

Promoting the Quality of Medicines (PQM) Program

FY 2019 Second Quarter Report Date: May 1, 2019

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About the Promoting the Quality of Medicines (PQM) Program

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The Promoting the Quality of Medicines (PQM) program is a Cooperative Agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to address critical medicines information and quality 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 April 2019, USAID supports PQM's work in 17 countries, 1 regional mission, 1 Cross Bureau program, and 3 core health programs.

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Acronyms

ADE	adverse drug event
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CHX	chlorhexidine
CRO	clinical research organization
CRP	Collaborative Registration Procedure
CTD	common technical document
DFDA	Department of Food and Drug Administration [Myanmar]
DGDA	Directorate General of Drug Administration [Bangladesh]
DRAP	Drug Regulatory Authority of Pakistan
DT	dispersible tablet
EFDA	Ethiopian Food and Drug Authority
EFMHACA	Ethiopian Food, Medicine and Healthcare Administration and Control Authority
eRIS	electronic regulatory information system
FPP	finished pharmaceutical product
GBT	Global Benchmarking Tool
GCP	good clinical practices
GFDA	Ghana Food and Drug Administration
GLP	good laboratory practices
GMP	good manufacturing practices
HPLC	high-performance liquid chromatography
IR	Intermediate Result
LIF	laboratory information file
LMHRA	Liberia Medicines and Health Products Regulatory Authority
LMIC	low- and middle-income country
LNCQM	Laboratório Nacional de Controlo da Qualidade de Medicamentos [Mozambique]
MDR-TB	multidrug-resistant tuberculosis
MNCH	maternal, newborn, and child health
MQDB	Medicines Quality Database
MQM	medicines quality monitoring
MRA	medicines regulatory authority
	Medicines Regulatory Harmonisation
NAFDAC	National Agency for Food and Drug Administration and Control [Nigeria]
NCLVB	National Control Laboratory for Vaccines and other Biologicals [Nigeria]
NMCP	National Malaria Control Program
NQCL	national quality control laboratory
	neglected tropical disease
	U.S. President's Emergency Plan for AIDS Relief
PIC/5	Phalmaceulical Inspection Co-operation Scheme
PIVIS PO	
	Promoting the Quality of Medicines
	nrequalification team
00	
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 2019, from January 1 to March 31, 2019.

Medical products are instrumental to any health system, but only if they are safe, effective, and quality assured. 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. In Q2, in Nigeria, the National Agency for Food and Drug Administration and Control's (NAFDAC) National Control Laboratory for Vaccines and other Biologicals (NCLVB) achieved ISO/IEC 17025:2005 accreditation of 14 test methods, including test methods for rapid diagnostic kits. PQM provided minimal technical assistance, as staff from NAFDAC's accredited laboratory in Yaba provided technical assistance to their NCLVB counterparts. NCLVB's accreditation positions the laboratory to provide quality and safety data for diagnostics developed locally or imported into the country to protect public health. In Ethiopia, to improve the guality management systems of the Ethiopian Food, Medicine and Healthcare Administration and Control Authority's inspection functions and processes, PQM supported the development of more than 16 standard operating procedures (SOPs): 3 of these were recommended to be used as guidelines, and 5 new SOPs were identified for development. The approval and implementation of these SOPs will contribute to the continual improvement of inspection practices, which will in turn facilitate progress toward international accreditation of the inspection function. In Uzbekistan, the Agency for Development of the Pharmaceutical Industry provided a draft selfassessment based on Pharmaceutical Inspection Co-operation Scheme (PIC/S) indicators. Based on the final selfassessment, gaps will be identified and a roadmap for PIC/S membership will be developed.

A continuous supply of quality-assured products is necessary to address national health priorities and plans. PQM works with manufacturers to improve compliance with international guality standards to meet local and global demand for guality-assured medicines. Since 2015, PQM has been providing extensive technical assistance to a manufacturer of clofazimine, an essential medicine for treating multidrug-resistant TB (MDR-TB) and a priority product for USAID. In Q2, the Global Fund's Expert Review Panel conducted a quality risk review and determined no objection to the manufacturer's clofazimine 100 mg soft capsules. This is a significant achievement, as clofazimine is very complex and challenging to develop, which has limited the number of manufacturers that produce it. This achievement ensures that a quality-assured generic product is now available on the market, and it is expected that increased competition should reduce the price of the product. Another PQM-supported manufacturer achieved World Health Organization (WHO) pregualification for a different essential medicine for treatment of MDR-TB, linezolid 600 mg tablet. In Indonesia. PQM has been providing technical assistance to a manufacturer toward WHO pregualification of its levofloxacin 500 mg tablets, which WHO announced as pregualified on February 22, making it the first Indonesianmanufactured anti-TB medicine to be pregualified. PQM also provided technical assistance to another Indonesian manufacturer to register a high-priority MNCH medicine, oxytocin injection, in Pakistan through WHO's Collaborative Registration Procedure mechanism. In addition, PQM supported manufacturers of two active pharmaceutical ingredients (APIs) for anti-TB products in Q2. In support of clofazimine API, PQM provided technical assistance to a manufacturer to draft the response for WHO prequalification assessment queries, which was submitted to WHO along with supporting documents. For rifapentine API, PQM visited two manufacturers to follow up on implementation of corrective and preventive actions for good manufacturing practices and on API Master File preparation.

Evidence-based decision-making 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. In Ethiopia, PQM continued building the capacity of the national pharmacovigilance center to improve its performance. PQM provided technical assistance in recording 273 adverse drug event reports into the pharmacovigilance data recording system, 53 of which were shared with the WHO Uppsala drug safety monitoring center. Based on an investigation conducted on the product following reported deaths at one referral hospital and informal complaints from others, the regulatory authority made the decision to take action on benzathine penicillin injection. A thorough investigation, including a causality assessment, was conducted, with a PQM staff member in attendance, to see whether the deaths were related to the benzathine penicillin batches in question. In parallel, quality control tests were

conducted on the product. The final decision was made based on the WHO scale of causality, which showed a possible causal relation with the deaths at the hospital. Finally, the regulatory authority recalled the batches, mandating the responsible bodies to collect the product from all over the country. This action is expected to save the lives of many who might otherwise have continued using the product.

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 toward lifesaving 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. PQM moved forward in terms of technology transfer of Umbipro (chlorhexidine digluconate gel 7.1%) from GSK to PQM and preparation of its transfer to interested manufacturers. Based on information and documents provided by GSK, the technology transfer report has been developed, and preparations are underway for a workshop on increasing access to quality-assured essential medicines through technology transfer to local manufacturers, with Umpibro as the case study.

One-sixth of the world's people—almost exclusively impoverished populations living in rural areas and urban slums of low-income countries—suffer from one or more NTDs. A major constraint to the effective scale-up of NTD control and elimination programs is the scarcity of quality-assured medicines suppliers and the limited number of products. PQM continues to support manufacturers to achieve prequalification of anti-NTD medicines, and preparation and implementation of all three PQM-supported bioequivalence studies are progressing well. One praziquantel finished pharmaceutical product (FPP) manufacturer completed bioequivalence dosing, initiated analysis, and will submit the interim report to PQM by the end of April 2019. A second praziquantel FPP manufacturer received bioequivalence protocol approval from the ethical committee, and the study is scheduled to start by mid-April 2019. The albendazole bioequivalence protocol for a pivotal study has been finalized and is under approval, tentatively scheduled to start by May 2019.

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).

This quarter, PQM implemented projects for 20 USAID country missions, 1 regional mission, 1 Cross Bureau program, and 3 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 2019 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 (QC) laboratories during the medicines registration process, when implementing corrective actions for poorquality 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 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 2019 Second Quarter IR1 Achievements

Key Results and Highlights

In Q2, the National Agency for Food and Drug Administration and Control's (NAFDAC) National Control Laboratory for Vaccines and other Biologicals (NCLVB) in Nigeria achieved ISO/IEC 17025:2005 accreditation of 14 test methods, including test methods for rapid diagnostic kits. Minimal technical assistance was provided by PQM, as staff from NAFDAC's accredited laboratory in Yaba provided technical assistance to their NCLVB counterparts to resolve all identified nonconformances. This approach is part of PQM's collaborative learning model, which promotes sustainability and self-reliance of laboratory activities. Given that many medical decisions are based on in vitro diagnostic test results, NCLVB's accreditation positions the laboratory to provide quality and safety data for vaccines (including bacille Calmette-Guerin (BCG) used for TB prevention) and diagnostics (e.g., HIV test kits, rapid diagnostic tests) developed locally or imported into the country to protect public health.

To improve the QMS of the Ethiopian Food, Medicine and Healthcare Administration and Control Authority's (EFMHACA) inspection functions/processes, PQM supported the development and implementation of different standard operating procedures (SOPs). More than 16 SOPs were reviewed and validated in a workshop conducted in Q2. During the review, three of the SOPs were recommended to be changed into guidelines, and five new SOPs were identified for development; PQM provided technical assistance in the development and final review for approval of the SOPs. The approval and implementation of these SOPs will contribute to the continual improvement of inspection practices, which will in turn facilitate progress toward international accreditation of the inspection function.

In Uzbekistan, the Agency for Development of the Pharmaceutical industry provided a draft self-assessment based on Pharmaceutical Inspection Co-operation Scheme (PIC/S) indicators. PQM reviewed the draft, and the next steps were agreed upon with the counterparts; PQM will review the provided QMS documents, then visit the country to work with the PIC/S working group to be established by the Agency for Development of the Pharmaceutical Industry and complete the self-assessment. Based on the self-assessment, the gaps will be identified and a roadmap for PIC/S membership will be developed.

Key IR1 Indicators for FY 2019 Q2

Number of QC laboratories accredited or reaccredited	1 (Nigeria)
Number of QC laboratories that have passed the proficiency test/inter- laboratory test	2 (Indonesia, Nigeria)
Number of sampling sites added for MQM/PMS activities by MRA	6 (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, NTDs, 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, stockouts, 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 medical 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 of 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 2019 Second Quarter IR2 Achievements

Key Results and Highlights

The Expert Review Panel (ERP) of the Global Fund determined no objection for clofazimine 100 mg soft capsules produced by Dong-A after quality risk review. This is a result of PQM's extensive technical assistance to the manufacturer, which began in December 2015 after PQM and Dong-A signed a memorandum of understanding. Clofazimine is an essential medicine for treating multidrug-resistant TB (MDR-TB) and a priority product for USAID. This is a significant achievement, as this product is very complex and challenging to develop due to its highly variable

characteristics. This complexity has limited the number of manufacturers that produce this product. This achievement ensures that now a quality-assured generic product is available on the market, and it is expected that increased competition should reduce the price of the product in the public health market.

PQM-supported manufacturer Celltrion achieved WHO PQ for its linezolid 600 mg tablet in Q2. Linezolid is also an essential medicine for treatment of MDR-TB.

In Indonesia, PQM has been providing technical assistance to manufacturer PT Kalbe Farma toward WHO PQ of levofloxacin 500 mg tablets. On February 22, 2019, WHO announced Kalbe's levofloxacin 500 mg as prequalified, making Kalbe the first Indonesian manufacturer to have a TB medicine prequalified. After levofloxacin was listed as a prequalified TB product, PQM facilitated a series of meetings with key stakeholders to prepare for a press conference with PT Kalbe Farma and USAID, as well as a meeting between PT Kalbe Farma and Global Fund ATM to discuss the local and global market opportunities.

In Q2, PQM also provided technical assistance to another Indonesian manufacturer, Sanbe Farma, to register a highpriority MNCH medicine oxytocin injection in Pakistan through WHO's Collaborative Registration Procedure (CRP) mechanism. With this activity, PQM pursues two goals: first, registering Sanbe Farma's oxytocin in Pakistan would ensure availability of the quality-assured product on the local market; secondly, this would be the first Drug Regulatory Authority of Pakistan (DRAP) product registered though the WHO CRP process, which would provide DRAP with experience to help in registration of other quality-assured products approved by WHO PQ or SRA.

PQM also supported manufacturers of two APIs for TB products in Q2. In support of clofazimine API, PQM provided technical assistance to a manufacturer to draft the response for WHO PQ assessment queries, which was submitted to WHO along with supporting documents. For rifapentine API, PQM visited two manufacturers to follow up on GMP corrective and preventive action (CAPA) implementation and API Master File preparation.

Key IR2 Indicators for FY 2019 Q2

Number of priority medicines that achieved WHO PQ, SRA, or ERP approval	3 (clofazimine, linezolid, levofloxacin)
Number of current or potential medicine shortages averted as the result of PQM's direct intervention	1 (clofazimine)
Number of approved site inspection report (FPP, API) received by a PQM- supported manufacturer from the local MRA	2 (Indonesia, Kazakhstan)

Number of Manufacturers Provided with Technical Assistance in FY 2019 Q2

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	3	magnesium sulfate injection, oxytocin injection, amoxicillin dispersible tablets (DT)
Core TB	8	clofazimine FPP, clofazimine API, rifapentine API, rifapentine FPP, kanamycin FPP, rifampicin/isoniazid/ethambutol/pyrazinamide tablets, linezolid FPP
Core NTD	4	praziquantel API, praziquantel FPP, albendazole FPP
Bangladesh	1	chlorhexidine solution
Ghana	1	artemether/lumefantrine tablets
Nigeria	8	zinc sulfate DT, sulfadoxine/pyrimethamine tablets, chlorhexidine gel, artemether/lumefantrine tablets, oxytocin injection, magnesium sulfate injection, ready-to-use therapeutic foods
Indonesia	3	levofloxacin, fixed-dose combination rifampicin 150 mg/isoniazid 75 mg, moxifloxacin
Kazakhstan	1	levofloxacin
Pakistan	6	amoxicillin DT, chlorhexidine gel, zinc sulfate DT
Uzbekistan	1	levofloxacin

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 QA, 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 QA 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 2019 Second Quarter IR3 Achievements

Key Results and Highlights

In Ethiopia, PQM has continued building capacity of the national pharmacovigilance center to improve its performance. In Q2, PQM provided technical assistance in the recording of 273 adverse drug event (ADE) reports into the pharmacovigilance data recording system, 53 of which were shared with the WHO Uppsala drug safety monitoring center. In Q2, one regulatory action was taken on benzathine penicillin injection. The decision was made based on an investigation conducted on the product following reported deaths at one referral hospital and informal complaints from others. A thorough investigation, including causality assessment, was conducted, with a PQM staff member in attendance, to see whether the deaths were related to the benzathine penicillin batches in question. In parallel, QC tests were conducted on the product. The final decision was made based on the WHO scale of causality, which showed a possible causal relation with the deaths at the hospital. Finally, a decision was made by the regulatory authority to recall the two batches. A letter was issued to responsible bodies to collect the product from all over the country. This action is expected to save the lives of many who might have continued using this product.

Key IR3 Indicators for FY 2019 Q2

Number of regulatory actions made by the MRA	1 (Ethiopia)
Number of PQM-supported awareness raising or advocacy events promoting quality of medical products	1 (Bangladesh)
Number of publications issued and presentations made on medical products quality assurance at national or international level that are presented or authored	2 (Indonesia, Cross Bureau)

Africa



Benin

I. Quarter 2 Highlights

PQM completed activity implementation in Benin in January 2019 and developed a final project report that was submitted to the Mission.

Burkina Faso

I. Quarter 2 Highlights

PQM completed activity implementation in Benin in February 2019 and developed a final project report that was submitted to the Mission.

Ethiopia

I. Quarter 2 Highlights

Regulating medicines import, distribution, and retail outlet networks is a key aspect of ensuring guality of medicines. In previous guarters, PQM supported EFMHACA to develop and implement an audit-based inspection system, including a manual and checklists. In Q2, PQM began supporting the inspection of medicine retail outlets in Addis Ababa. The inspection is expected to cover about 800 medicine retail outlets. In collaboration with the federal Ministry of Health (MOH), EFMHACA had a plan to identify model institutions involved in medicines import/distribution and retail. The goal is to identify those establishments that fully implemented good distribution and dispensing practices and acknowledge investments in quality services so that others can learn from them. PQM supported EFMHACA in the development of a guide for selection of model institutions and relevant checklists. In an effort to improve EFMHACA's QMS of inspection functions/processes, PQM supported the development and implementation of different SOPs. More than 16 SOPs were reviewed and validated in a workshop conducted in Q2: 3 SOPs were recommended to be changed into guidelines, and 5 new SOPs were identified to for development. PQM provided technical assistance in the development and final review for approval of the SOPs, which will contribute to the continual improvement of inspection practices and facilitate progress toward international accreditation of the inspection function. This is part of the larger effort to strengthen EFMHACA's inspectorate be able to conduct impartial inspections that are consistent with international best practices, which will eventually assist EFMHACA to become a PIC/S member.

In Q2, EFMHACA launched its electronic regulatory information system (eRIS) in the presence of Minister of Health H.E. Dr. Amir Aman, USAID representatives, and various other partners and stakeholders. The eRIS is a comprehensive software application that was developed to automate various regulatory functions, including medicine registration, inspection, and licensing. The system's modules include i-import, i-register, and i-license, which are designed to manage import, registration, and licensing operations, respectively. The tool is meant to achieve efficiency in institutional performance in those key regulatory functions and improve transparency by reducing manual operations and enhancing visibility in decision-making processes. PQM played a key role in the development of eRIS, providing technical assistance in mapping the processes, defining the requirements, developing new tools or updating existing ones in support of the automation, testing the software, training relevant staff and continually enhancing the system to improve its functions or accommodate emerging needs. PQM has continued to provide technical assistance in the different modules of the eRIS.

In response to a USAID request, PQM has been supporting EFMHACA in strengthening its pharmacovigilance system since mid-2017. In Q2, 273 ADE reports were entered into the pharmacovigilance data recording system, 28 of which were product defects., and 53 adverse drug reaction reports were shared with WHO Upsala drug safety monitoring center. Feedback in the form of acknowledgment letters were provided to 35 healthcare providers who actively reported ADR on continuous basis. In connection to reports on product defects, further investigation was initiated in communication with the inspection directorate on 13 medicines. In Q2, one regulatory action was taken on benzathine penicillin injection, when the regulatory authority decided to recall two batches of the product from all over the country. The investigation on this product was based on a death report following administration of the product, which ultimately indicated possible association. This decision is expected to save the lives of many who could have had the chance to use these products.

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 plans 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 became the 42nd country validated for MNTE. The joint mission from UNICEF and the WHO Africa Regional Office made the final validation assessment and noted 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 health products for Ethiopians.

III. Quarter 2 Progress by Objective

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

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

During the current year, as part of the Expediting Medicine Market Authorization Strategy 2017, which was developed with the PQM's support, EFMHACA wanted to use external human resources to reduce the backlog of dossier applications and thereby increase access to medicines. In support of this effort, PQM provided technical assistance to EFMHACA in creating pool of experts by providing relevant training in four rounds, two of which were provided Q2. The training was provided in two levels: basic and advanced dossier assessment. A total of 44 participants took part in the basic dossier evaluation training, 3 of whom were from EFMHACA. In the advanced dossier assessment training, 50 participants attended, 16 of whom were from EFMHACA. The rest of the participants in these trainings came from Schools of Pharmacy from different Ethiopian universities. EFMHACA had entered into a service level agreement with Jimma University to conduct the scientific assessment of dossiers and is in the process of doing the same with other selected academic institutions. PQM provided technical assistance in the design of the training program, preparation of training materials, and delivery of the training. Two PQM staff participated as trainers. EFMHACA covered the cost of all these trainings, indicating the commitment and preparedness of the authority to sustain some of the efforts in regulatory workforce capacity building, most of which were previously supported by PQM. The additional pool of expertise created through this training is expected to assist in speeding up review of dossiers in backlog. This in turn will improve the market authorization of new products, thereby contributing to increased access to essential medicines needed for addressing priority health challenges in Ethiopia.

With the goal of achieving international standards, EFMHACA has been working to strengthen its inspection functions. The QMS of inspection functions and processes has been identified as a critical area for improvement. Accordingly, EFMHACA, in collaboration with PQM, developed and implemented relevant SOPs. In Q2, a workshop was organized to validate and finalize the SOPs, and more than 16 SOPs were reviewed and discussed. During the discussion, three of the SOPs were recommended to be changed into guidelines, and five new SOPs were identified for development. PQM provided technical assistance in the development and final review of the SOPs, which will contribute to the continual improvement of inspection practices and facilitate progress toward international accreditation of the inspection function.

In Q2, EFMHACA officially launched eRIS in the presence of Minister of Health H.E. Dr Amir Aman. eRIS is a comprehensive software system that was developed to automate various regulatory functions, including medicine registration, inspection, and licensing. The system has different modules, including i-import, i-register, and i-license to manage the import, registration, and licensing operations, respectively. H.E Dr Amir Aman officially announced the launching of eRIS in the national event attended by representatives from various stakeholders and partners. The Minister, USAID representatives, JSI/AIDSFree representatives, and EFMHACA's Director General provided a keynote address highlighting the benefits of automating regulatory functions to achieve efficiency and transparency and improve access to information for decision-making in various aspects including those related to supply chain. The event, which included a demonstration of eRIS, received broad media coverage (both electronic and paper) and was attended by more than 110 participants from relevant government organizations, professional associations, civil societies, media, pharmaceutical manufacturers, importers, and development partners. PQM played a key role in the

development of eRIS from inception to its development, testing and implementation. We provided technical assistance in mapping the processes, defining the requirements, development of new tools or updating existing ones in support of the automation, testing the software, training of relevant staff and continued enhancement of the system to improve its functions or accommodate emerging needs. PQM was officially recognized by both the government client (EFMHACA) and the partner in charge of software development (AIDSFree) at the launching event for its contribution to the development and implementation of the system. EFMHACA used the event to popularize the new proclamation approved by the government to reform EFMHACA into the Ethiopian Food and Drug Authority (EFDA). In connection to this, a PQM staff member, along with a few other experts/officials, received special recognition by H.E Dr. Amir for their significant contribution to the current proclamation.

PQM has continued providing technical assistance in to implement the different eRIS modules. As part of implementing i-register, support included identifying gaps and offering suggestions for new features to improve systems performance and assistance to clients when they encounter problems while submitting applications through the system. Technical assistance was also provided in developing pharmaceutical facility licensing information system (i-license), which is a software solution for automating the licensing of medicine facilities. In relation to this application, system requirements, checklists, forms, certificates, process flows, and other related tools were developed. Subsequently, the system was developed, tested, retested, and made ready for implementation. The working group assigned for this task is chaired by PQM staff. The major accomplishments regarding development of this module (i-license) include:

- Following establishment of i-license task force, terms of reference were prepared for the taskforce.
- Different meetings were conducted, and consensus was established on how to proceed with developing the system.
- The situation was assessed, and the existing tools, tools to be updated/modified, and new tools to be developed were identified.
- System requirements were developed.
- Relevant checklists, certificates, application forms and notification letters were prepared.
- Process mapping was conducted, and licensing processes were optimized.
- Data cleaning is in progress.

While implementing eRIS and medicine registration guidelines, experts at the authority and PQM observed deficiencies when clients submitted applications for medicines registrations. Based on these observations, it was determined that training applicants in necessary. Accordingly, PQM supported the development of a training proposal and identified training topics in Q2. The training on medicine dossier submission compilation to clients (manufactures and importers) is planned to be provided in Q3.

On a related effort, based on a request from EFMHACA, PQM supported the development of the Medical Device Information System (MDIS). MDIS is meant to automate the import and registration of medical devices in the country. Technical assistance was provided in the system analysis, system requirement development, and actual development of the software system. The current processes for medical device registration were mapped and optimized. In addition, different checklists for screening and evaluating applications were developed. The import permit approval system for medical devices (i-import) was developed and implemented. The i-import for medical devices was launched, and a preliminary design of the medical device registration system was developed. The fullscale implementation of this system will improve the transparency and efficiency of registration and import of medical devices, thereby increasing access to quality products (including diagnostic test kits) in support of priority health programs.

PQM has long been engaged in building capacity for local production of medicines, which helped in the development and implementation of the GMP roadmap and National Strategy and Plan of Action (NSPA) for local pharmaceutical production. To realize the implementation of the GMP roadmap and NSPA, building the capacity of the regulatory authority to have a strong GMP inspection capability is critical. As part of this effort, PQM supported the development of the Pharmaceutical Manufacturer GMP Inspection Directive. This directive requires that inspectors be qualified to be nominated for inspection of manufacturing facilities. To meet the need for adequate and capable inspectors, PQM has supported EFMHACA in two ways: (1) PQM supported the development and administration of evaluation tools that can help EFMHACA select competent inspectors who meet the minimum requirements, and (2) PQM has continued providing technical support to EFMHACA in the creation of adequate pool of inspectors by training experts in the field. In Q2 only, PQM provided training to 256 experts selected from EFMHACA and other relevant sectors.

Regulating medicine import, distribution, and retail outlet networks are a key aspect of ensuring medicines quality. In line with this, in previous quarters PQM supported EFMHACA to develop and implement an audit-based inspection system. This practice involves rigorous inspection of all supply, inventory, and dispensing of related medicine transactions and helps to identify the presence of malpractice and illegal dealings that involve substandard and falsified medicines. Accordingly, a manual and checklists were developed for this purpose. In Q2, PQM began

supporting inspection of medicine retail outlets in Addis Ababa, which is expected to cover about 800 medicine retail outlets. EFMHACA collaborated with MOH to identify model institutions involved in medicines import/distribution and retail. The goal of this effort is to identify those establishments that fully implemented good distribution and dispensing practices and acknowledge investments in quality services so that others can learn from them. In this line, PQM supported EFMHACA in developing a guide for selection of model institutions and relevant checklists.

To effectively monitor medicines circulation in Ethiopia, EFMHACA has been working to establish systems on pharmaceutical products traceability. The authority has developed a pharmaceutical products traceability strategy and directives. With PQM's technical assistance, the Pharmaceutical Products Barcoding Guideline was prepared, and an internal review among the technical working group was conducted in Q2. EFMHACA is in the process transitioning to EFDA, and the new proclamation (number 1112/2019) is under publication. To implement the transition, a new institution must be established with mandates indicated in the proclamation. This requires new regulation to establish the new institution. In Q2, PQM provided technical assistance to prepare EFDA's establishment regulation.

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

During this planning period, PQM has continued supporting EFMHACA to maintain the accreditation of its QC laboratory and transit its QMS from ISO17025:2005 to ISO17025:2017, the updated version. In Q2, PQM provided training on the new standards to 17 staff from EFMHACA's QC laboratory. Moreover, PQM provided technical assistance in the development of relevant QMS documents as per the new standard. Critical documents, including a confidential policy, impartiality policy, and quality risk management SOP, were developed in Q2 as part of meeting the requirements for the new standard.

While providing support to strengthen the QC laboratory, PQM has also been working with EFMHACA toward transitioning the accreditation body from ANAB to ENAO, a local organization. To facilitate this transition, technical assistance was provided to prepare the EFMHACA laboratory for the final onsite assessment by ENAO. The assessment was already conducted, and EFMHACA is now working to meet ENAO requirements, some of which were new or not required by ANAB. As this transition was taking more time than anticipated, EFMHACA has already reapplied to ANAB for this year, and the complete transition is expected in the following year.

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

As part of supporting the PMS of antimalarial medicines, PQM provided essential supplies, including reference standards, high-performance liquid chromatography (HPLC) columns, and reagents in Q2. The supplies are distributed to each branch laboratory of EFMHACA where the quality testing will be conducted. PQM also conducted supportive supervisions at the four branch laboratories to mentor, build staff capacity, and fill gaps, if any, in preparation for testing of PMS samples. The involvement of branch laboratories in conducting PMS at full scale is a huge step forward for EFMHACA to expand its PMS capabilities and improve national coverage, which will help provide a better understanding of the national situation with regard to the circulation of substandard and falsified medicines. Following the supportive supervision and delivery of essential supplies, testing of the PMS samples has already been started and is expected to be completed in the coming 2 weeks. In addition to Ethiopia's regular PMS program, NQCL will conduct testing of all samples (156 samples of oxytocin injection, amoxicillin DT, and ampicillin suspension) collected form the six IGAD countries. The testing of samples has begun and is showing good progress. The joint PMS program being undertaken by the IGAD member states will serve as a good example of what can be done among countries with regard to implementation of the harmonization agenda that PQM has long been supporting.

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

Sub IR 2.1 Quality-assured priority medicines produced locally increased

During the past few years, implementation of NSPA has been a key priority of the Ethiopian government. Accordingly, EFMHACA was one of the institutions given responsibility to support its implementation. Therefore, there was a plan by EFMHACA to develop local capacity on GMP by providing training to at least 300 experts from relevant institutions. To implement this plan, training of trainers was provided in FY 2018. PQM has continued supporting scale-up training planned for this year. The scale up training is being provided in collaboration with the School of Pharmacy of Addis Ababa University. In Q2, training materials were developed, and training was provided to a total of 256 experts in 4 rounds (74, 58, 64, and 60 experts in each round). Two PQM staff members actively participated in providing the training. The cost of this training was fully covered by EFMHACA through Addis Ababa University based on a contract between the two institutions. The availability of this trained workforce will help advance proper implementation of the GMP roadmap and NSPA, thereby contributing to increased availability of quality-assured essential medicines produced by local manufacturers. The processes involved in this training program are unique in that the activity is contracted out to another local organization (Addis Ababa University), instead of EFMHACA doing it on its own. This process will help facilitate the building of capacity in another local organization that will continue providing technical assistance to EFMHACA in the future.

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

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

As part of strengthening the national pharmacovigilance system, PQM has provided technical assistance in the restructuring of the pharmacovigilance center, including the type and number of experts needed to fill essential positions and carry out the work. Technical assistance was also provided in developing a roadmap for the national pharmacovigilance center, which will help inform subsequent decisions to strengthen its funding, workforce, and systems.

PQM has also continued building the capacity of the national pharmacovigilance center. In Q2, PQM provided technical assistance in recording 273 ADE reports into the pharmacovigilance data recording system, and 53 ADE reports were shared with the WHO Uppsala drug safety monitoring center. Acknowledgment letters were provided to 35 healthcare providers who reported ADE on a regular basis. Of those 273 ADE reports, 28 were related to product defects, and further investigation was initiated on 13 medicines. In Q2, regulatory action was taken on one of the products. This is part of PQM's effort to build EFMHACA's capacity using the routine pharmacovigilance system to detect and/or prevent the circulation of substandard and falsified medicines. The regulatory actions taken on products following the evidence generated through the pharmacovigilance system will augment those efforts through PMS and inspection systems, thereby enhancing EFMHACA's overall capability to ensure patient safety.

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

In Q1, regulatory action was taken on benzathine penicillin injection. The decision was made based on an investigation conducted on the product following reported deaths a referral hospital and informal complaints from others. A thorough investigation, including causality assessment, was conducted, with a PQM staff member in attendance to see whether the deaths were related to the benzathine penicillin batches in question. In parallel, QC tests were conducted on the product. The final decision was made based on the WHO scale of causality, which showed a possible causal relation with the deaths at the hospital. Finally, a decision was made by the regulatory authority to recall the two batches. A letter was issued to responsible bodies to collect the product from all over the country. This action is expected to save the lives of many who might otherwise have continued using this product.

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

Activities under this objective were completed in previous quarters. There are no additional updates for Q2.

IV. Key Challenges

The continual changing of priorities at EFMHACA, one of PQM's key stakeholders, resulted in the postponement of some of the activities. With the approval of the new proclamation, EFMHACA is currently in a transition mode, potentially leading to additional delays to planned activities. Staff at key positions are changing and/or being reappointed with a different responsibility. In addition, restructuring of the organization is in progress, with a potential to temporarily disrupt existing progresses. PQM is working closely with EFMHACA to mitigate the challenges and complete activities on time.

V. Lessons Learned

During the current planning period, PQM encountered a significant reduction in funding, substantially reducing the ability to invest in implementation of activities. However, PQM was able to implement most of its activities due to resetting prioritization and leveraging funding from local partners. In addition, PQM's experience indicates that, with appropriate intervention and/or advocacy, local governments can significantly contribute resources to support program implementation as per the example of EFMHACA.

Ghana

I. Quarter 2 Highlights

The Ghana Food and Drug Administration (GFDA) continues to have discussions with MOH to address the quality of oxytocin injection on the Ghanaian market. The high-level consultations are aimed at ensuring that public sector facilities only procure GFDA-registered medicines. There are also plans for other regulatory actions, including the removal of failed medicines from the market.

II. Country Context

Malaria is a leading cause of morbidity and mortality in Ghana. The goal of the U.S. President's Malaria Initiative (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 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 artemisinin-based combination therapies 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

Following the PMS of oxytocin injections and ergometrine injections conducted in Q1, sample analyses were concluded in Q2 by the GFDA laboratory. Preliminary test results from the analysis indicate that analytical tests for assay were conducted on 85 of the 105 oxytocin injections samples collected and that 41.2 percent (35/85) did not meet specifications. For ergometrine, 11 samples were collected, 5 samples were tested, and 80 percent (4/5) did not meet assay specifications. These results represent significant failures. A detailed discussion of the results and subsequent regulatory actions taken by GFDA will be provided after GFDA issues the report of the surveillance in Q3.

It is worth noting that PQM has collaborated with GHSC-PSM, seeking a coordinated response to the observed failure of oxytocin injection in the supply chain in Ghana. These efforts are multifaceted, with PQM contributions focused on technical guidance based on PMS results and findings.

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

In line with ongoing technical assistance to local manufacturers in Ghana, PQM continues to provide technical assistance to Entrance Pharmaceuticals Limited (EPL), including technical reviews in Q2. A key item for EPL is the bioequivalence study for artemether/lumefantrine. PQM provided a review of the bioequivalence protocol, which has now been sent to the selected CRO for institutional review board and ethics committee approval prior to the start of the study.

From a project timeline perspective, EPL continues to experience unplanned delays. There were delays with obtaining approval for beginning the bioequivalence study, and the earlier delays related to importation of equipment have been completely resolved. Commitment from EPL management to address these issues is encouraging. Following a technical review meeting with EPL, the project timeline is further extended to allow for the conduct of the bioequivalence study (which is a required component of the dossier) and its results to be available. EPL is now expected to have its dossier submitted for WHO PQ by June 30, 2019.

Guinea

I. Quarter 2 Highlights

In Q2, PQM began key activities after a short hold due to changes in key leadership at Direction de la Pharmacie et du Médicament (DPM) and Laboratoire National de Contrôle des Médicaments (LNCM). The new leadership changed its priority from previously agreed-upon PMS and GMP to registration and import control. However, due to the short period of activity implementation before the PQM project in Guinea closes, the new direction was determined to significantly impact PQM's approved work plan. PQM management intervened and discussed the associated risks

with the USAID Mission and new leadership of DPM and LNCM. Following this intervention, PQM reached agreement with the Mission, DPM, and LNCM to complete planned activities of PMS and GMP inspection training.

Currently, the PQM team is working to develop and update the PMS protocol, conduct sampling and testing of antimalarial products, and train key DPM inspectors in GMP. Detailed accomplishments of these intervention will be provided in the next quarter, as these activities are ongoing at the start of Q3.

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 also helping to strengthen the country's 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 local pharmaceutical manufacturers and depends on importation for all required essential medicines. Proper registration of medicines is a necessary step to ensure that only quality-assured medicines are licensed and available in the market; in addition, registration fees generate 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 gaps and challenges identified.

III. Quarter 2 Progress by Objective

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

No updates for this quarter.

Objective 2 – Continue strengthening DNPL capacity in product registration

No updates for this quarter.

Objective 3 – Enable DNPL to assume MQM responsibilities

No updates for this quarter.

Objective 4 – Strengthen QC capacity of LNCQM

No updates for this quarter.

IGAD

I. Quarter 2 Highlights

Highlights in Q2 include the collection of samples from cross-border sites. Six Member States were able to collect samples from facilities identified based on risk assessments and as per the protocol developed by the IGAD– Medicines Regulatory Harmonisation (MRH) Expert Working Group on PMS with technical support from PQM during the workshop conducted in Q1. Samples were shipped to Ethiopia for testing at the EFMHACA laboratory.

II. IGAD Context

IGAD comprises eight countries in the horn of Africa region: Djibouti, Eritrea, Ethiopia, Kenya, Somalia, South Sudan, Sudan, and Uganda. The region experiences migration and cross-border mobility due to economic uncertainty and political conflicts. The cross-border mobile populations face major barriers to access of basic healthcare due to the complex sociopolitical dynamics of the public health system in the context of migration and cross-border mobility. IGAD hopes to reduce regional health disparities and risks associated with cross-border mobility of people through interventions to reduce maternal and child morbidities, improve unmet demand for family planning among women and girls, prevent outbreaks of communicable diseases, prevent and control TB and HIV, monitor the safety and quality of medicines, and reduce and control the movement of substandard and falsified medical products.

The IGAD Health and Social Development division has sought to implement an MRH for the horn of Africa in line with the vision and goals of the African Medicines Regulatory Harmonization initiative. With funding from USAID/East Africa Regional, the PQM program will implement targeted interventions, including establishment of an EWG to identify pharmacovigilance/PMS document gaps, provide recommendations for implementation of pharmacovigilance/PMS activities in the region, and facilitate a survey to determine the prevalence of substandard and falsified medicines at selected cross-border sites to inform future interventions. Details of the planned activities are delineated in the approved PQM work plan.

The activities of the PQM work plan were adopted from the proposed IGAD health program activities and align with IGAD's strategic interventions #1 and #3: (#1) To institutionalize a system for monitoring safety and quality of medicines used at IGAD cross border points, and (#3) Develop and institutionalize IGAD regional cross-border health policies and sector-specific strategies on RMNCH, MRH, TB, and HIV/AIDS. These IGAD strategic interventions are aligned to two of the three Development Objectives (DOs) of USAID's Regional Development Cooperation Strategy, 2016–2021: Improved management of risks that transcend borders (DO2) and East African institutions' leadership and learning strengthened (DO3).

III. Quarter 2 Progress by Objective

Objective 1 – Establish a Regional Expert Working Group (PV/PMS-EWG) on Pharmacovigilance and Post Market Surveillance

No activity to report this quarter.

Objective 2 – implement a survey to determine the prevalence of Substandard and Falsified (SF) medical products used in the MCH-FP/TB/HIV-AIDS at selected IGAD cross-border areas

In continuation of activities to implement regional PMS, sample collection was facilitated in Q2. IGAD-MRH and PQM experts facilitated the collection of samples by regulators in respective member countries. Although sample collection was delayed due to logistical challenges (availability of funds and scheduling), six Member States collected 153 samples as of March 2019. The table below illustrates the number of samples collected during the sampling exercise.

Country	Oxytocin injection	Amoxicillin DT	Amoxicillin suspension
Djibouti	2	0	0
Ethiopia	14	12	2
Kenya	22	4	12
Sudan	13	0	9
Uganda	26	14	3
Somalia	10	6	3
Total (153)	87	37	29

All samples were subsequently shipped to EFMHACA laboratory for analysis. The analysis results are expected in Q3. Expert Working Group workshops to validate and disseminate the results are planned for Q3 as well.

Objective 3 – IGAD Cross-border draft health policy developed and shared with stakeholders

PQM followed up with the IGAD-MRH secretariat on this activity. Per the work plan, PQM is expected to provide a technical review of the portion of the draft health sector policy that addresses the pharmaceutical sector. Based on communication with the IGAD-MRH secretariat, a consultant to prepare the draft health policy is in the process of

being recruited. PQM has communicated the urgency for this activity, taking into consideration the program's period of performance, and continues to liaise with IGAD.

Kenya

I. Quarter 2 Highlights

In Q2, the suspension on activity implementation was lifted, and the FY19 work plan was approved by the Mission. PQM conducted an initial implementation planning visit to the country, when it was able to revitalize the PMS/Pharmacovigilance Technical Working Group, and also engaged Kisimu and Kissi counties in PMS planning and implementation. Subsequent activities and events are planned in the coming months. PQM also initiated the procurement of laboratory supplies needed for the upcoming PMS direct implementation.

II. Kenya Context

USAID funding is provided for health systems strengthening interventions, including strengthening of the health workforce, the health information system, and supply chain management for HIV/AIDS, malaria, and family planning materials. In this context, PQM has been engaged to help strengthen the pharmaceutical regulatory system and to improve medicines quality. Kenya and other countries in Africa are disproportionally affected by the burden of poor-quality medicines. The best way to combat this public health challenge—and to increase the impact of other interventions in the malaria, TB, HIV/AIDS, and MNCH programs—is to strengthen the national regulatory authority to ensure that medicines are properly registered and tested, and MRAs take corrective regulatory actions related to substandard or falsified products and unlicensed pharmaceutical outlets. These interventions are aligned with Kenya's overall strategy of attaining sustainability of established capabilities by strengthening the country's institutions as well as fostering regional cooperation.

Liberia

I. Quarter 2 Highlights

In Q2, PQM continued to provide capacity-building assistance to the laboratory and helped the Liberia Medicines and Health Products Regulatory Authority (LMHRA) redesign its newsletter in terms of content and appearance. PQM also began planning for a joint closeout meeting that will follow the upcoming LMHRA dissemination meeting in the first week of May 2019.

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 international partners, the NMCP has made significant efforts to scale up malaria prevention interventions as well as improve public–private partnership to increase access to quality-assured 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 the appropriate regulatory actions when poor-quality medicines are identified. As a result of 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 been subsequently banned through a regulatory action by LMHRA and since then have become less prevalent. Although results from various MQM activities and subsequent regulatory actions have been encouraging, the data continue to show that falsified and substandard medicines are still a major concern in Liberia.

PQM activities in Liberia are focused on:

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

As part of the approved work plan, PQM provides technical assistance toward building the QC capacity of the existing LMHRA QC laboratory and attaining compliance with international standards (ISO 17025), strengthening and expanding quality monitoring of antimalarials, promoting regulatory actions when falsified and substandard medicines are identified, and increasing awareness about the quality of medicines.

III. Quarter 2 Progress by Objective

Objective 1 – Rebuilding capacity of LMHRA QC laboratory

PQM supported LMHRA's QC laboratory to transition to a temporary facility and provided assistance during the installation of laboratory equipment procured with World Bank funding. During a site visit on February 25–27, PQM staff engaged in the following activities:

- Assisted the laboratory in developing risk management safety measures and SOPs to be implemented during their routine activities. This process is critical for the safety of the laboratory and its personnel and will help prevent another fire incident.
- Through a donation from USP, provided the motherboard for the HPLC's computer, which was needed to run the equipment.
- Followed up with the laboratory on the status of the QC testing of medicines as part of the LMHRA fixed amount award (FAA).
- Conducted 1-day monitoring of the screening of samples that were collected as part of the FAA activities.

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

No updates for this quarter.

Objective 3 – Build LMHRA capacity to take appropriate regulatory actions

No updates for this quarter.

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

No updates for this quarter.

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

To improve the dissemination of regulatory actions and raise awareness about poor-quality medicines, PQM has been assisting LMHRA to redesign its newsletter in terms of content and appearance. During this quarter's site visit, PQM conducted the following activities:

- Shared with LMHRA an enhanced, user-friendly format that includes information aimed at raising awareness about poor-quality medicines.
- Shared the electronic format and provided guidance on how to display content and photos of regulatory actions taken by LMHRA.
- Shared with LMHRA samples of newsletters and various costs of printing.

Upon completion, LMHRA adopted the newsletter provided by PQM.

IV. Key Challenges

The implementation of the work plan saw some delays due to transition of management within LMHRA and a delay in the laboratory receiving the new equipment procured by the World Bank.

Mali

I. Quarter 2 Highlights

All major work plan activities were completed in the last quarter. An ongoing FAA with the University of Bamako (USTTB) for a study of resistance of antimalarial medicines is ongoing and will be closed by the end of July 2019. The final project report will be submitted at that time.

Mozambique

I. Quarter 2 Highlights

In Q2, PQM continued to provide technical assistance to the National Directorate of Pharmacy (DNF) and Laboratório Nacional de Controlo da Qualidade de Medicamentos (LNCQM) to build capacity and strengthen QA systems to protect public health. PQM worked with DNF staff to update the PMS protocol, which was necessary after the natural disaster in Sofala province prompted the selection of a different province for sample collection based on established risk criteria. PQM also supported procurement of "office in a container" additional space to promote GLP and procurement of reagents, equipment parts, and Minilab™ replenishment kits for a planned PMS exercise in Q3.

II. Country Context

PQM has been providing technical assistance to Mozambique since 2010. Activities have focused on strengthening the QA/QC capabilities of Mozambique's MRA, the pharmacy department (PD). In 2016, PD and MOH updated the pharmaceutical law of Mozambique, which transitioned the MRA from PD to DNF. The law was approved by the Parliament in early 2017 and signed by the President in September 2017.

PQM conducted a rapid assessment of PD's QA/QC capabilities in December 2010, which revealed that LNCQM's infrastructure, equipment, and staff were inadequate to provide required QC services. The assessment also identified a lack of medicines quality PMS. 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 aware of the country's vulnerability and exposure to poor-quality medicines. This new legislature, including Article 4 (which addresses quality), offers a great opportunity for PQM and other supporting partners to make long-lasting contributions to strengthen medicines regulation and eliminate substandard and falsified products.

III. Quarter 2 Progress by Objective

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

In Q2, PQM supported LNCQM to procure and install "offices in a container" to supplement the current laboratory work space. This great stride will help LNCQM achieve an ideal work flow that would meet specification for GLP and sets the stage for LNCQM to meet an international standard, ISO17025 accreditation. It was necessary to address the problem of space constraints faced by LNCQM, which required staff to sit in the same open space where medicine sampling and testing was carried out. With procurement of this additional space, staff can be relocated and the laboratory rearranged to improve work flow and promote better quality services.

PQM also supported procurement and shipment of reagents required for LNCQM to perform their statutory roles of testing medicines (pre- and post-market) to ensure only quality-assured medicines are available and circulating in Mozambique.

Objective 2 – Support and strengthen post-marketing surveillance

As a result of the cyclone Idai natural disaster that affected Sofala province, the draft protocol developed for the planned medicines surveillance exercise was revised to substitute Sofala with another province for sample collection. The selection of the next province with the highest risk for poor-quality medicines was determined using Medicines Risk-based Surveillance (MedRS), a tool that contains a set of criteria for determining medicine risks to support selection of what medicines, what geographical locations and what outlets to collect medicine samples. The province selected to replace Sofala was Niassa. The sample collection is planned for next quarter.

PQM also procured and shipped reagents and supplies required for levels 1–3 PMS testing, including reference standards, equipment parts, and Minilab[™] replenishment kits required for planned PMS sampling and testing.

Objective 3 – Provide technical assistance to the Pharmaceutical Department

In Q2, PQM continued to follow up and provide technical support to DNF's PMS team. In an effort to build capacity and promote country ownership and self-reliance, DNF led the development of the risk-based PMS protocol with technical support from PQM. The PMS unit, under DNF's pharmacovigilance department, was recently established after the new pharmaceutical law was promulgated. PMS had previously been under LNCQM, which was not properly equipped to carry out follow-up activities outside of sample testing to ensure appropriate actions are taken to remove medicines that do not meet minimum standard requirements from the market. Upon PQM's advice, the PMS unit was established under DNF to better address this gap. PQM built the capacity of DNF on risk-based PMS principles and worked closely with the team to plan and coordinate the entire activity. PMS implementation is planned for Q3.

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

Activities under this objective were completed in Q1.

Nigeria

I. Quarter 2 Highlights

PQM continues to provide technical assistance to strengthen regulatory system functions in Nigeria. Integral components of PQM technical support includes strengthening NAFDAC's NQCL to raise laboratory standards; strengthening local manufacturers' capacity to attain international GMP standards necessary for the supply of quality medicines; strengthening NAFDAC's PMS function to remove poor-quality and substandard products from the market; and reinforcing the use of data for public health impact.

Highlights in Q2 included:

- NAFDAC's National Control Laboratory for Vaccines and other Biologicals (NCLVB) achieved ISO/IEC 17025:2005 accreditation of 14 test methods, including test methods for rapid diagnostic kits.
- Two other NAFDAC laboratories renewed their accreditation status and migrated to new ISO 17025:2017.
- Test results of sampled antimalarial medicines concluded; showing 1.3 percent failure (12 samples failed).
- Assessment of all pharmaceutical manufacturing facilities in Nigeria concluded. Analysis of the collated findings is ongoing.

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 antimalarial medicines to support PMI's overarching goal to reduce malaria-associated mortality in Nigeria by 50 percent.

Through Maternal and Child Health funding, USAID/Nigeria is also working to increase the availability of medicines for MNCH in support of the UN Commission on Life-Saving Commodities for Women and Children, established in April 2012 to improve access to affordable 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 Commission recommended 13 essential health commodities for women and children that it considered will have the greatest impact on achieving health-related UN Sustainable Development Goals.

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

III. Quarter 2 Progress by Objective

Objective 1 - Strengthen national quality assurance and regulatory systems

NAFDAC completed testing of samples collected in FY18 as part of its PMS program in Q1. In Q2, compilation of the findings was completed. Findings for antimalarial medicines sampled and tested indicated that five samples of sulfadoxine/pyrimethamine tablet; two samples each of artemether/lumefantrine, quinine, artesunate tablets; and one sample of artesunate amodiaquine did not meet quality requirements. The total percentage of antimalarials sampled and tested that failed QC tests was 1.3 percent.

Product	# samples tested	# samples passed	# samples failed	% failure
Artemether/lumefantrine	421	419	2	0.5
Artesunate/amodiaquine	134	133	1	0.8
Sulfadoxine/pyrimethamine	195	190	5	2.6
Quinine	76	74	2	2.7
Dihydroartemisinin/piperaquine	41	41	0	-
Artesunate	24	22	2	9.0
Mefloquine	1	1	0	-
Pyrimethamine	3	3	0	-
Arterolane + piperaquine	3	3	0	-
Artesunate + mefloquine	4	4	0	0
Proguanil + chloroquine	1	1	0	-
Proguanil	1	1	0	-
Artemisinin + piperaquine + primaquine	1	1	0	-
Artesunate + sulfadoxine/pyrimethamine	1	1	0	-
Amodiaquine	1	1	0	-
TOTAL	907	895	12	1.3

Of the samples that failed, 78 percent were imported, 21 percent were locally manufactured, and less than 1 percent had no country of manufacture. NAFDAC has planned regulatory measures for all failed samples. Recall of the products from the market, further investigative inspections, and regulatory measures on the manufacturers are among planned measures discussed during the dissemination of the results to key stakeholders in Q2. In attendance were a WHO representative, Pharmaceutical Manufacturers Group of Manufacturers Association of Nigeria (PMGMAN) members, the Chairman of the National Association of Community Pharmacist of Nigeria, representatives from the Food and Drug division of the federal MOH, and others. Updates on regulatory actions and findings from FY18 PMS for maternal and child health medicines will be available next quarter.

In line with Nigeria's FY19 work plan activity, the last round of PMS of antimalarial medicines commenced in Q2 with sampling of 1,050 samples of antimalarial medicines from 6 states and the federal capital territory. Analysis of sampled antimalarial products will be completed next quarter.

Objective 2 – Capacity for medical products' quality assurance workforce sustainably improved

Last quarter, PQM conducted a mock audit of NAFDAC'S NCLVB using the ISO/IEC 17025:2005 audit checklist ahead of a third-party audit of the laboratory by ANAB. In Q2, NCLVB achieved ISO/IEC 17025:2005 accreditation of 14 test methods, including test methods for rapid diagnostic kits. Minimal technical assistance was provided by PQM, as staff from NAFDAC's accredited laboratory in Yaba provided technical assistance to their NCLVB counterparts to resolve all identified nonconformances. This approach is part of PQM's collaborative learning model, which promotes sustainability and self-reliance of laboratory activities. Given that many medical decisions are based on in vitro diagnostic test results, NCLVB's accreditation positions the laboratory to provide quality and safety data for vaccines

(including BCG used for TB prevention) and diagnostics (e.g., HIV test kits, rapid diagnostic tests) developed locally or imported into the country to protect public health.

The NQCL in Kaduna and NIPRD both achieved ISO/IEC 17025:2015 accreditation in FY18 and retained the accreditation status in Q2. Following the training conducted for all PQM-supported accredited laboratories to upgrade their status of accreditation to International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) 17025:2017, both laboratories successfully upgraded to the new ISO/IEC 17025:2017, and official certification will be granted next quarter. Equipment calibration for both laboratories was done by a local calibration company, NQA&CA. The engagement of a local calibration company had a positive effect on the cost of calibration. Also, most associated costs for the reaccreditation of the NAFDAC Kaduna laboratory, including logistics, were paid for by NAFDAC without financial support from PQM.

Objective 3 – Supply of quality-assured priority medicines produced locally increased

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 develop and submit dossiers for WHO PQ. PQM also provides technical assistance and guidance to manufacturers for the local production of medicines, which may decrease reliance on international donation and help establish a sustainable local supply with national resources.

In line with the work plan, activities in Q2 centered on providing technical assistance to a local manufacturer toward WHO PQ of two products (oxytocin injection, magnesium sulfate) and to local manufacturers interested in products of interest (zinc sulfate tablet, oral rehydration salt, chlorhexidine, amoxicillin DT, artemether/lumefantrine, oxytocin injection, magnesium sulfate injection, and ready-to-use therapeutic food). PQM provided technical support to eight local manufacturers in Q2.

Last quarter, PQM GMP team provided technical assistance to Juhel Pharmaceuticals in the update of data for its oxytocin dossier. The updated oxytocin dossier was submitted to the East African Community dossier assessment team in Q2. The PQM GMP team will continue to monitor the accelerated study for more data after the conduct of photosensitivity and bacteria retention tests for both magnesium sulfate and oxytocin injections in preparation for submission to the WHO PQ team (PQT).

PQM provided continuous tailored technical assistance to Emzor Pharmaceuticals to produce quality-assured sulfadoxine/pyrimethamine. The Medical Export Group (MEG), an international distributor, visited Emzor to discuss prospects for increased procurement of sulfadoxine/pyrimethamine and other products of public health interest. Emzor management indicated its capacity to meet the increased volume, and 2 million doses of sulfadoxine/pyrimethamine were delivered to MEG in Q2. The PQM GMP team will continue to provide technical assistance to prepare for production of batches of artemether/lumefantrine that will be used to monitor stability at the new facility recently built by Emzor.

Last quarter, PQM Nigeria collaborated with NAFDAC to commence a countrywide assessment of pharmaceutical manufacturing facilities in Nigeria. The third phase of the inspection was concluded in Q2, with the inspection of 133 pharmaceutical companies. As part of planned mitigation of noncompliances observed during the assessment, PQM organized a meeting with the Director of NAFDAC's Drug, Evaluation and Research directorate to discuss a CAPA plan for the local manufacturers. A key outcome of the meeting included plans to organize a 2-day CAPA training for all active pharmaceutical manufacturers in the three geopolitical zones of the country simultaneously next quarter to help manufacturers identify gaps and take corrective measures to address them. Comprehensive assessment findings for the GMP roadmap activity will be disseminated to key stakeholders next quarter.

Other activities included:

- As part of ongoing technical assistance to Swipha, PQM followed up on the registration of zinc sulfate DT with NAFDAC and monitored progress on other priority medicines (artemether/lumefantrine and sulfadoxine/pyrimethamine).
- PQM provided technical assistance to May & Baker on the stability study of reformulated artemether/lumefantrine (currently in its 15th month).
- Following the successful partnership of Nemel Pharmaceutical Limited and MCSP (completed USAID funded program targeted at reduction of newborn and maternal mortality), a partnership facilitated by PQM, the company has continued to replicate the model to increase access to quality-assured amoxicillin DT for newborn babies in the rural and semi-urban communities through trained proprietary patent medicine vendors (non-pharmacist managed drug shops). For 3 years, PQM provided technical assistance to Nemel to produce NAFDAC-approved quality-assured amoxicillin DT. The government of Cross Rivers state in southern Nigeria made a procurement request for 14,000 doses of amoxicillin DT.

Objective 4 – Utilization of medical product quality information for decision making by regulatory and academia increased

PQM Nigeria attended a meeting with the new leadership of the Pharmaceutical Society of Nigeria (PSN). The objective was to acquaint the new leadership on accomplishments in the pharma space as a result of USAID's contributions through the PQM program in Nigeria. The PSN president applauded PQM's achievements, particularly in the field of local manufacturing in Nigeria. He expressed the need for more collaboration as the institution's agenda gears toward a roadmap for a sustainable and prosperous pharmaceutical sector in Nigeria. The visit helped bring forward burning issues surrounding the quality of medicines in the Nigeria.

USAID/Nigeria and PQM, along with other stakeholders (including WHO, UNICEF), received merit awards for their outstanding support to strengthen NAFDAC and medicines QA in the country to protect public health. The award was presented during NAFDAC's 25th anniversary celebration at the Presidential Villa in Abuja. The event was attended by Nigeria's First Lady, Aisha Buhari; First-Class King Ooni of Ife, Oba Adeyeye Ogunwusi; past NAFDAC Directors General; and others.

Senegal

I. Quarter 2 Highlights

During a February 18–22 site visit, PQM staff reviewed the FAA activities carried out by LNCM as part of the riskbased PMS protocol. PQM also assisted DPM in developing a communication campaign about substandard medicines. As PQM Senegal activities will finish in FY19 Q3, PQM has begun closing out the project.

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 August 2015, PQM collaborated with DPM, the regulatory authority, to organize 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 other 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 participated in 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's QC capacity, 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 that led staff members not to fulfill their assigned duties; insufficient numbers of laboratory staff with the technical capacity to conduct QC testing of medicines according to compendial methods; 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 fully employed personnel, as opposed to contractual staff, which led to high turnover; periodic turnover and restructuring; 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, the 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

Nothing to report this quarter.

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

During a February 18–22 site visit, PQM staff completed the following:

- Reviewed the FAA activities carried out by LNCM as part of the risk-based PMS protocol.
- Conducted a desk review of the FAA milestones' supporting documents.
- Visited the LNCM Dakar site to observe sample collection and testing.
- Facilitated the preparation of the next phase post-submission of LNCM results to DPM. The sampling phase started late because of the presidential campaign.

Objective 3 - Support DPM in improving its regulatory functions

During the February 2019 site visit, PQM staff facilitated a meeting with the National Committee, DPM Director, and representatives from the National Service of Education and Information (SNEIPS). The main outcomes of the meeting included agreement on the location of the upcoming campaign (Touba city) and the activities to be conducted.

Sierra Leone

I. Quarter 2 Highlights

In Q2, PQM conducted an assessment of the Pharmacy Board of Sierra Leone (PBSL)'s ability to effectively support functions and processes that ensure the quality of medicines in the country. An in-depth assessment of the National Pharmaceutical Quality Control Laboratory (NPQCL) was conducted to identify areas for improvement to support development of a roadmap toward ISO 17025 accreditation. The WHO Global Benchmarking Tool (GBT) was utilized for this assessment, along with PQM's *Medicines Regulatory, Quality Assurance and Quality Control Systems Assessment Tool* (MRAT) for PBSL. Also utilized were PQM's Stepwise Assessment Tool towards Accreditation (SATTA), which measures laboratory capacity against the requirements for ISO 17025 and WHO PQ, and PQM's Laboratory Capacity Maturity Model (LCMM) tool, which assesses laboratory staff knowledge and skills for basic, intermediate, and advanced analytical testing techniques.

Data analysis and assessment report development is underway.

West Bank and Gaza

I. Quarter 2 Highlights

In January 2019, PQM completed activity implementation in West Bank and Gaza and developed a transition plan that was submitted to the Mission.





Bangladesh

I. Quarter 2 Highlights

Highlights of PQM's activity in Bangladesh during Q2 included the following:

- PQM assisted National Control Laboratory (NCL) management to develop an action plan to identify gaps based on the WHO assessment and subsequently provided guidance and technical know-how to address the gaps. From February 25 to 27, two WHO auditors and two observers conducted a peer audit at NCL, and their feedback was positive. PQM local experts participated in the peer audit to look at the issues raised by the auditors, which will help PQM to support NCL in developing CAPA against the observations. This will ultimately help NCL to sustain the ISO 17025 standard and move toward the WHO PQ process.
- PQM assisted the Directorate General of Drug Administration (DGDA) and NCL in developing SOPs, key documents, and CAPA implementation. In Q2, four new SOPs were developed and implemented at NCL, and four were revised. PQM also assisted in following up on 65 CAPAs, which had been generated from the observation of WHO interim benchmarking assessment held on September 16–20, 2018.
- PQM continued supporting DGDA's PMS committee to implement risk-based PMS and facilitate the development of a risk-based PMS guideline. Implementation of the guideline will ensure effective use of data for evidence-based decisions for public health impact. On March 25, one PQM expert conducted a review session on risk-based PMS approach with DGDA's committee and NCL staff to finalize the guideline for Bangladesh. Agreed-upon comments and recommendations were added to the guideline. DGDA Director General Major General Md. Mustafizur Rahman acknowledged the guideline as final. DGDA has also taken proactive steps to explore funding opportunities for activities such as Minilab[™] procurement and setup at district-level offices to strengthen the screening and monitoring of PMS samples toward regulatory actions.

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, as well as discussions and consultations with the USAID Bangladesh Mission, DGDA, SIAPS, and other relevant partners/stakeholders.

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/input to NCL to strengthen its QMS toward attaining compliance with international standards, and NCL recently was accredited for the ISO/IEC 17025:2017 standard. PQM is working to maintain this accreditation standard and to also move forward with the WHO PQ accreditation process.

PQM is working alongside NCL management and technical staff to follow up on the progress of the CAPA plan, which was developed based on the findings from the internal audit and recently conducted peer audit by the WHO assessor. In Q2, CAPAs were addressed and ongoing support was provided to close several of them.

With the assistance of PQM technical staff in Bangladesh, NCL continued to develop SOPs to improve internal processes to sustain its ISO 17025:2017 standard and move forward with WHO PQ. PQM also provided support to review calibration reports; out-of-specification, deviation, and change control reports around investigations; root cause analysis; risk assessment; action plans; and logbooks. The following are some key accomplishments in Q2:

- PQM continues to support NCL to sustain its QMS and QA/QC systems. In Q2, PQM assisted NCL
 management to develop an action plan to identify gaps based on the WHO assessment. PQM provided
 guidance and technical know-how to resolve the issues. On February 25–27, two WHO auditors and two
 observers conducted a peer audit at NCL and provided positive feedback. PQM local experts participated
 in the peer audit to fully understand the identified issues and develop CAPAs in order to help NCL sustain
 the ISO 17025 standard and move forward with the WHO PQ process.
- In October 2018, NCL Dhaka achieved ISO/IEC 17025:2017 accreditation from ANAB. To maintain its
 recently achieved ISO accreditation status as well as to apply for WHO PQ, NCL will continue to perform

proficiency testing (PT)/inter-laboratory testing (ILT). This will allow for the continued assessment of NCL staff competency to perform testing. As part of PT/ILT support, PQM provided three PT for its microbiology laboratory and one ILT for the chemical laboratory. With PQM assistance, NCL staff will complete this testing in April 2019.

On March 3–6, DGDA and USP jointly organized the 5th Annual Asia chapter of Network of Official Medicines Control Laboratories (NOMCoL) technical workshop in Bangladesh. At the inauguration ceremony, keynote remarks were provided by Md. Ashadul Islam, Health Services Division Secretary, MoHFW; Caroll Vasquez, USAID OPHNE Director; and Dr. Emily Kaine, USP-GPH SVP. Other distinguished guests from PQM, DGDA, the Bangladesh Association of Pharmaceutical Industries (BAPI), WHO, and member countries were also in attendance. All participants agreed on the importance of this network, which serves as a platform to resolve shared challenges in QC testing, report on national and international advances, and exchange data, insights, and lessons learned for member countries. Twenty-four technical and metrology staff from member countries and Bangladesh, along with local PQM technical staff, attended the technical session of the workshop. The countries represented in the workshop included Bangladesh, Laos, Nepal, Papua New Guinea, Sri Lanka, Thailand, and Myanmar. During the technical session, all the participants were updated on the recent developments in relation to QMS, data integrity, uncertainty measurement, analytical instrument qualification, computer systems validation, equipment and software validation processes, balance performance verification, and pH calibration.

Summary of Key Laboratory Documents Developed, Reviewed and CAPA Progress from January to March 2019				
Items Number of Items completed				
Approved and implemented new SOP through PQM review	 Four (04): Operation, cleaning and calibration of Refractometer, Operation and monitoring of Cascada Water Purification system, Operation, cleaning and calibration of Fume hood, Operation, cleaning and calibration of Hardness tester 			
Revision of SOP	 Four (04): Analytical method validation Purchase, receipt, store, handling and disposition of all materials using for analysis Vendor qualification & listing in NCL Preparation and maintenance of mobile phase and solutions 			
CAPA status in Q2 FY19:				
An internal audit was conducted on October 28-30, 2018 and 10 CAPAs were developed	7 (6 - in Q1 FY19: & 1 - in Q2 FY19): 3 in development process			

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

As of February 2019, of the seven manufacturers selected by BAPI, only ACI Limited has shown interest in producing first-line anti-TB drugs with the WHO PQ standard. Techno Drugs Limited (which is not on the BAPI list) has also shown interest in producing first-line anti-TB drugs. Techno Drugs has written letters to BAPI and DGDA expressing its interest in WHO PQ and PQM technical assistance to achieve the standard. Both companies have submitted their expressions of interest (EOIs) through providing an initial evaluation questionnaire as part of PQM's evaluation of the company's readiness for participation in the PQM program. The initial evaluation questionnaire determines the eligibility and readiness of the manufacturer to participate in this program. On March 19, DGDA invited a PQM HQ expert to visit Bangladesh to conduct GMP gap assessments of the two companies' facilities.

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

Several activities were implemented to enhance DGDA's regulatory capacity. These include strategic planning, monitoring and evaluation of its functions, capacity building of human resources, and improved PMS. PQM Bangladesh staff continued to support DGDA functions, providing guidance and review of developed SOPs and guidelines.

- To strengthen DGDA's MQM, PQM continued supporting DGDA's PMS committee to implement risk-based PMS and facilitate the development of a risk-based PMS guideline to enable sustained efforts on the use of data for evidence-based decisions for public health impact. On March 25, one PQM HQ expert visited Bangladesh and conducted a review session on risk-based PMS approach with DGDA's committee and NCL staff toward finalizing the guideline. At the meeting, agreed-upon comments and recommendations were added to the guideline. DGDA Director General Major General Md. Mustafizur Rahman acknowledged the guideline as final. DGDA has taken proactive steps to explore funding opportunities for activities, such as Minilab[™] procurement and setup at the district-level offices, to strengthen the screening and monitoring of PMS samples, which will support improved enforcement through regulatory actions.
- PQM staff continued to assist DGDA in addressing the CAPAs based on the WHO interim benchmarking
 assessment observations and recommendations by the WHO assessor from September 2018. A total of 65
 CAPAs were raised in relation to the observations of the 5 regulatory functions (regulatory inspection,
 marketing authorization, clinical trials oversight, laboratory testing, and lot release), and PQM has been
 providing technical assistance to address these CAPAs. The closure of CAPAs has strengthened DGDA's
 regulatory functions over time and helped it move toward the WHO Maturity Level III benchmark.

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

PQM continues to facilitate the development of National Quality Assurance Guidelines (NQAG) for medical products. In Q2, PQM Bangladesh continued responding to recommendations received from the team and committee members.

SL/ No.	Training	Date	Laboratory Designation	Gender	Total Trained	Technical Areas	Training conducted by
1	Training on internal audit and CAPA management for DGDA's QMS unit	1/1/19	DGDA, NCL	26M, 4F	30	QMS	Local Staff
2	Training on document control system for DGDA	1/2/19	DGDA, NCL	20M, 6F	26	QMS	Local Staff
3	Refresher training on column management	1/15/19	NCL	11M, 6F	17	ALS	Local Staff
4	Refresher training on ILT	1/17/19	NCL	15M, 9F	24	ALS	Local Staff
5	Training on SOP of measurement uncertainty	1/24/19	NCL	10M, 7F	17	ALS	Local Staff
6	Refresher training on OOS procedure	2/10/19	NCL	14M, 5F	19	QMS	Local Staff
7	Training on system suitability and method transfer	2/11/19	NCL	9M, 13F	22	ALS	Local Staff
8	Training on training effectiveness evaluation questionnaire	2/18/19	NCL	11M, 6F	17	QMS	Local Staff
9	Training on data integrity and user management, waste management and titrimetric technique of analysis	3/27/19– 3/28/19	NCL	15M, 6F	21	ALS	HQ Staff
	Total in Q2 FY19			131M. 62F	193	ALS=101. QMS=92	

Summary of Trainings conducted in Q2 FY19

IV. Key Challenges

- Utilization of Government of Bangladesh resources, along with USAID support, is important. If government resources do not materialize as anticipated, it will hamper the achievement of the overall program objectives.
- Safety and security remain a concern in Bangladesh. Since June 2018, 1.2 million Rohingya refugees have
 arrived in the southeast region of Bangladesh, near the border with Myanmar. The current Rohingya refugee
 crisis is a global concern. The PQM country focal person is closely working with the global security director to
 monitor the security situation.

V. Sustainability, Partner Contributions, and Ownership

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

Activities targeting beneficiaries of the quality of medicines and health products (priority health program managers under other MOH directorates, program implementing partner nongovernment organizations, and patients) must be incorporated for awareness and sustainability of the program. A strong voice from the user end is important to face the problem of substandard and falsified medicines.

Indonesia

I. Quarter 2 Highlights

In Q2, PQM Indonesia's major accomplishments were as follows:

- Levofloxacin tablet 500 mg, produced by PT Kalbe Farma, was listed as a prequalified product by WHO on February 22 (https://extranet.who.int/prequal/news/pt-kalbe-farma%E2%80%99s-levofloxacin-tablet-prequalified). This is a major achievement by PQM Indonesia following its continuous support to PT Kalbe Farma since 2014. PQM will continue to advocate that PT Kalbe Farma maintain and roll out its PQ experience to its 12 sister companies that produce more than 200 medicines for Indonesia's population.
- After extensive technical assistance support to the BPOM NQCL to build its capacity and prepare for WHO
 PQ, a second inspection by WHO was conducted on February 18–20. The inspection was satisfactory, with
 one major and five minor findings. BPOM is required to submit a CAPA plan within 1 month of receiving the
 inspection report. PQM provided technical assistance support to assist with developing the CAPA and
 implementation plans, and BPOM committed to submitting the plans to WHO the first week of April 2019.
- PQM provided support to PT Sanbe Farma to prepare the product dossier for levofloxacin tablets 500 mg. The product dossier was successfully submitted in January 2019 and was accepted by WHO PQ assessor for review. In addition, PQM provided technical assistance on strengthening the capacity of GMP implementation at PT Sanbe Farma/Carprifarmindo through a mock audit and training.
- PQM Indonesia also supported PT Imedco Djaja and PT Pharos in product formulation and process development to manufacture the new first line regimen, rifampicin/isoniazid 150/75 mg and moxifloxacin tablets 400 mg, a second-line treatment for MDR-TB.
- PQM's ongoing support to the provincial QC laboratory at Denpasar to achieve WHO PQ standard is
 progressing well, and the laboratory is on schedule to submit the laboratory information file (LIF) to WHO PQ
 in 2019.

II. Country Context

PQM receives field support funding through TB and 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

FY18 Carryover Activities:

In the process of preparing to apply for WHO PQ for the Denpasar BBPOM QC Laboratory, PQM Indonesia provided intensive training and technical assistance, including training, development and revision of technical procedures, and compilation of the laboratory information file. Furthermore, PQM also provided input into the laboratory upgrades required to comply with WHO standards.

An ILT scheme consists of testing the same medicine samples by different laboratories and comparing the results to assess the reliability of the test results of the participating laboratories. To ensure laboratories maintain the skills obtained through PQM technical assistance, annual participation in ILTs is warranted. Since 2016, PQM Indonesia has facilitated the participation of BBPOM Denpasar in two ILTs, in which the laboratory achieved a 100-percent success rate. The most recent ILT completed by Denpasar involved HPLC to determine the amount of active ingredient in albendazole tablet samples. Preliminary results indicate the data submitted by the Denpasar laboratory was within specification and will result in the laboratory continuing to have a 100-percent ILT success rate.

FY19 Activities:

The result of the WHO PQ audit of NQCL was encouraging. PQM Indonesia continued to provide intensive technical assistance for preparation of the WHO PQ reinspection that occurred on February 18–20. The WHO PQ inspection report was received by the laboratory on March 12 and showed only one major and five minor findings. Since then, PQM has continued to provide technical assistance to develop the CAPA plan to be submitted for WHO PQ in the first week of April 2019.

Technical assistance to the pharmaceutical chemistry QC laboratory at the Faculty of Pharmacy, University of Indonesia (UI), has primarily been to build the capacity of the laboratory to perform QC testing of medicines. Since September 2018, UI has received equipment donations to build the Faculty of Pharmacy's ability to deliver preservice training to pharmacy students. Key laboratory equipment has been donated by USP in support of UI. Recent donations have included HPLC software, which was subsequently followed by training of five UI laboratory staff (three male and two female) as future trainers on operations, maintenance, and troubleshooting.

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

FY18 Carryover Activities:

PQM continued to provide technical assistance to PT Sanbe Farma to compile the product dossier for levofloxacin tablets 500 mg. The product dossier was submitted for WHO PQ on January 11 and subsequently accepted for screening. PQM provided technical assistance to address queries received from WHO PQT, which were submitted along with the revised dossier on March 6.

In preparation for the WHO PQ audit, PQM provided training on handling out-of-specification results on February 11; this training was attended by 46 participants (9 male and 37 female). Computerized system validation training was conducted on February 12 and was attended by 30 participants (18 male and 12 female).

On February 13–15, PQM verified the implementation of 70 percent of the CAPAs stemming from the findings of the audit conducted in 2018. The remaining CAPAs were verified by PQM in mid-March. This was also followed by a mock audit on March 19–20.

FY19 Activities:

In Q4 of FY18, PQM conducted a GMP audit at PT Imedco Djaja. This manufacturer is being supported to produce moxifloxacin tablets 400 mg, which is recommended for treating patients who have intolerance or resistance to isoniazid and as a component of treatment regimens against MDR-TB. Intensive technical assistance was provided to Imedco to develop the CAPA plan, revise and develop SOPs, finalize the CAPA report, and verify implementation of

the CAPA plan resulting from the initial GMP audit. As follow up in Q2, PQM reviewed and verified the CAPA report through a visit that on January 24.

PQM has also provided several trainings to strengthen GMP implementation at PT Imedco Djaja, such as a training on process validation conducted on January 23 with 17 participants (6 male and 11 female); training on computerized system validation on March 4 with 20 participants (8 male and 12 female); and engagement in the development and review process of various SOPs at PT Imedco Djaja.

PQM provided support to PT Kalbe Farma to achieve WHO PQ of levofloxacin 500 mg tablets. PQM provided technical assistance in drafting a response on the quality section of the levofloxacin 500 mg dossier for WHO PQ and a review of the TB information; a Quality Information Summary was also performed for submission for WHO PQ. On February 22, WHO announced Kalbe's levofloxacin 500 mg as prequalified, making Kalbe the first Indonesian manufacturer to have a TB medicine prequalified and thereby reducing the need to import and the length of the supply chain. (An article can be found at https://extranet.who.int/prequal/news/pt-kalbe-farma%E2%80%99s-levofloxacin-tablet-prequalified.)

After levofloxacin was listed as a WHO-prequalified TB product, PQM facilitated a series of meetings with key stakeholders to prepare for a press conference with PT Kalbe Farma and USAID, as well as a meeting between PT Kalbe Farma and Global Fund ATM to discuss the local and global market opportunities.

Given the need of Indonesian manufacturers to produce generic products that are bioequivalent to innovator products, PQM has also been providing support to three CROs to conduct these studies. In Q1 of FY18, PQM provided GLP/GCP training and audited three CROs (Equilab International, Pharma Metrics, Sanclin Eq). PQM also provided training to PT Pharma Metric Lab on data integrity (attended by 25 participants, 5 male and 20 female).

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

FY19 Activities:

PQM developed the terms of reference for a workshop on "Risk-based approaches to PMS in LMICs." The MedRS tool, an algorithm that applies risk-based principles, was shared with BPOM/DitKMEI. The workshop will also assess the cost effectiveness of the Minilab[™] screening technology. PQM is awaiting approval and a date from Directorate of KMEI and the NQCL of BPOM.

To strengthen collaboration and knowledge in the professional community, PQM was invited for the fourth time to participate in the Annual Scientific Meeting of Indonesia Pharmacists Association. A PQM Indonesia staff member delivered a presentation on "Electronic Data Integrity."

Objective 4 – Monitoring and Evaluation for specific activities

FY19 Activities:

In Q2, PQM began preparing for project closeout. This included the development of a closeout plan using the closeout checklist and other related tools. A closeout kickoff meeting was held on March 11, which was attended by the HQ closeout team and the field office closeout team to ensure smooth coordination on the implementation of closeout-related activities. The plan is to have a monthly closeout meeting between the HQ team and the Indonesia closeout team to ensure all intended closeout activities are conducted in timely manner.

In Q1, the draft of the official goods and services handover document (referred to as a BAST document) was prepared and submitted to BPOM and USAID for review. USAID signed the BAST on March 1, and PQM facilitated the transfer to BPOM for signature. PQM is currently waiting for BPOM to countersign the BAST document.

IV. Key Challenges

One of the challenges faced by PQM in Q2 was the resignation of Christopher Raymond, Chief of Party, effective February 11. PQM management decided to appoint Eddy Bahfen, Senior Operations Manager, to Acting Chief of Party. Additional technical support will be provided by USP HQ and from the USP Singapore office, including more frequent management visits.

Another challenge faced in Q2 was the processing of the BAST, which took much longer than anticipated. The BAST process requires review and approval by BPOM and USAID. Management turnover with BPOM staff now overseeing new and unfamiliar PQM activities required orientation of the new staff and additional review time.

Since January, PQM has been awaiting approval and a date of availability from BPOM to hold the risk-based PMS workshop. Given there is one quarter of implementation remaining for PQM, an alternative activity will be recommended to USAID if BPOM does not finalize a date by the second week of April.

Myanmar

I. Quarter 2 Highlights

The protocol for the baseline study on the quality of anti-TB medicines was finalized in Q1. In Q2 PQM with the support of staff from the Department of Food and Drug Administration (DFDA) collected 217 samples in 7 geographical regions: Yangon, Mon, Kayin, Shan, Bongo, Kayah, and Mandalay. The test results report will be completed and shared with the Mission in Q3.

PQM facilitated the implementation of the protocol for screening and observed compendial testing of anti-TB medicines. Prior to the visit, PQM performed an evaluation of PC laboratory's readiness to perform analytical testing of the TB samples being collected. Based on the data provided, the PC laboratory provided its test results for a pyrazinamide sample. PQM had minor comments but the laboratory was ready and able to perform analytical testing. During the visit, PQM observed a need for training on titrimetry and delivered a refresher training to the DFDA PC Laboratory staff. PQM held an in-depth discussion on the importance of data integrity and measured uncertainty practices and the impact these will have on the survey report.

During a March 22 meeting, PQM briefed the Myanmar Mission on the remaining activities: technical assistance to Mandalay laboratory toward ISO 17025 accreditation and technical assistance associated with the relocation of Nay Pyi Taw laboratory. Both are likely to be postponed due to the extensive delays in both Mandalay and Nay Pyi Taw laboratory construction. The project closeout process was also discussed with the Mission, and planning for a local closeout event is underway.

II. Country Context

Malaria has been a key public health burden in Myanmar, and the spread of drug-resistant malaria poses a major challenge, especially in the border areas. The combined effort of Myanmar 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 Myanmar. As DFDA is undergoing rapid expansion with field offices and laboratories being opened in every state/division and region of Myanmar, 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's laboratory will serve as the reference laboratory in Myanmar 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 Myanmar, 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, must 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 Myanmar to revise the current cost structure for quality testing to enable the Nay Pyi Taw laboratory to become self-sustainable

All activities under Objective 1 have been completed.

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

All activities under Objective 2 have been completed.

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

No updates for this quarter.

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

No updates for this quarter.

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 updates for 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

Nothing to report this quarter; activity is on hold by DFDA. The procurement of Raman devices is on hold by DFDA.

Objective 7 – Understanding of anti-TB medicine quality in public and private sectors increased

The baseline survey of the TB protocol for PMS implementation was conducted in Q2. Sampling was done in alignment with DFDA, with the field offices taking responsibility for sample collection in seven geographical areas (Yangon Region, Mandalay Region, Bago Region, Kayin State, Kayah State, Mon State, and Shan State). A total of 217 samples were collected from the private sector, 88 of which were selected for quality testing. Ten samples from the public sector will be sent to DFDA laboratory in April. First-line anti-TB medicines were given priority over the second-line anti-TB medicines, and samples from high-TB incidence areas (Yangon and Mandalay Regions) were given priority over the low-TB incidence areas during the selection process.

Testing began in the third week of March, which coincided with the supervisory visit from PQM. During the visit, PQM observed the DFDA laboratory performing quality testing on the two samples of four-fixed-dose-combination anti-TB medicines (isoniazid, rifampicin, Ethambutol, and pyrazinamide). The laboratory performed satisfactorily, and the two samples were found to conform to the specifications.

Knowing that this would be PQM's last technical assistance visit, the team made careful observations of the laboratory workflow for testing and found the need to deliver a refresher training on titrimetry. Eight laboratory analysts were trained in manual titration and automated titration. The critical training on this subject focused on back titration (also known as residual titration). Calculation regarding this type of titration was discussed, and calculation regarding titrimetric methods in general was revisited.

PQM discussed the electrodes that must be used in a potentiometric titration. This is important because use of a wrong electrode can result in false identification and consequently erroneous quantification. Data integrity as applied to antimalarial testing and TB testing and uncertainty measurement were discussed at length, since this impacts data reporting.

At the end of PQM's visit to the DFDA PC Laboratory, a debriefing meeting was scheduled with the Deputy Director General to discuss the current data from the ongoing survey of TB medicines in Myanmar, as well as and PQM's project closeout.

IV. Key Challenges

The Mission was briefed on the technical issues regarding the testing of streptomycin for injection and amikacin for injection. The laboratory does not have an electron capture detector for chemical assay testing. PQM team informed the Mission that bioassay will be done for these medicines and chemical assay will not be done.

There are concerns on the dissemination of findings after the study has been completed. Sensitive findings such as the wide availability of anti-TB medicines that can be bought freely although they are classified as "Prescription Only Medicines" will need to be addressed. As a result of these findings, the Ministry of Health and Sports might not be willing to accept the negative findings, and the Mission has already experienced such reaction from the Ministry in other studies. PQM recommends that the dissemination of survey results be done through DFDA to avoid conflict with the Ministry.

Pakistan

I. Quarter 2 Highlights

In Q2, PQM continued its technical assistance to selected laboratories toward attaining internationally recognized certifications, such as ISO 17025 and/or WHO PQ. With PQM support in Q2, another regulatory laboratory, the Drug Testing Laboratory (DTL) Rawalpindi, attained ISO 17025:2005 certification by the Pakistan National Accreditation Council. Moreover, with PQM support, LIFs from DTL Faisalabad, DTL Lahore, and DTL Multan have been submitted to WHO PQT.

To facilitate DRAP's achievement of WHO GBT Maturity Level III, in Q2 PQM continued providing support to DRAP to reassess its GBT self-assessment scores based on the new WHO GBT version. With PQM's support, DRAP will submit the revised WHO GBT self-assessment report in Q3 and will invite WHO for an onsite audit in October 2019. PQM continued to support DRAP in developing a QMS as per GBT and ISO requirements. DRAP addressed the ISO clauses requirement by developing the required documents and procedures. PQM also supported DRAP in reviewing, revising, adapting, and preparing documents in accordance with its institutional developmental plans.

II. Country Context

Chlorhexidine (CHX) is one of the 13 life-saving commodities identified by the 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 Pakistan's effort to reduce the mortality of newborns (currently at 200,000 deaths/year, about 22 cases/hour) caused by cord infections that can be prevented by use of quality CHX gels.

PQM is tasked with providing technical assistance to potential manufacturers of CHX gel to improve their manufacturing quality standards. PQM will also help strengthen DRAP's capacity, improving medicines registration processes, PMS, and other key functions, including enabling the QC laboratories to work 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 Pakistan. 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 preand 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 that received registration of CHX and to other potential MCH product manufacturers to improve their current GMP standards to qualify for WHO PQ, ERP, and local registration

Activity 1.1: Technical assistance to manufacturers of priority products

As per the 2019 work plan, PQM continued to provide support to the manufacturers of maternal and child health (MCH) medicines. PQM technical assistance remained focused on the products that are not produced in Pakistan or are in short supply; have issues of quality, safety, and efficacy; and fill a public health need in the country. Technical assistance to manufacturers in Q2 remained focused on four products:

- Amoxicillin DT: Globally, pneumonia remains the leading infectious cause of death among children under 5, killing approximately 2,400 children a day. In Pakistan, pneumonia accounted for approximately 16 percent of the 5.6 million under-5 deaths, killing around 880,000 children in 2016.¹ The antimicrobial of choice for treatment of pneumonia in children is amoxicillin DT. In Pakistan, PQM identified two potential manufacturers to produce amoxicillin DT.
 - Macter International: This manufacturer showed steady progress in implementing PQM-recommended corrective actions, completing 93 percent of CAPAs, with the remaining corrective actions likely to be completed by June 2019. With significant investment in equipment and technology, the manufacturer has developed a stable formulation of amoxicillin DT that is currently undergoing stability testing. Following the initial stability testing, Macter was able to develop trial and pilot batches for enhanced stability and palatability testing. It is anticipated that Macter will soon be able to fill gaps in the demand for amoxicillin DT in the public sector, thereby contributing to the management of childhood pneumonia in Pakistan.
 - CSH Pharmaceuticals: PQM audited this manufacturer in September 2018 and shared recommendations with management. The manufacturer developed corrective plans and has started addressing the observations raised during the audit. PQM continues to monitor CSH's progress in implementing the agreed-upon CAPA plan. CSH Pharmaceuticals is providing evidence for closure of its CAPAs. Verification of this evidence will take place in Q3.
- Zinc DT and zinc DT/oral rehydration salts (ORS) co-pack: Diarrheal disease is the second leading cause of death in children under 5. It is both preventable and treatable. Globally, there are nearly 1.7 billion cases of childhood diarrheal disease every year. In Pakistan, diarrhea kills around 525,000 children under 5 annually. The treatment of diarrhea includes rehydration with ORS solution and with zinc (micronutrient) supplements. Zinc reduces the duration and frequency of a diarrhea episode by 25 percent and is associated with a 30-percent reduction in stool volume.² Zinc DT was not available in the country, so PQM identified three manufacturers that were interested in manufacturing it. All three manufacturers are receiving PQM technical assistance toward zinc DT production.
 - M/s Pharmevo: WHO inspected the manufacturer for PQ in FY18 Q4. M/s Pharmevo submitted a response to WHO's observations and is now waiting to receive WHO's response. Management is committed to addressing any points raised by WHO PQT, and PQM will continue to provide technical assistance to address any further WHO PQT observations.
 - Atco Laboratories: Through PQM's support, Atco developed a stable formulation for zinc DT. The manufacturer has built a dedicated new section for commercial production of zinc DT, which was recently approved by DRAP. Atco will manufacture pilot batches for stability studies and palatability studies.

ORS and zinc are cost-effective treatments for childhood diarrhea. In combination, they reduce the severity and duration of symptoms and the risk of recurrence in the immediate short term. UNICEF is supporting governments to scale up the use of ORS and zinc by sourcing and promoting quality co-packaged ORS and zinc in order to facilitate access.

 Atco is already manufacturing an ORS and zinc solution, which is registered with DRAP as "Zincat OD Syrup," but this product does not comply with WHO-recommended formulations. The manufacturer has now registered another product for export, "Zincviet OD Syrup," which is compliant with the WHO-recommended formulation. Atco Laboratories will produce pilot batches for stability studies and palatability studies. The initial application for the co-pack was deferred by DRAP, as the product was not available in reference countries notified by DRAP. PQM is

¹ https://data.unicef.org/topic/child-health/pneumonia/

² https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease

supporting Atco for resubmission of its co-pack registration application to DRAP, along with a reference from UNICEF.³

- Aspin Pharma: This manufacturer produced 1 pilot batch (100,000 tablets) and 2 small batches (each of 30,000 tablets) of zinc DT in July 2018. A 9-month stability study is now complete and shows satisfactory results, as they complied with the compendial specification. In Q2, the dossier (quality part) with 6-month stability data was submitted to WHO for screening. After addressing the observations of the WHO review, a final version will be submitted to WHO PQT.
- Chlorhexidine gel: PQM has been assisting four manufacturers to develop and manufacture CHX 7.1% gel. PQM has been successful not only in getting the product developed by the four manufacturers but also in getting it registered in only 2 years. Now CHX 7.1% gel is being marketed by all four manufacturers (Atco Laboratories, Aspin Pharma, Zafa Pharma, and Akhai Pharma) and is freely available in the market to meet patients' needs and for procurement by government agencies. Two manufacturers, Atco Laboratories and Aspin Pharma, were interested in getting their products supplied to UNICEF and requested PQM's support. PQM provided support, and both companies submitted their dossiers and were registered with UNICEF. They are now awaiting the procurement tender by UNICEF for the ERP. UNICEF informed both manufacturers that the ERP review will be conducted once the tender for procurement is completed. Aspin Pharma and Zafa Pharma for CHX 7.1% gel, as neither manufacturer was interested in UNICEF ERP applications. Nevertheless, PQM has been monitoring the quality of products made by these manufacturers to ensure high-quality products remain available in the marketplace. PQM is now confident that the CHX 7.1% gel produced by these manufacturers is of standard quality and is likely to remain so; therefore, further monitoring of the product beyond June 2019 may not be required.

The table below presents updated information on MCH manufacturers receiving PQM assistance.

List of manufacturers receiving Feel TA and associated mort product of interest					
Manufacturer	MCH Product of Interest	Existing TA recipient			
Atco Laboratories Karachi Sindh	CHX gel	Existing			
Atco Laboratories Karachi Sindh	Zinc DT	Existing			
Atco Laboratories Karachi Sindh	Zinc syrup	Existing			
Aspin Pharma Karachi Sindh	CHX gel	Existing			
Aspin Pharma Karachi Sindh	Zinc DT	Existing			
CSH Pharma Lahore Punjab	Amoxicillin DT	Existing			
Macter International Karachi Pakistan	Amoxicillin DT	Existing			
Pharmevo	Zinc DT	No further assistance			
Atco Laboratories Karachi Sindh	Zinc DT+ORS co-pack	Existing			

List of manufacturers receiving PQM TA and associated MCH product of interest

Activity 1.2: Conduct batch analytical tests of all priority medical products in Pakistan

To ensure the manufacturers maintain the quality of CHX 7.1% gel produced through PQM assistance, PQM tested the in-market batches of the manufacturers' products in Q1. The results showed that all the samples collected were of standard quality and met the stringent requirements set out in the USP Compendium. PQM will collect another lot of samples from the market of products produced by the four manufacturers and will have these samples tested at an ISO 17025-certified laboratory in Q3. The objective is to ensure that the batch-to-batch quality of CHX 7.1% gel is maintained.

Activity 1.3: Continue to provide dossier preparation and GMP training to manufacturers and staff of DRAP on the common technical document (CTD) implementation and adaptation

With PQM's advocacy, DRAP decided to shift to the CTD template for registration application of all medicines. In FY 2018, DRAP officially declared the CTD as the only format for submitting medicine registration applications as of January 2019. However, due to technical challenges, DRAP extended the deadline for mandatory submissions to March 7, 2019.

CTD review requires specific technical skills, so in Q3 PQM will conduct a hands-on training for review of the CTD dossier (actual submitted) for DRAP staff involved in the review process. The training will include the practice of assessor report writing. This will be the last training on CTD that was part of DRAP's transition toward implementation of CTD for medicine registration. By conducting this training, PQM is confident that the evaluators' skill level will be enhanced to conduct a detailed evaluation of CTD dossiers being submitted to DRAP, which will result in better decision-making based on medicines quality.

³ ORS and Zinc: UNICEF Suppliers and Product Range, February 2016

Objective 2 - Strengthen the capacity of quality control laboratories to meet international standards

Substandard and falsified medicines cause treatment failure and adverse reactions, increase morbidity and mortality, and contribute to the development of drug resistance. Poor-quality medicines also increase healthcare costs to both patients and the health system as a whole, wasting resources that could otherwise be used to benefit public health. PQM's laboratory support program contributes to systems strengthening and industry stability with healthy competition for safe and quality-assured medicines in Pakistan. Reliable quality testing utilizing a risk-based PMS approach is increasing the detection of substandard and falsified medicines, including in the Afghanistan–Pakistan border regions. This is evident in that recently the antimicrobials for newborn health (e.g., imported CHX gel) tested by PQM-supported laboratories was found to be substandard, having impurity above limits. Through this program, economic support windows are widening by saving the costs to patients and healthcare systems through the reduction of treatment failures. In addition, the QA infrastructure strengthened through PQM support can forestall the negative impact of poor-quality medicines, such as the earlier incidents of contaminated cardiac medicines and cough syrup that took the lives of more than 400 people in Pakistan in 2011 and 2012. These types of tragedies could have been averted or their risk of occurrence reduced through reliable testing facilities, which now exist to support timely investigation.

PQM's technical support to QC laboratories is centered along three processes:

- Laboratory quality assurance system assessment: PQM conducts a targeted assessment of the QA system to obtain baseline data on the functionality of existing laboratory activities and the level of technical skills. The assessment highlights existing opportunities for improvement and helps to customize practical and feasible laboratory interventions. The initial assessment revealed a need for improvement in the overall quality management and document control systems, update of the responsibility matrix, establishment of a Laboratory Information and Management System (LIMS) to integrate the laboratory equipment and testing activities, SOPs for complaints, and revision of out-of-specification and CAPA SOPs.
- 2. Implementation of proposed technical interventions: After the assessment, recommendations for specific interventions and/or continuous improvement were developed to address identified gaps in capacity and other areas for improvement. Interventions include supporting the development of frameworks to enhance medicines quality testing (e.g., adoption of pharmacopeia standards as legal documents); training and building the capacity of technical personnel on QMS and analytical testing; advising on specifications for procuring analytical instruments; and implementing long-term preventive maintenance plans for the continuous provision of QC activities.
- **3. Monitoring and evaluation**: Quality improvement of interventions through effective monitoring and evaluation is a key component of PQM's laboratory system strengthening. PQM incorporates risk identification and mitigation as well as measurement indicators in all of its interventions. Performance indicators (e.g., compliance with pharmacopeial requirements, SOPs developed and implemented, staff adequately trained to perform tests, score for inter-laboratory comparison) are measured continuously throughout the implementation lifecycle and revised where necessary.

Activity 2.1 Conduct comprehensive assessment of laboratories

DTL Rawalpindi

DTL Rawalpindi is one of the provincial regulatory laboratories, established under the Drug Act of 1976/DRAP Act of 2012, for PMS of quality of medicines. PQM is providing technical assistance to DTL Rawalpindi based on the three-step approach mentioned above. In Q2, with PQM support, DTL Rawalpindi attained ISO 17025:2005 accreditation by the Pakistan National Accreditation Council. (The accreditation certificate number is LAB 166; it is valid until December 26, 2021.) With this accomplishment, six PQM-supported laboratories have now achieved ISO certification. PQM is currently providing subsequent support to DTL Rawalpindi to prepare its LIF for WHO PQ. Through PQM support, DTL Rawalpindi is expected to submit its LIF for WHO PQ by the end of Q3.



DTL Bahawalpur

DTL Bahawalpur (situated in south Punjab, an underserved region) is a provincial regulatory laboratory that was established under the Drug Act of 1976/DRAP Act of 2012. In Q1, DTL Bahawalpur attained ISO 17025:2005. In Q2, PQM supported DTL Bahawalpur in preparing its LIF for WHO PQ. This technical assistance includes revision of

SOPs related to deviation, change control, analyst authorization, control of documentation and records, personnel training, equipment qualification, materials handling, safety plans, validation of analytical procedures, and investigation of out-of-specification results. It is expected that, through PQM support, DTL Bahawalpur will submit its LIF for WHO PQ by the end of Q3. Prequalification for this laboratory will provide reliable testing services for surveillance of medicines quality to two divisions of Punjab (Bahawalpur and Sahiwal), benefiting 18.8 million people who are more vulnerable to substandard and falsified medicines. The laboratory will also play an important role in curbing poor-quality medicines, a major factor in the development of antimicrobial resistance.

Federal Government Appellate Laboratory, NIH Islamabad

The Federal Government Appellate Laboratory in Islamabad faces challenges that include infrastructure development, staffing, and procurement of modern equipment. The laboratory has an approved PC-1 (Developmental Plan) by the federal government, but the required funding is not currently available. PQM has successfully negotiated to leverage funds from the Global Fund for very essential equipment for the laboratory. In the meantime, PQM has trained laboratory staff on laboratory techniques to support them in their application for ISO 17025 accreditation.

In Q2, PQM supported the laboratory to prepare basic SOPs for QMS, including job descriptions with key performance indicators; a laboratory organogram; document control SOPs; measurement of uncertainty; analyst authorization; a training need assessment and training plans; operational logs templates; and logs for calibration, qualification, and cleaning. It is expected that all SOPs will be completed by the end of Q3, and during this time PQM will provide trainings on SOPs and internal self-audits.

Activity 2.3 Continue to support the CDL Karachi, DTLs and PDTRC Lahore quality control laboratories in improving standards of practice

CDL Karachi

In Q2, PQM continued to provide support to CDL Karachi for ISO and WHO PQ accreditation. Below is the summary of key activities in Q2:

- 1. PQM reviewed CDL Karachi's organization chart and job descriptions. The observations were communicated to the laboratory, and staff will finalize the actions by the end of the second week of Q3.
- 2. PQM reviewed over 53 QMS SOPs and helped to draft the missing SOPs. All the finalized SOPs are expected to be approved by the concerned authority in the first month of Q3.
- 3. About 50 operational SOPs were completed, and the remaining 20 will be completed by the first week of Q3.
- 4. PQM is supporting the preparation of the LIF for WHO PQ. The LIF, along with the EOI, will be submitted to WHO by the end of Q3.
- 5. The plan for the follow-up training program on all newly developed SOPs for CDL staff has been finalized and is expected to start in the second week of Q3. It was agreed that all the training would be organized on a Saturday to avoid any interruption in the routine functions of the laboratory.

PDTRC Lahore

Since its inception, the Pakistan Drugs Testing and Research Center (PDTRC) has been working under Punjab Industrial Estates Development and Management Company; in Q2 PDTRC was handed over to the Government of Punjab Health Department. PQM briefed the Provincial Health Minster about PQM/USAID technical assistance and progress on WHO PQ. In Q2, PQM continued its technical assistance to PDTRC for submission of its CAPA plan to WHO. WHO accepted the CAPA plan but requested a few additional evidence documents. PQM is assisting PDTRC in sharing the required information with WHO PQT.

Prequalification of the laboratory will provide testing facilities for the prequalification of locally manufactured medicines, especially for integrated disease programs, as well as for testing of medicines to be exported to comply with the requirements of certain importing countries. This laboratory will also be used for pre- and post-marketing of pharmaceuticals as required. It is expected that the laboratory will also provide QC services for pharmaceutical products to UN agencies and their partners, procurement agencies serving national authorities, and UN agencies and/or national authorities of WHO Regional Member States. This will lead to savings by local pharmaceutical manufacturers by foregoing the high cost of foreign testing, as well as revenue generation from marketing their QA products.

DTL Lahore

In Q2, through PQM technical assistance, DTL Lahore prepared and submitted its LIF for WHO PQ. The LIF is under review by WHO PQT, and PQM will continue to support DTL Lahore to address any further queries by WHO PQT for final acceptance of the LIF.

DTL Faisalabad

In Q2, with PQM continuous support, DTL Faisalabad removed all major observations that were required for submission of its LIF to WHO. DTL Faisalabad prepared its EOI application and LIF for WHO PQ and successfully summitted these to WHO PQT. WHO PQT is reviewing the LIF, and PQM will continue to support DTL Lahore to address any further queries by WHO PQT for final acceptance of the LIF. Prequalification of this laboratory will provide reliable testing services for surveillance of medicines quality to three divisions of Punjab (Faisalabad, Gujranwala, and Sargodha), benefiting 38 million people who may be exposed to the dangers of substandard and falsified medicines.

DTL Multan

In Q2, with PQM support, DTL Multan addressed the identified gaps and removed all major nonconformances that were required for the EOI application to WHO PQT. PQM extended its technical assistance to develop the LIF in accordance with WHO requirements. DTL Multan's EOI application and LIF for WHO PQ were submitted to WHO PQT. PQM will continue to provide technical assistance to laboratory staff to address any query from WHO PQT for successful acceptance of the LIF and further preparation for the WHO peer audit visit. Prequalification of this laboratory will provide reliable testing services for surveillance of medicines quality to two divisions of Punjab (Multan and Dera Ghazi Khan), benefiting a population of 15.7 million people. The DTL Multan catchment area (administrative division of cities where laboratories provide testing services) is in the southern part of Punjab, which has the highest vulnerable population due to poverty, poor health facilities, and ongoing conflict and violence.

Activity 2.4: Continue to provide technical support to DRAP and provincial health authorities in the establishment of inter-laboratory testing and an inter-laboratory comparison network among QC laboratories in Pakistan

An independent assessment of the technical performance of a laboratory is necessary to assure the validity of measurements or tests and should be part of an overall quality strategy. (The term "measurement" used in this document covers methodology, staff competency, measurement, and tests.) A common approach to this independent assessment is the use of independent Inter-Laboratory Comparison Testing (ILC-T) schemes.

PQM is providing technical assistance to selected laboratories for participation in this scheme. In FY 2018, 10 laboratories (DTL Rawalpindi, DTL Faisalabad, DTL Multan, DTL Bahawalpur, DTL Lahore, PDTRC Lahore, CDL Karachi, DTL Quetta, Pakistan Army Laboratory Lahore, and LNCM Morocco) participated in the second round of ILC-T for four-fixed-dose-combination anti-TB formulation. PQM provided the test material to each laboratory along with USP standards for analysis. In Q2, the expected report from the Morocco laboratory was received, and results are being compiled. The final report will be shared with all participatory laboratories for necessary action, if required.

Activity 2.5: Continue to support the establishment of a post-marketing surveillance (PMS) program with special focus on MCH medicines to ensure effective and robust monitoring of product quality

This activity is linked with objective 4, which is capacity building of inspectorates at federal and provincial levels to perform their role effectively in pharmaceutical establishments licensing, PMS, and enforcement action. For a detailed update, please see objective 4 updates.

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

Activity 3.2 Supporting DRAP in establishing organizational Quality Management System (QMS) as per WHO GBT Level-III

Quality Management System (ISO 9001:2015 Certification): QMS implementation in the national regulatory regime will help to coordinate and direct DRAP's activities to meet customer needs, meet regulatory requirements, continually improve effectiveness and efficiency, and see the acceptance/recognition of DRAP regulatory decisions by other international regulatory authorities. This means that all DRAP processes, authorities, and responsibilities are well-defined and documented; performance indicators are developed to achieve targets; performance is monitored; risks are assessed for each critical process; and risk mitigation strategies are in place.

In Q2, DRAP addressed gaps identified in ISO clauses 4 to 10, with support from PQM. Below is a brief update on major clauses (further details can be found in Progress Report: ISO 9001 Certification of DRAP, Ministry of National Health Services Regulation & Coordination).

 Clause 4.4 – Quality management system and its processes: Each DRAP division identified functions as per device methodology, followed by development of SOPs and work instruction where required. In accordance with ISO requirements, process risks and their mitigation in each SOP were addressed.

- Clause 5.2 Quality policy: The draft quality policy has been prepared as per the ISO requirement. The draft
 was circulated among QMS coordinators and members of top management for their review and finalization.
 It is expected that the final quality policy will be disseminated in Q3.
- Clause 5.3 Organizational roles, responsibilities and authorities: Job descriptions of each sanctioned posts were developed, including key performance indicators. The division developed a specific organogram for annual planning and a target-setting exercise.
- Clause 6.2 Quality objectives and planning to achieve them: In Q2, hands-on training was conducted to prepare SMART quality objectives. Divisions are working to finalize their SMART objectives.
- Clause 7.1.5 Monitoring and measuring resources: SOPs to ensure valid and reliable results when monitoring or measuring are used to verify the conformity of products and services.
- Clause 7.4 Communication: Before the implementation of QMS, there was no SOP for communication among divisions and externally. With PQM support, a detailed SOP for internal and external communication has been developed as per ISO standards.
- Clause 7.5 Documented information: An SOP for document and record management is developed and implemented. Necessary documents are being developed on a standardized format, along with proper codification. A master list of all the documents/records will be developed, including the electronic dashboard.
- Clause 8.2 Requirements for products and services: Requirements for different processes have been identified in the form of checklists and annexed in the relevant SOPs.
- Clause 8.7 Control of nonconforming outputs: An SOP on control of nonconformances has been established and is in the process of implementation.
- Clause 9.1 Monitoring, measurement, analysis and evaluation: PQM is supporting DRAP to conduct an annual planning workshop to set targets and monitor performance.
- Clause 9.2 Internal audit: An SOP to conduct management review has been developed and is currently in the process of approval. As per ISO requirement, the management review will be conducted after an internal audit. The internal audit for all DRAP divisions is planned for the end of Q3.
- Clause 10 Improvement: An SOP for corrective action has been developed and is expected to be implemented in Q3. After the implementation, opportunities for continual improvement will be included in all processes.

The bar charts below shows the clause-wise gaps and DRAP conformity status during the initial gap assessment and during Q2.



Activity 3.3 Support development and/or revision of policies/strategies, adoption of guideline and regulations In Q2, PQM supported DRAP in reviewing, revising, adapting, and/or preparing the following documents as per institutional developmental plans:

- DRAP communication strategy with external and internal stakeholders.
- DRAP framework on core competencies for all technical positions.
- HR performance-based monitoring system (including development of key performance indicators).
- Draft guidelines for sterile manufacturing.
- Draft guidelines for non-sterile manufacturing.
- QMS repository dashboard.
- Good pharmacovigilance practices.
- Draft rules on DRAP independent QA board.

Technical Assistance to DRAP for achieving WHO GBT Level III compliance

WHO's GBT assists regulators worldwide in evaluating the developmental status of their regulatory systems and related functions. In Q2, WHO rolled out the latest version of its benchmarking tool for evaluating the progress of national regulatory authorities toward meeting WHO QA targets. DRAP requested PQM support to achieve WHO GBT Maturity Level III, the minimum acceptable level for a stable, well-functioning, and integrated regulatory system. By achieving Maturity Level III, DRAP would attain WHO Listed Authority status, which would help it to perform functions using systematic regulatory approaches; enable good quality, safety, and efficacy assessments; safeguard patients from substandard and falsified medicines; ensure consistency and transparency in decisions; and achieve worldwide recognition of its



regulatory decisions. In Q2, PQM continued providing support to DRAP to reassess its GBT self-assessment scores based on the new GBT version. WHO is expected to share the findings on DRAP's self-assessment report in Q3. DRAP submitted its self-assessment report last year, with support from PQM. PQM will consider WHO's observations on the DRAP GBT self-assessment report as it continues to support DRAP in submitting its revised WHO GBT self-assessment report before inviting WHO for an onsite audit in October 2019.

Objective 4 – Capacity Building of Inspectorates at federal and provincial levels to perform their role effectively in pharmaceutical establishments licensing, and post-marketing surveillance of medicines quality, and enforcement action.

Ensuring the availability of quality medicines and eliminating substandard and falsified products from the supply chain is the main objective of all PQM efforts. PMS is a requirement to achieve the above-stated objective. The USAID Country Development Cooperation Strategy identified priority areas of intervention, including PMS activities in border regions. PQM has been working with DRAP to prepare a regulatory framework for effective PMS and conducted a consultative meeting with stakeholders (DRAP and provinces) in 2017 and a workshop on risk-based PMS in March 2018. The workshop recommendation called for the development of a common protocol for risk-based PMS.

PQM assisted in developing this protocol, which is now fully developed and will be presented at a stakeholders meeting in Q3. The objective of the meeting is to review, update, and approve the draft protocol for the adoption of a uniform national PMS framework.

Participants will present the framework to authorities in their respective provinces for approval and adoption. The implementation plan for rolling out the framework will be finalized at a second meeting in May 2019. The implementation of this framework will enhance collaboration and capacity of the inspectorates of both DRAP and provincial governments for PMS. The new regulations will not only strengthen enforcement against substandard and falsified products in the supply chain but also improve coordination/communication among the regulatory functions divided between DRAP and provincial health authorities.

A training of selected Drug Inspectors from DRAP and each province will be conducted as a training of trainers in June 2019 on the newly developed risk-based PMS framework. The selection of inspectors will be based on their seniority and length of remaining service. This is to ensure that the master trainers remain available for a longer period to impart the training to their peers and to new inspectors. This will in turn enhance sustainability of the program by creating a team of trainers for future transfer of knowledge.

IV. Key Challenges

The existence of a travel advisory remains a programmatic challenge for PQM. PQM encountered various challenges working with manufacturers of FPPs, including additional capital investment to comply with CAPAs and GMP compliance, which are required for WHO PQ. PQM worked closely with manufacturers to develop a framework to guide future planning and investment by defining potential barriers to market access. This is leading to increased demand for assistance to manufacturers. With an eye toward sustainability, PQM always considers including those that may be better addressed by other technical assistance entities, especially with respect to business development and capacity of the national regulatory regime for continuous technical assistance.

Another challenge that PQM faces is that effective regulation can ascertain more issues. For example, PQM's technical support to laboratories and PMS is expected to lead to increased detection of substandard medicines. PQM is also advocating for risk-based PMS, which is cost effective in contrast to sporadic surveillance without any plan or risk consideration. In effect, the outcomes of PQM's work may not be evident in the realm of QA systems strengthening, but the impact may be reflected elsewhere in the system and vice versa. This is not an issue unique to PQM—it is common to all health system interventions. PQM can measure how its work contributes to systems strengthening only with an in-depth understanding of how systems behave (complex system theory) and how the health systems in which it works function.

PQM has been working collaboratively and maintaining open communication with key regulatory stakeholders in Pakistan (e.g., DRAP, Ministry of National Health Services Regulations and Coordination, provincial governments, WHO). Past experience has shown that provincial governments are less inclined toward strengthening QA and QC systems, which negatively impacts the performance of many QC laboratories. Punjab is an exception: with PQM support, one more laboratory achieved ISO 17025 accreditation in Q2, raising the total number of ISO certified laboratories in the country to five.

V. Lessons Learned

PQM works closely with DRAP to strengthen its regulatory capacity. However, a review of provincial health authorities revealed 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 areas of risk-based PMS and strengthening of the provincial QC laboratories. Continued technical assistance is needed to sustain the interventions and progress made so far, as well as to implement new mandatory functions required for attaining Level III compliance based on WHO GBT (pharmacovigilance, clinical trial, risk-based PMS).

To ensure sustainability, PQM has concluded that it must continue to work in parallel with all stakeholders (federal government, DRAP, provincial governments, and the pharmaceutical industry).

VI. Cross-Cutting Issues

Availability of quality-assured treatments for extensively drug-resistant typhoid

Azithromycin is an affordable and effective treatment for extensively drug-resistant typhoid and is readily available in the market. However, due to lack of finished product testing capabilities at the manufacturers' end, the quality of available brands is questionable. In order to tackle this issue, a complete assessment of antimicrobial regulations, manufacturing techniques, and testing capability is required. There should be an increased focused on PMS, along with regulatory strengthening at both the federal and provincial levels.

Bioequivalence studies center and bioequivalence regulations

Recent changes in international support mechanisms (e.g., the Global Fund to Fight AIDS, Tuberculosis and Malaria is reducing its support for supplies) are likely to affect Pakistan. Pakistan has one of the highest TB burdens in the region, and the National TB Control Program depends on Global Fund supply of WHO-prequalified anti-TB medicines to treat patients. PQM is supporting two Pakistani manufacturers that are producing first-line fixed-dose combinations, neither of which has achieved WHO PQ. Through USAID financial assistance, these manufactures will acquire their bioequivalence studies abroad. There is a need to strengthen the capacity of bioequivalence facilities and CROs in Pakistan to conduct bioequivalence studies according to international GCP and GLP standards.

Laboratory QMS for public health laboratories

PQM support to develop QMS for medicines quality testing laboratories has also highlighted the need to support public health laboratories for disease surveillance. Communicable diseases still remain a major public health concern and are the prime cause of morbidity and mortality in Pakistan. Pakistan bears a significant portion of the regional burden of many communicable diseases, including HIV/AIDS, Hepatitis B and C, and TB. MDR-TB also poses a significant public health threat. Moreover, a recent outbreak of extensively drug-resistant typhoid and increasing trends of antimicrobial resistance have put more emphasis on the role of public health laboratories. Both sets of laboratories (medicines quality testing and public health laboratories) are critical components of the health care system. The fundamental principle of QMS are the same for both, and PQM can play a vital role in strengthening the network of public health laboratories to strengthen the quality of care and surveillance to align with the global health security agenda.

Eastern Europe & Central Asia



Kazakhstan

I. Quarter 2 Highlights

In Q2, PQM continued technical assistance to the Karaganda medicines QC laboratory of the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM) to strengthen its QMS in preparation for WHO PQ. In Q2, as a follow-up of Karaganda NQCL participation in the WHO PQT peer review conducted in FY 2018 Q4, PQM provided technical assistance to the laboratory to prepare a CAPA plan addressing observations by WHO PQT. In Q2 Karaganda laboratory submitted its CAPA plan to WHO PQT.

PQM also continued work with Nobel Almaty Pharmaceutical Factory, a manufacturer of second-line anti-TB medicines. As part of technical assistance to the manufacturer, in Q2 PQM provided technical assistance in development of a CAPA plan based on PQM's cross-contamination risk assessment visit in FY18.

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-burden MDR-TB country; MDR-TB reached 26 percent among new cases and 58 percent among previously treated cases.

In response to these challenges, Kazakhstan adopted a strategic document, "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 MRA, 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), about 40,000 units of falsified medicines in 40 cases 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, published in 2011, revealed Kazakhstan had the highest overall proportion of substandard samples (23.3%). Although 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 enforcement of medicines regulatory actions.

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 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 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

In Q2, PQM continued remote technical assistance to the Karaganda medicines QC laboratory. As a follow-up to WHO PQT's peer review audit, PQM provided extensive support to the laboratory in development of the CAPA plan in response to WHO PQT's observations. The CAPA plan was developed and submitted to WHO PQT in mid-February 2019. However, despite PQM's recommendation to prepare and submit the documents demonstrating implementation of CAPA, there is a delay in preparation of those documents by the laboratory. PQM has been following up with the laboratory and stakeholders to ensure that the documents are prepared, reviewed by PQM, and submitted to WHO PQT.

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 Q2, PQM continued remote support to Nobel Almaty Pharmaceutical Factory for its anti-TB product, levofloxacin. PQM provided technical assistance to finalize CAPAs developed by the manufacturer after PQM's GMP and cross-contamination risk assessment visits. PQM provided additional recommendations on mitigation of risks for cross-contamination between the products. Currently, the manufacturer is working on implementation of the CAPA.

Uzbekistan

I. Quarter 2 Highlights

In Q2, as a follow-up of PQM's GMP assessment and risk assessment visits to the new manufacturing site of Nobel Pharmsanoat, PQM visited the manufacturer and provided technical assistance in the form of roundtable discussions on current laboratory and manufacturing concerns. PQM will continue technical support and provide further recommendations to the manufacturer. In Q2, PQM conducted a training on the fundamental principles of GLP for the staff of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment under the Agency for Development of Pharmaceutical Industry, Ministry of Health of the Republic of Uzbekistan. The training was followed by question-and-answer sessions with staff members. In Q2, three pieces of laboratory equipment purchased by PQM were delivered to the medicines QC laboratory.

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 3 of 7 samples of rifampicin capsules and 3 of 11 samples of isoniazid tablets failed quality tests in Uzbekistan. Although 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 Q2, PQM continued to provide technical support to Nobel Pharmsanoat for its anti-TB product, levofloxacin. Based on PQM's cross-contamination risk assessment visit, the manufacturer developed a CAPA plan for risk mitigation. In Q2, PQM made a 1-day visit to Nobel Pharmsanoat to provide technical assistance in the form of roundtable discussions on current laboratory and manufacturing concerns. The objective of the discussions was to provide a better understanding of best practices associated with specific operations. The team discussed both production and laboratory practices and was able to respond to 22 questions, ranging from general method verification to manufacturing process validation points.

PQM will continue providing technical support to the manufacturer and will perform a laboratory assessment of the physical chemical and microbiology laboratories with guidance and recommendations provided as needed. PQM will prepare an implementation plan for alignment of laboratory QMS and technical operations to international standards.

Objective 2 – Strengthen the medicines quality control system

In Q2, PQM continued providing technical assistance to the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment under the Agency for Development of Pharmaceutical Industry, Ministry of Health of the Republic of Uzbekistan, to strengthen medicines QC capabilities. PQM provided a 4-day training to 24 representatives from various departments within the State Center on the fundamental principles of WHO GLP and practical applications as they relate to medicines QC laboratories. The training provided an overview of the underlying principles of quality assurance and integrity of non-clinical laboratory testing that supports research or marketing permits for products regulated by government agencies. The training aimed to enhance participants' ability to identify key good practices and perform self-assessments of quality and technical operations. The training sessions involved presentations on indicated topics with general principles based on international standards, targeted exercises, and group discussions. The training provided participants with the base for creating a quality-centered environment focusing on generating accurate, complete, and consistent data.

The training was followed up by 2-day question-and answer sessions with the Quality Manager and staff members of the State Center in relation to CAPA implementation, reference standards management, equipment qualification, specifications for microbiology and physical chemistry laboratory, document creation, and other areas of concern. As a result of the roundtable discussions and the progress of CAPA implementation, it was recommended that the State Center establish an independent quality unit to manage its quality system improvement activities as well as routine quality activities. In Q2, three laboratory instruments purchased by PQM were delivered to the medicines QC laboratory. In February, the QC laboratory began renovation of the physiochemical laboratory area to improve its compliance with the ISO 17025 standard and GLP. After completion of the renovation, the vendor will install the equipment and train staff to use it appropriately.

PQM will continue technical assistance to the medicines QC laboratory and will conduct a QA training for the members of the quality unit in May 2019. PQM will prepare an implementation plan for international accreditation or WHO PQ of the laboratory.

Objective 3 – Strengthen GMP inspection system

In Q2, the Agency for Development of the Pharmaceutical industry provided a draft self-assessment based on PIC/S indicators. The draft was reviewed by PQM, and next steps were agreed to with the counterparts: PQM will review the provided QMS documents, then visit the country to work with the PIC/S working group to be established by the Agency for Development of the Pharmaceutical Industry and complete the self-assessment. Based on the self-assessment, the gaps will be identified, and a roadmap for PIC/S membership will be developed.

Core Portfolio



Core MNCH

I. Quarter 2 Highlights

PQM moved forward in terms of technology transfer of Umbipro (CHX digluconate gel 7.1%) from GSK to PQM and preparation of its transfer to the interested manufacturers. Based on information and documents provided by GSK, the technology transfer report has been developed. The workshop on "Increasing access to quality-assured essential medicines through technology transfer to local manufacturers" with the case study of Umbipro technology transfer has been announced, and preparations are underway.

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 toward lifesaving 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 assures an uninterrupted supply of quality-assured medicines, but also strengthening medicines regulatory capacities to protect populations 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: PQM continued technical assistance to the manufacturer in China on magnesium sulfate injection. In January 2019, the WHO GMP team conducted a GMP inspection of the manufacturing site for manufacturing activity related to magnesium sulfate injection. At the beginning of March, PQM visited the manufacturer to follow up on the WHO audit and dossier preparation. The draft dossier for magnesium sulfate was prepared, and all the data required for submission are available. PQM reviewed the Quality Overall Summary of Module 2, Module 1, and Module 3. The manufacturer has completed the draft dossier and is expected to submit the full dossier to WHO by May 2019.

In December 2018, WHO PQT conducted a GMP inspection of the magnesium sulfate manufacturer in Ukraine. The manufacturer received additional data query for the magnesium sulfate dossier submitted to WHO. In Q2, PQM provided assistance to the manufacturer in the preparation and implementation of the GMP CAPA plan and additional dossier query response.

- Amoxicillin DT FPP: In December 2018, PQM staff visited the amoxicillin manufacturer in Ghana. The PQM GMP team provided a risk assessment of the beta-lactam cross-contamination issues related to the amoxicillin DT manufacturing process. The manufacturer is working on CAPA to address the cross-contamination due to the beta-lactam manufacturing lines.
- **Oxytocin FPP:** PQM continued technical assistance to the manufacturer in China on oxytocin injection. Following the WHO GMP inspection, PQM visited the manufacturer in March to follow up on the WHO audit and dossier preparation. The manufacturer has developed the primary batches for oxytocin injection and placed them under stability monitoring. The 6-month stability data will be available by July 2019; by then, the dossier will be prepared for submission to WHO.

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

With PQM's support, the Nigerian manufacturer Juhel submitted dossiers for its oxytocin and magnesium sulfate products for the 9th EAC joint assessment meeting, which was held December 2018 in Entebbe.

The EAC joint assessment meeting requested additional information from Juhel. PQM provided follow-up support to respond to the queries from EAC, which Juhel submitted in March. The final decision about approval of Juhel's products will be made in April 2019 at the 10th EAC joint assessment meeting.

In Q2, PQM continued providing assistance to the Indonesian manufacturer Sanbe to register its high-priority MNCH medicine oxytocin injection in Pakistan via the WHO CRP mechanism. With this activity, PQM pursues two goals: (1) registration of Sanbe's oxytocin in Pakistan would ensure the availability of a needed quality-assured product on the local market, and (2) the experience gained by DRAP in registering its first product through the WHO CRP process would help in registration of other quality-assured products approved by WHO PQT or SRAs.

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

In Q2, PQM continued working with GSK a technology transfer for Umbipro (CHX gel) to PQM, so that PQM can share the information and help to build capacity of interested manufacturers in LMICs. Based on the information and documents provided by GSK, PQM developed a technology transfer report. The report will be finalized in Q3 and will be ready for sharing with interested manufacturers in LMICs.

PQM began to prepare for the workshop on "Increasing access to quality-assured essential medicines through technology transfer to local manufacturers" to be held in Accra, Ghana, in May 2019. Umbipro (CHX digluconate gel 7.1%) technology transfer will be presented as a case study. The workshop will discuss technology transfer requirements and procedures, production, and QC. Also, Umbipro technology transfer information will be shared on the plenary session and via one-to-one meetings with the manufacturers. The workshop announcement and preliminary agenda has been developed and shared with manufacturers in Africa and Asia.

Core NTD

I. Quarter 2 Highlights

Preparation and implementation of all three PQM-supported bioequivalence studies are progressing well. One praziquantel FPP manufacturer completed bioequivalence dosing, initiated analysis, and will submit the interim report to PQM by the end of April 2019. A second praziquantel FPP manufacturer received bioequivalence protocol approval from the ethical committee, and the study is scheduled to start by mid-April 2019. The albendazole bioequivalence protocol for a pivotal study has been finalized and is under approval, tentatively scheduled to start by May 2019.

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 an 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 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, which allows a manufacturer to partake in a rapid quality risk assessment of its product dossier and 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**: With PQM support, one manufacturer in China, Jiangsu Chengxin Pharma, received WHO GMP approval and full WHO PQ for micronized and non-micronized praziquantel API in Q1. PQM continued to provide support to the second manufacturer in China to prepare its responses for WHO PQ assessment. The manufacturer submitted the response letter to WHO and received feedback from WHO on the dossier and GMP desk review. The manufacturer plans to submit a GMP desk review response at the beginning of Q3.
- **Praziquantel FPP**: One of the two manufacturers in India received bioequivalence protocol approval from the ethical committee. The manufacturer has placed all three batches on stability, and the 6-month stability studies will be available by the end of June. The dossier is being prepared, and PQM began reviewing several supporting documents for the dossier. The dossier by the second manufacturer is being prepared, and PQM will receive the dossier for review by the end of April. PQM visited the facility in January to conduct document verification, review the investigation report and CAPA plan, and finalize the project timeline. PQM continues to provide technical assistance at various stages to ensure that the manufacturers are making progress toward WHO PQ.
- Albendazole FPP: In Q1, PQM selected a manufacturer in India to receive financial and technical support for a bioequivalence study of albendazole. In January, PQM conducted the initial GMP assessment of the manufacturing facility to evaluate compliance against WHO GMP and WHO PQ requirements for manufacturing of albendazole chewable 400 mg tablet. The manufacturer has completed the stability study and stability data for 18 months are available. The dossier is being prepared, and PQM began reviewing several documents for the dossier.

Objective 2 – Technical support for bioequivalence study

In Q2, PQM continued technical assistance to two manufacturers of praziquantel FPP in support of bioequivalence study preparations: One of the manufacturers has successfully completed bioequivalence dosing for all the four folds, initiated bioequivalence analysis, and will submit the interim report for review by PQM by the end of April.

The second manufacturer received bioequivalence protocol approval from the ethical committee, and the study is scheduled to start by mid-April. The bioequivalence protocol for a pivotal study for albendazole FPP is under approval, and the pilot study is tentatively scheduled to start by May 2019.

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

PQM submitted a sub-award package to USAID for the selected vendor for development of the GMP online training module. After approval, the vendor will start development of the online module with PQM's oversight. This activity will be cost-shared with the Core TB program.

Core TB

I. Quarter 2 Highlights

After a quality risk review, the Global Fund ERP determined no objection for clofazimine 100 mg soft capsules produced by Dong-A. This is a result of PQM's extensive technical assistance to the manufacturer, which began in December 2015 after a memorandum of understanding between PQM and Dong-A was signed. Clofazimine an essential medicine for treatment of MDR-TB and a priority product for USAID. This is a significant achievement, as the product is very complex and challenging to develop due to its highly variable characteristics. This complexity has limited the number of manufacturers that produce this product. This achievement ensures that a quality-assured generic product is now available on the market; it is expected that increased competition will result in a reduction in price of the product.

PQM also provide technical assistance to Celltrion, which achieved WHO PQ for its linezolid 600 mg tablet. Linezolid is also an essential medicine for treatment of MDR-TB.

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 the availability of affordable quality-assured anti-TB medicines.

Consistent themes within these publications are safeguarding treatment for all people with TB, including drugresistant 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

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

- **Clofazimine FPP**: PQM provided assistance to the manufacturer in Korea to draft the response for submission to the Global Fund. In Q1, the response was submitted to the Global Fund. PQM provided further assistance to respond to the questions and queries from the Global Fund ERP, and in January 2019 the product received ERP approval for 2 years after a quality risk review that determined no objection for clofazimine 100 mg soft capsules manufactured by Dong-A.
- **Clofazimine API**: PQM provided technical assistance to the manufacturer to draft the response for WHO PQ assessment queries. The response and supporting documents were submitted to WHO.
- **Rifapentine API**: PQM visited two manufacturers to follow up on GMP and API Master File preparation. Following the onsite discussion, one manufacturer agreed to develop and provide the first draft of the drug master file to PQM by June 2019 and planned to complete the pending GMP CAPA by April 2019. The second manufacturer has revised its API Master File based on the recommendation provided by PQM.
- **Kanamycin FPP**: In January 2019, the WHO team conducted a GMP inspection of the manufacturing site for Kanamycin injection. At the beginning of March, PQM visited the manufacturer in China to follow up on the WHO audit. During the visit, PQM reviewed the final QA request from WHO on kanamycin full prequalification and discussed the queries regarding analytical purity with the manufacturer. The manufacturer revised the Quality Information Summary of its kanamycin dossier after the WHO QA query, and the application is close to its final stage of prequalification.

- Linezolid FPP: With PQM support, one manufacturer in Korea, Celltrion, received WHO PQ for linezolid 600 mg tablet on February 6.
- Rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC): In Q2, PQM visited manufacturers in Pakistan to provide hands-on assistance on dossier compilation and final GMP assessment of the facility. One manufacturer is waiting for bioequivalence protocol approval from the local regulatory and ethics committee, and the study is planned to start by mid-April. The manufacturer has placed all three batches on stability and is waiting for satisfactory results of 6-month stability data. The manufacturer is currently preparing the dossier. The second manufacturer is also waiting for bioequivalence protocol approval from the local regulatory and ethics committee, and the study is planned to start by mid-April. The manufacturer is currently preparing the dossier. The second manufacturer is also waiting for bioequivalence protocol approval from the local regulatory and ethics committee, and the study is planned to start by mid-April. The manufacturer has placed all three batches on stability and sent 3-month stability data to PQM for review. The manufacturer is in the process of compiling the dossier.

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

PQM submitted a sub-award package to USAID for the selected vendor for development of the GMP online training module. After approval, the vendor will start development of the online module with PQM's oversight. This activity will be cost-shared with Core NTD.

Cross Bureau

I. Quarter 2 Highlights

- International meetings: Following the December 2018 NEPAD/PQM/WHO coordinated workshop to promote local production and supply of quality-assured medicines in Africa, PQM developed a draft document on "Points to Consider: Enabling Local Production of Quality Assured Medicines in Africa." The document was shared with WHO, which will review and disseminate the final version.
- MedRS: A web-based version of MedRS (PQM developed risk-based PMS tool) has been completed and will be available at PQM's website in Q3 for direct use by country MRAs. Demonstration of the Excel version was performed in Uganda, Mozambique, Indonesia, and Cambodia, the latter during a risk-based PMS workshop funded by WHO. Comments and recommendations from these and future deployments are being gathered for final refinement before being made available on PQM's website.
- **E-course**: All sessions of the e-course on the importance of ensuring medical product quality for health systems strengthening, to be published at the Global Health eLearning Center, have been completed and are currently under review.
- **Regulatory system country profiles**: Drafts of country's regulatory system profiles for Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan finalized by PQM and submitted to countries' MRAs for review, completion of missing information and final approval. Approval received from Ethiopia and Myanmar.
- Quality-assured medicines in UHC: A service agreement with the University of North Carolina was completed. The scope of work was finalized for development of an article and white paper on the "Importance of Medicine Quality in Achieving Universal Health Coverage."

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

Following the NEPAD/PQM/WHO coordinated workshop to present and discuss key enabling factors for successful local production and supply of quality-assured medicines held in FY19 Q1, PQM developed a draft document on "Points to Consider: Enabling Local Production of Quality Assured Medicines in Africa." This document was shared with WHO, which will review and disseminate the final version.

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

Activity 2.2: Contribute to the increase in competency in bioequivalence dossier review

PQM planned to continue to provide technical assistance and support to the East African Community MRAs to develop competence in bioequivalence dossier review, including hands-on guidance for bioequivalence data evaluation. With the capacity developed through previous trainings, and with ongoing support provided to EAC regulators during subsequent joint dossier assessment exercises by WHO and Swiss-medic as technical experts, the planned PQM follow-up hands-on training on bioequivalence data review was no longer a priority. As a result, this activity was discontinued.

Objective 3 – To improve risk-based quality assurance systems and create models for self-sufficiency and sustainability

Activity 3.1: Rollout of risk-based quality assurance framework

Specialists at Ethiopia and Nigeria PQM offices began development of questionnaires for the baseline assessment of the current status of GMP inspections, dossier evaluation, PMS, analytical testing, and regulatory actions at the MRAs of Ethiopia (EFMHACA) and Nigeria (NAFDAC).

Activity 3.2: Finalize online risk-based PMS tool (MedRS)

All components of the web-based version of MedRS have been completed. In Q2, demonstrations of the Excel version took place in Uganda, Mozambique, Indonesia, and Cambodia, the latter during a risk-based PMS workshop funded by WHO. Comments and recommendations from these deployments were gathered for the final refinement of the online version. PQM is delivering information sessions on the web-based version for new MedRS users; user feedback and comments will be documented before the tool is made available at PQM's website for country MRAs.

Activity 3.3: Rollout of risk-based approach for post-market surveillance

The rollout is currently being implemented as part of MRAs' allocated budgets for PMS; Bangladesh and Indonesia are also drafting their own national risk-based PMS guidelines. Use of MedRS will also be implemented in Ghana, Indonesia, Mozambique, and Uganda. As a result, support through Cross Bureau has been discontinued.

Objective 4 - Development of e-Learning course on medicines quality assurance

All nine sessions of the e-course on the importance of ensuring medical product quality for health systems strengthening have been completed and are currently under internal review. Internal and external review of contents as well transfer to the Global Health eLearning platform and publication will be completed in Q3.

Objective 5 – Establish regulatory system country profiles

Drafts of all remaining country profiles (Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan finalized by PQM) were finalized and submitted to country MRAs for review, completion of missing information, and final approval. Comments to MRA's revised versions were sent back to Ghana. The Bangladesh profile had been approved by the MRA in Q1. The Ethiopia and Myanmar profiles were approved in Q2. All reports will be submitted to USAID in the final format in Q3.

Objective 6 – Provide guidance on the importance of medicines quality in Universal Health Coverage (UHC) schemes

The service agreement with the University of North Carolina (UNC) was completed. At a kickoff meeting between PQM and the UNC team, the final scope of work for developing an article and white paper on the "Importance of Medicine Quality in Achieving Universal Health Coverage" as well as the delivery timelines for drafts and the final version was agreed upon. All deliverables expected to be completed in Q3.

Management Overview

In Q2, PQM hosted a webinar "Implementing a Risk-Based Approach to Medicines Quality Surveillance." The webinar was preceded by the launch of a two-part video that outlines how designing and implementing programs that monitor medicines quality through a risk-based approach allows countries to tailor activities according to local needs, optimize limited resources, and focus efforts on areas that present the greatest risks to public health. Following the video launch, participants were invited to participate in a live Q&A session on February 28 with PQM Principal Program Manager, Timothy Nwogu. The video is available on the PQM website at https://www.usp-pqm.org/resources/knowledge-sharing-videos.

Also in Q2, a journal article "Falsified and Substandard Drugs: Stopping the Pandemic," coauthored by PQM Senior Program Manager, Mustapha Hajjou, was published by the *American Society of Tropical Medicines and Hygiene*. This publication was a follow-up to Cross Bureau-funded PQM participation in a discussion panel at the 2017 Consortium of Universities for Global Health meeting. The article is available at http://www.ajtmh.org/content/journals/10.4269/ajtmh.18-0981;jsessionid=LH_WVRPXq0cfq6utxEeoUAC4.ip-10-241-1-122.

On March 27, PQM Senior Director Jude Nwokike, participated in USAID's Office of Health Systems' consultative meeting, "From fragile to resilient health systems: a journey to self-reliance." The meeting brought together health system and resilience leaders, policymakers, and development experts to share experiences, innovative practices, successes, and challenges for shifting health systems from fragile to resilient.⁴

⁴ https://www.eventbrite.com/e/from-fragile-to-resilient-health-systems-a-journey-to-self-reliance-tickets-55426514196