bottleneck for approval of this product by the WHO PQ team. PQM developed and provided a concept note containing recommendations to resolve the comparator product issue (no comparator product currently available). The concept note was provided to the WHO TB team, who will use it in discussions with the WHO PQ team to advocate for a solution, as the

product is greatly needed for treatment of MDR-TB as a part of the short-term regimen. The manufacturer supported by PQM is still in the product development phase.

- **Kanamycin API**: PQM provided remote assistance to one of the manufacturers in Q2. PQM has provided input in the search of a new intermediate source. PQM also provided remote assistance in compiling the API MF to be submitted to PQM for review. PQM also conducted an initial GMP assessment of a second API manufacturer in February 2018. This manufacturer was identified from the workshop "Ensuring the Quality of Priority Medicines" organized by PQM in Bangkok in July 2017. Upon assessment of the facility, it was concluded that this manufacturer will only be moving forward with the non-sterile API for WHO PQ.
- **Kanamycin FPP**: With PQM's support, the manufacturer provided a response to the latest round of dossier queries from the WHO PQ team. The facility has already been accepted for GMP compliance.
- **Linezolid FPP**: The manufacturer received U.S. FDA inspection in November 2017, and the result was positive, with no critical or major observations. The manufacturer is awaiting final product approval from the U.S. FDA in late April.
- **Rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC)**: The PQM field office team conducted a visit to one of the 4 FDC manufacturers on March 13–15 to verify and close out GMP observations, review the product dossier, and discuss project timelines and planning for the bioequivalence study. A second manufacturer is expecting local regulatory approval from DRAP at the end of March; a bioequivalence study protocol has been submitted to WHO for review and comments. Comments were received, and the manufacturer and CRO are incorporating the comments into the protocol.

To contribute to ensuring an uninterrupted supply of anti-TB medicines for the U.S. market, PQM selected a manufacturer to benefit from technical assistance toward approval of their product (rifampicin FPP) by U.S. FDA. Bringing new suppliers to the U.S. market will decrease the risk of a shortage of medicines and may also have a positive impact on medicines price reduction. In addition, U.S. FDA approval makes medicines eligible for supply through Stop TB Partnership's GDF, so the intervention potentially can increase the number of international quality-assured suppliers not only in the United States but also on the global public health market.

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

The PQM staff prepared a workshop proposal for submission to the 49th Union Conference on Lung Health to be held at The Hague, Netherlands.

The PQM team also started working to engage one of the academic institutions to collaborate on the online GMP training modules.

PQM is working on conducting an orientation for technical consultants. The objective is to orient the consultants on the PQM program, updated technical goals and objectives, and updated technical processes. It will also provide participants with the opportunity to learn from various field experiences on regulatory landscape, and bioequivalence study design and protocol development. This orientation will be held in early Q3 (April).

Cross Bureau

I. Quarter 2 Highlights

During this quarter, Cross Bureau continued implementing carry-over activities from the FY 2017 work plan, as indicated for Objectives 1, 2, and 5.

- Media reports and analysis of incidents of poor-quality medicines delivered by a data analysis company did not meet PQM requirements and expectations. Starting next quarter, PQM will gather and analyze media reports from selected EPCMD countries internally and will develop the corresponding dashboard.
- Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries was completed. The associated tool (MedRS) is at the final stages of development.
- All modules for an e-course on medicines QA are completed and currently under review. PQM will notify the USAID Bureau of Global Health eLearning (GHeL) team of its interest in creating the course in GHeL's platform, and upon approval will submit a detailed course proposal.

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 2 Progress by Objective

Objective 1 – Increase awareness of the importance of medicines quality

A company contracted in Q1 to analyze media information on poor-quality medicines delivered a report for the period October 2016 to June 2017 that did not meet PQM requirements and expectations. Consequently, starting on Q3, PQM will gather and analyze internally poor-quality medicines incidents reported for EPCMD countries since October 2017, and will develop and update quarterly the corresponding country dashboards.

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

The "Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries" document was finalized. Building on WHO guidelines for conducting quality of medicines surveys and medicines testing, as well more than 15 years of experience in supporting LMICs to establish and implement medicines monitoring activities, these guidelines aim to support regulatory agencies to implement technically sound, cost-effective, and sustainable national PMS programs. For this, PQM introduces risk-based elements for both the sampling process (e.g., medicines characteristics, geographical location, types of facilities) as well as for testing (e.g., multilevel testing approach for both field and laboratory QC). Implementation of these risk-based approaches will help countries allocate limited human and financial resources for continuous monitoring of the quality of medicines in the market to ensure their efficacy and safety when they reach patients. PQM is already working with selected countries for the prompt use of these guidelines when establishing their national PMS programs.

The associated risk-based web tool (MedRS) is at the final stage of development after feedback provided during this quarter. Completion and launching is projected during Q3.

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

No updates this quarter.

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

There is nothing to report in this quarter, as the tool was previously finalized.

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

The six modules of the e-course have been completed and are currently under review; module 2 was adapted to an e-course platform utilizing tools designed to integrate images and media with interactive elements. However, before pursuing additional modules in this platform, a proposal will be submitted for inclusion of this course in the Global Health e-Learning Center.

Objective 6 – Establish regulatory system country profiles

No updates this quarter.

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

In Q1, the Federation of African Pharmaceutical manufacturers Association (FAPMA), in collaboration with the African Medicines Regulatory Harmonization (AMRH) had requested PQM GMP support. According to the FAPMA request letter, “An intervention in the form of site quality inspections will serve as an important gap analysis and will afford the participating manufacturers an opportunity to address the shortcomings that will progressively bring them closer to undergoing a full WHO PQP inspection.”

Recognizing the need for coordinated support to this regional body and the potential intervention required, PQM sought to collaborate with WHO to ensure any interventions are aligned with other support being provided in the region. In Q1, an initial teleconference meeting was held between PQM and the WHO GMP technical support team to discuss the FAPMA request and seek out areas of potential collaboration. After initial deliberations, all parties reached consensus to reconvene to further deliberate what approach may be most suited to address FAPMA’s request.

In Q2, a follow-up teleconference was held with representatives from WHO, AMRH, and PQM, There was consensus for a workshop to strengthen capacity for local pharmaceutical production for FAPMA members with technical assistance from both PQM and WHO. It was agreed that WHO will draft a proposal for this workshop, which will be shared with PQM. PQM anticipates to receive this workshop proposal from WHO in Q3.

Core Malaria: The FY 2017 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 FY 2018.

Management Overview

During Q2, PQM worked with the USAID missions and core health element teams to obtain outstanding approvals for FY 2018 work plans. By the end of the quarter, 18 out of 21 work plans (86%) had been 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 77 percent and 73 percent of work plans approved, respectively, at the end of the Q2.

During this quarter, PQM finalized a key guidance document entitled *Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries,* an activity funded through PQM's Cross Bureau project. The document is currently being translated into French, and formal dissemination of the document is expected during the next quarter.

PQM also finalized three additional technical documents that highlight different facets of our work to improve access to quality-assured essential medicines:

- *Strengthening Manufacturing Capacity to Improve Access to Quality-Assured Essential Medicines*
- *Analytical Instrumentation Support for National Quality Control Laboratories*
- *Strengthening National Quality Control Laboratories in Low- and Middle-Income Countries to Improve the Quality of Medicines*

These technical documents are available on PQM's website and were disseminated externally through the e-drug list serv.

Finally, in February, PQM's Program Director, Jude Nwokike, along with other PQM and USP colleagues, published a *Perspectives* article in the Bulletin of the World Health Organization on the importance of addressing medicines QA to fight antimicrobial resistance (http://www.who.int/bulletin/volumes/96/2/17-199562/en/).

In January 2018, Director Nwokike had the opportunity to attend the Prince Mahidol Awards Conference and present at a side event on "Monitoring and Improving Medicines Quality through Antimicrobial Resistance (AMR) National Action Plans." Director Nwokike shared experiences in strengthening medicines quality surveillance systems and PQM's work towards reducing poor-quality medicines that contribute to AMR.