

Promoting the Quality of Medicines (PQM) Program

FY 2019 Third Quarter Report
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About the Promoting the Quality of Medicines (PQM) Program

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The Promoting the Quality of Medicines (PQM) program is a Cooperative Agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to address critical 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 18 countries, 1 regional mission, 1 Cross Bureau program, and 3 core health programs.

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Acronyms

ACT	artemisinin-based combination therapy
API	active pharmaceutical ingredient
CAPA	corrective and preventive action
CHX	chlorhexidine
CRO	clinical research organization
CRP	Collaborative Registration Procedure
DFDA	Department of Food and Drug Administration [Burma]
DGDA	Directorate General of Drug Administration [Bangladesh]
DRAP	Drug Regulatory Authority of Pakistan
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
FPP	finished pharmaceutical product
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
LMHRA	Liberia Medicines and Health Products Regulatory Authority
LMIC	low- and middle-income country
M&E	monitoring and evaluation
MDR-TB	multidrug-resistant tuberculosis
MNCH	maternal, newborn, and child health
MOH	Ministry of Health
MQDB	Medicines Quality Database
MQM	medicines quality monitoring
MRA	medicines regulatory authority
NAFDAC	National Agency for Food and Drug Administration and Control [Nigeria]
NMCP	National Malaria Control Program
NQCL	national quality control laboratory
NTD	neglected tropical disease
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PMI	U.S. President's Malaria Initiative
PMS	post-marketing surveillance
PQ	prequalification
PQM	Promoting the Quality of Medicines
QA	quality assurance
QC	quality control
QMS	quality management systems
SOP	standard operating procedure
SRA	stringent regulatory authority
TB	tuberculosis
UNICEF	United Nations Children's Fund
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WHO	World Health Organization

Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance in partnering countries to strengthen quality assurance (QA) systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance helps to build the capacity of medicines regulatory authorities (MRAs) and QA systems. PQM supports the manufacture of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH). PQM also provides support to increase the utilization of medical product quality information for decision-making. This report summarizes results achieved during the third quarter (Q3) of FY 2019, from April 1 to June 30, 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. With PQM's support, in Q3 the Pakistan Drugs Testing and Research Center (PDTRC) Lahore laboratory became the first public sector laboratory—not only in Pakistan, but in all of southeast Asia—to be prequalified by the World Health Organization (WHO). In Indonesia, the BPOM national quality control laboratory received the closing letter from WHO confirming it is compliant with WHO standards. In Uzbekistan, the president issued a Decree that complying with good practices, including good manufacturing practices (GMP) and good laboratory practices, will become mandatory beginning January 1, 2022, and that the Agency for Development of Pharmaceutical Industry must collaborate with the Pharmaceutical Inspection Co-operation Scheme. To promote sustainability in Nigeria, a proposition to increase product registration fees for market authorization holders was submitted to the National Agency for Food and Drug Administration and Control (NAFDAC), approved by the NAFDAC governing council, published in the agency's gazette, and made public; this achievement serves as an exit plan for the PQM program. In Guinea, PQM helped to facilitate the first post-marketing surveillance activity carried out by the regulatory authority at the national level.

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 quality standards to meet local and global demand for quality-assured medicines. In Q3, with PQM's technical assistance and advocacy efforts, the Drug Regulatory Authority of Pakistan (DRAP) endorsed a procedure for registration of product dossiers in accordance with the WHO Collaborative Registration Procedure process. Also in Q3, PQM organized a workshop with GSK on “Increasing access to quality-assured essential medicines through technology transfer to local manufacturers: The Umbipro case study” to give manufacturers access to critical information for developing and producing quality-assured chlorhexidine, with the goal of increasing the number of sources of quality-assured chlorhexidine in Africa and Asia. In Indonesia, PQM held a workshop with local manufacturer PT Kalbe Farma to share knowledge and experience from Kalbe's earlier successful WHO prequalification audit for levofloxacin 500 mg tablets. In Nigeria, Emzor Pharmaceuticals resolved all identified corrective and preventive actions (CAPAs) from PQM's GMP audit for the antimalarial sulfadoxine–pyrimethamine (SP) 500+25 mg tablet; Emzor has since received procurement requests for 2.1 million doses of SP for delivery to the Medical Export Group, an international distributor. Another Nigerian manufacturer, Juhel Pharmaceuticals, submitted its dossier for magnesium sulfate 50% w/v (used for treating preeclampsia/eclampsia) to the WHO prequalification team, which could bolster the availability of the product on the local market and allow it to be procured globally.

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. In Q3, the Liberia Medicines and Health Products Regulatory Agency (LMHRA) performed its sixth round of annual sample collection and testing, which revealed that nearly 14 percent of antimalarials collected failed to comply with one or more regulatory requirements. In response, LMHRA took action to remove and quarantine all noncompliant products and shared the findings with key stakeholders in a dissemination meeting. The Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) has continued using the routine adverse drug event reporting system as a mechanism to identify poor-quality medicines and take enforcement actions. In Q3, EFMHACA recalled a number of products found to be defective: disposable syringes, Z-Cold syrup, and rapid pregnancy test kits, and the manufacturer of the disposable syringe was asked to stop production until the root cause of the defect is identified and resolved. This practice, in conjunction with post-marketing quality surveillance and inspection, is expected to boost EFMHACA's capacity to detect and prevent substandard and falsified medicines from entering into the Ethiopian market.

Program Background

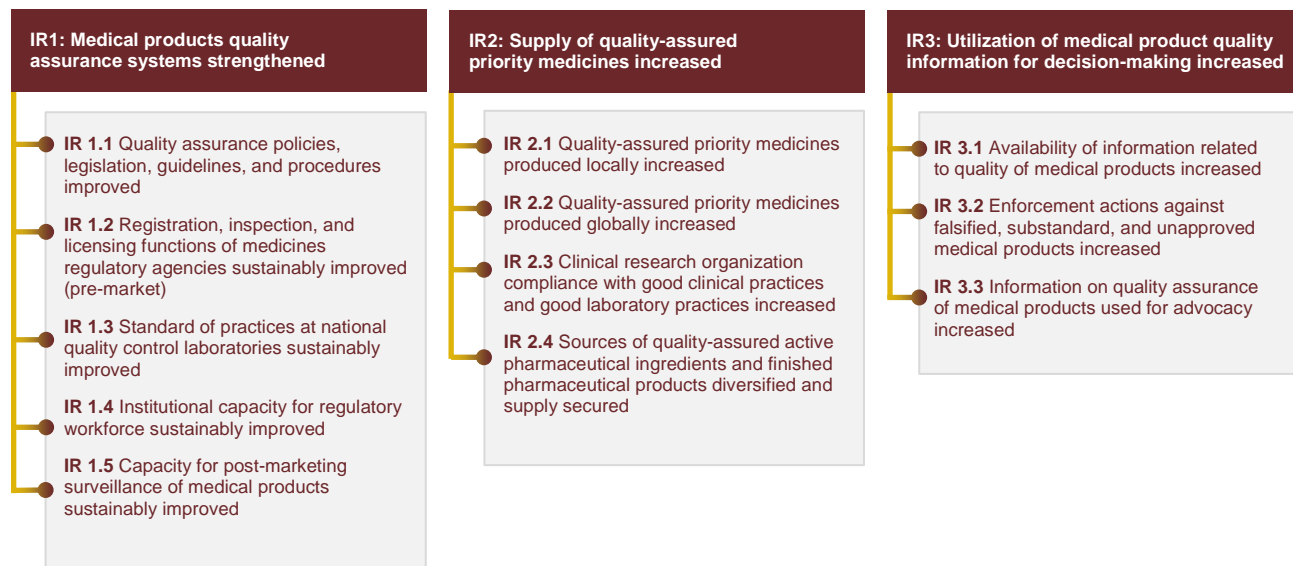
The Promoting the Quality of Medicines (PQM) program is a cooperative agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to support low- and middle-income countries (LMICs) in addressing critical issues 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 18 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.

PQM Goal: Quality assurance systems strengthened to sustainably ensure quality and safety of medical products and protect public health



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

Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved

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

PQM's in-service training programs, application of the Collaborative Learning Model, train-the-trainers approach, and hands-on support facilitate the transformation 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 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 Third Quarter IR1 Achievements

Key Results and Highlights

This quarter, two PQM-supported laboratories saw major results. The Pakistan Drugs Testing and Research Center (PDTRC) Lahore laboratory was prequalified by WHO. This is the first public sector laboratory—not only in Pakistan, but in southeast Asia—to be prequalified by WHO. In Indonesia, the BPOM NQCL received the closing letter from WHO PQ confirming the laboratory is compliant with WHO standards. These are both major achievements for Pakistan and Indonesia, as the laboratories will be recognized globally for their trusted capability to provide accurate and reliable results.

The president of the Republic of Uzbekistan issued a Decree this quarter for “Further measures for accelerated development of Pharmaceutical Industry in the Republic of Uzbekistan in 2019–2021.” The Decree includes some areas that PQM has advocated for regarding strengthening the country's medicines QA system. Complying with good practices, including GMP and GLP, will become mandatory for entities beginning January 1, 2022. The Decree also requires the Agency for Development of Pharmaceutical Industry to collaborate with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and develop a roadmap for PIC/S accession. According to the Decree, funding will be allocated for development of the new compound of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment, including a new medicines quality control laboratory.

In Nigeria, a draft proposition to increase product registration fee for market authorization holders (MAHs) was submitted to the National Agency for Food and Drug Administration and Control (NAFDAC) Director General by the pharmacovigilance (PV)/PMS director, subject to approval by the governing council. The proposition highlighted an increase in NAFDAC's annual retention fee for registered products that will be channeled to funding for PV/PMS activities. The document was approved by the NAFDAC governing council, published in the agency's gazette, and made public to MAHs. This achievement serves as an executed exit plan for the PQM program.

In Guinea, PQM collaborated with the regulatory authority and other stakeholders, including NQCL and health programs, to facilitate the first PMS activity carried out by the regulatory authority at the national level. The national PMS protocol was developed, and 333 samples (from both the public and private sectors) were collected at 3 sites along Guinea's borders with Liberia, Mali, and Senegal. One sample of amoxicillin lacked active pharmaceutical ingredient (API), and 13 samples were found doubtful using Minilab™. While the doubtful samples were not able to be confirmed using advanced analytical methods at the laboratory, it is worth noting that it took the regulatory authority and NQCL only 7 weeks to complete the PMS activities from the adoption of the protocol to the presentation of results to stakeholders. During the workshop that PQM organized for sharing PMS results, the stakeholders provided feedback and recommendations to address the challenges identified and improve future PMS activities, which are to be submitted to the Ministry of Health (MOH).

Key IR1 Indicators for FY 2019 Q3

Number of national medicine quality assurance policies, regulations, and legislations developed or updated and submitted for adoption	2
Number of quality control laboratories that have passed the proficiency test/inter-laboratory test	3
Number of quality control laboratories accredited or reaccredited	5
Number of in-service training programs developed or reformed to address QA/QC topics	1
Number of pre-service training curricula developed or reformed to address QA/QC topics	1

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, stock-outs, and poor-quality medicines. Further exacerbating supply challenges is the lack of economic incentives for manufacturers to produce essential medicines. PQM works with manufacturers to improve compliance with international quality standards to meet local and global demand for quality-assured medicines. PQM’s assistance ensures a steady supply of essential medicines of assured quality, safety, and efficacy, thus strengthening countries’ health systems to improve health outcomes.

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

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

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

To address global needs for essential medicines, PQM works with manufacturers to help them develop and submit dossiers for certification by the WHO PQ of Medicines Program for medicines to treat TB, malaria, and NTDs. Both WHO PQ and stringent regulatory authority (SRA) approval confirm that these medicines meet acceptable international standards for quality, safety, and efficacy, and can be purchased by international procurement agencies. In addition, by increasing the number of suppliers and creating a competitive environment, PQM helps shape the market for essential medicines and contributes to reducing the price of these essential 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 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 Third Quarter IR2 Achievements

Key Results and Highlights

In Q3, with PQM's technical assistance and advocacy efforts, the Drug Regulatory Authority of Pakistan (DRAP) endorsed a procedure for registration of product dossiers in accordance with the WHO Collaborative Registration Procedure (CRP) process. This is an important milestone, as it will facilitate accelerated registration of quality-assured medicines (such as those that are WHO prequalified or SRA approved) in Pakistan. This will help to increase access to quality-assured public health medicines by patients in the country. PQM continues to encourage the Indonesian manufacturer, Sanbe Farma, to register its high-priority MNCH medicine, oxytocin injection, in Pakistan via the WHO CRP mechanism, especially now that the procedure has been approved by DRAP.

Also in Q3, PQM organized a workshop with GSK on "Increasing access to quality-assured essential medicines through technology transfer to local manufacturers: The Umbipro case study." The workshop focused on the concepts of technology transfer and provided detailed insight into technology and manufacturing know-how for manufacturing Umbipro. The workshop was followed up by one-on-one sessions with participating manufacturers to address their specific concerns and confidential questions. The manufacturers now have access to information that is critical for developing and producing quality-assured chlorhexidine (CHX). It is expected that this will help increase the number of sources of quality-assured CHX in Africa and Asia.

Earlier this year, Indonesia's PT Kalbe Farma achieved WHO PQ for its levofloxacin 500 mg tablets. In Q3, PQM worked with Kalbe to hold a workshop to share knowledge and experience from the WHO PQ audit. Kalbe is now committed to developing a Quality Manual that will be adopted by all sister manufacturers under Kalbe's corporate structure, which is expected to boost implementation of international GMP standards across production sites.

In Nigeria, PQM has worked to build the capacity of local manufacturers. In Q3, Emzor Pharmaceuticals resolved all identified corrective and preventive actions (CAPAs) from PQM's GMP audit for production of the antimalarial sulfadoxine-pyrimethamine (SP) 500+25 mg tablet. Attaining production of quality-assured SP is a big leap for the country, providing opportunities to procure quality-assured SP by international distributors, donors, and the Nigerian government. So far, Emzor has received procurement requests of 2.1 million doses of SP for delivery to the Medical Export Group, an international distributor. Because of PQM technical assistance to overhaul Emzor's facilities QMS, other product lines benefited from the strengthened system. In Q3, Emzor supplied 1.62 million doses of cotrimoxazole (960 mg) tablets to the National Agency for Control of AIDS for various public health interventions in Nigeria.

Another Nigerian manufacturer, Juhel Pharmaceuticals, submitted its dossier for magnesium sulfate 50% w/v (used for treating preeclampsia/eclampsia in pregnant women) to the WHO PQ team for review in Q3. Having a locally produced, WHO-prequalified source of this product would ensure its availability on the local market and allow it to be procured globally.

Key IR2 Indicators for FY 2019 Q3

Number of priority medicines that achieved local approval with PQM's support	1
Number of dossiers accepted for review by WHO PQ or SRA	1

Number of Manufacturers Provided with Technical Assistance in FY 2019 Q3

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	3	magnesium sulfate injection, oxytocin injection, and amoxicillin dispersible tablets
Core TB	6	clofazimine FPP, clofazimine API, rifapentine API, kanamycin FPP, rifampicin/isoniazid/ethambutol/pyrazinamide (4FDC), and isoniazid API
Core NTD	4	praziquantel API, praziquantel FPP, and albendazole FPP
Bangladesh	2	chlorhexidine solution and 4FDC
Ghana	1	artemether-lumefantrine tablets
Nigeria	8	zinc sulfate dispersible tablets, sulfadoxine-pyrimethamine tablets, chlorhexidine gel, artemether-lumefantrine tablets, oxytocin injection, magnesium sulfate injection, ready-to-use therapeutic foods
Indonesia	5	levofloxacin, rifampicin/isoniazid (2FDC), and moxifloxacin, tenofovir/lamivudine/efavirenz
Kazakhstan	1	levofloxacin
Pakistan	6	amoxicillin dispersible tablets, chlorhexidine gel, zinc sulfate dispersible tablets, zinc sulfate oral solution
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 created the Poor-Quality Medicines ALERT feature. The ALERT provides rapid access to the most recent information on poor-quality medicines identified from PMS activities in PQM countries, including those performed independently of PQM assistance. Through collaborations with the World Wide Antimalarial Resistance Network and the newly formed Infectious Diseases Data Observatory, PQM is exploring ways to integrate information among these databases and expand the scope of medicines included.

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

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

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

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

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

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

Overview of FY 2019 Third Quarter IR3 Achievements

Key Results and Highlights

In Q3, the Liberia Medicines and Health Products Regulatory Agency (LMHRA) performed its sixth round of annual sample collection and testing. About 600 samples were collected, 85 percent of which were antimalarial medicines. The preliminary report indicated that nearly 14 percent of the antimalarials failed to comply with one or more regulatory requirements (e.g., country registration, proper labeling, expiry date, package inserts, manufacturer, disintegration rate, amount of active ingredients, and dissolution testing). Following the outcome, LMHRA took action to remove and quarantine all products that were found noncompliant with the regulatory requirements of the country. The outcome was also shared with key stakeholders in a dissemination meeting.

The Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) has continued using the routine adverse drug event (ADE) reporting system as a mechanism to identify poor-quality medicines (product defects) and take enforcement actions. In Q3, EFMHACA recalled the following products found to be defective: disposable syringes, Z-Cold syrup (paracetamol 125 mg phenylephrine hydrochloride 5 mg + chlorpheniramine maleate 1 mg) and human chorionic gonadotropin (HCG) rapid pregnancy test kits, following investigation of information received through a routine adverse drug reaction (ADR) reporting system. In fact, the manufacturer of the disposable syringe was asked to stop production until the root cause of the defect is identified and resolved. These actions, especially the removal of the pediatric paracetamol from the market, are expected to keep the Ethiopian public from being harmed. The action taken on the rapid pregnancy kit is also critical, as it protects individual mothers from getting false positive and false negative results. Since spontaneous ADE reporting happens mostly from serviced delivery points, which are closest to patients, regulatory actions guided by product defect reports will have the highest potential for public health benefits. This practice in conjunction with post-marketing quality surveillance and inspection is expected to boost EFMHACA's capacity to detect and prevent substandard and falsified medicines from entering into the Ethiopian market.

Key IR3 Indicators for FY 2019 Q3

Number of PQM-supported awareness raising or advocacy events promoting the quality of medical products	7
Number of publications issued, and presentations made on medical products quality assurance at the national or international level that are presented or authored by PQM	6
Number of regulatory actions made by an MRA	29

Africa



Ethiopia

I. Quarter 3 Highlights

In Q3, supportive supervisions were conducted at four EFMHACA branch laboratories. The supervision helped to resolve some key issues identified. The laboratory in Dire-Dawa was unable to test antimalarial samples collected because of high-performance liquid chromatography (HPLC) instrument malfunctioning (leakage and pressure drop). This problem was resolved by PQM mentors during the supportive supervision visit, thereby allowing the facility to resume routine testing services. In addition, the water distillation system at Mekelle branch laboratory was non-functional, so staff were unable to provide key testing services for the Authority. However, PQM provided technical assistance to make the system functional. In other branches, the team discussed the progress of the laboratories and helped to address bottlenecks associated with providing quality laboratory services to the population. Based on the findings at each branch, immediate action was taken to resolve some issues, while an action plan was developed for those issues that require additional time and resources.

As part of support to regional regulatory bodies, PQM, in partnership with EFMHACA, conducted supportive supervision and mentoring of regulators in various regions. The team provided technical assistance to validate regionally selected model institutions in response to the national effort to identify exemplary institutions (importers, wholesalers, and pharmacies) that can serve as benchmarks for others to learn from. The activities included development of a proposal to conduct validation of model institutions previously selected by respective regional authorities. The validation team inspected the proposed model institutions in Adama, Addis Ababa, Bahirdar, Dessie, Hawassa, Jimma, and Shashemene. The validation teams were composed of staff from EFMHACA, regional regulatory bodies, the Ethiopian Pharmaceutical Association, universities' schools of pharmacy, and private organizations from respective regions.

In Q3, PQM continued building the capacity of the national PV center to improve its performance. PQM provided technical assistance in recording 110 ADE reports into the pharmacovigilance data management system. A total of 35 ADE reports were shared with WHO Uppsala Monitoring Centre. Feedback in the form of acknowledgment letters were provided to 26 healthcare providers who reported ADEs. Of those 110 ADE reports, 35 were related to product defects. In connection to reports on product defects, further investigation was initiated through communication with the inspection directorate on 11 medicines. Regulatory action was taken on three of the products. This is part of PQM's effort to build EFMHACA's capacity to use the routine PV system to detect and prevent the circulation of substandard and falsified medicines. The regulatory actions taken on products following the generation of evidence through the PV system augments PMS and inspection efforts, thereby enhancing EFMHACA's overall capability to ensure patient safety and protect public health.

In Q3, EFMHACA recalled the following products found to be defective: disposable syringes, Z-Cold syrup (paracetamol 125 mg phenylephrine hydrochloride 5 mg + chlorpheniramine maleate 1 mg) and HCG rapid pregnancy test kits, following investigation of information received through a routine ADR reporting system. In fact, the manufacturer of the disposable syringe was asked to stop production until the root cause of the defect is identified and resolved. These actions, especially the removal of the pediatric paracetamol from the market, are expected to keep the public out of harm.

II. Country Context

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

The impact-level targets sets 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 Ethiopia's national health targets and goals through ensuring the availability of quality-assured, safe, and efficacious medicines that address the priority health needs of the people of Ethiopia.

III. Quarter 3 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)

In Q3, a 5-day workshop entitled “Revision of Medicine Registration Guideline and Development of Medicine Registration Directive” was organized by EFMHACA in collaboration with PQM. The revision was triggered by implementation of the electronic regulatory information system, best practices in other countries, complaints gathered from relevant stakeholders, bottlenecks encountered during implementation, and enactment of the new Proclamation No.1112/2019. The workshop participants were from EFMHACA and PQM. Key published resources used as input included WHO guidelines such as TRS 986 Annex 6; TRS 992, Annexes 7 and 8; TRS 1010, Annex 10; and other guidelines. Other countries’ best practices were also reviewed and considered in the revision of the guidelines and preparation of the directive.

During this planning period, the Federal Ministry of Health announced it would identify model pharmacies that could be considered model sites for providing quality services to the public. To implement this high-level plan, EFMHACA planned to select pharmacy establishments that go beyond fulfilling minimum regulatory requirements and could be trusted to provide the anticipated high standard of services. Though not involved in selecting the model sites, PQM incorporated the selection into the supportive supervision plan for regional regulatory bodies. In partnership with EFMHACA, PQM conducted supportive supervision and mentoring of regulators in regions to help build capacity on inspection. Combined with this activity, PQM provided technical assistance in validation of model institutions selected by regions in response to the national effort to identify exemplary institutions (importers, wholesalers, pharmacies) that can serve as a benchmark for others to learn from. The activities included development of a proposal for validating model institutions previously selected by respective regional authorities. The validation team inspected the proposed model institutions in Adama, Addis Ababa, Bahirdar, Dessie, Hawassa, Jimma, and Shashemene. The validation teams were composed of staff from EFMHACA, regional regulatory bodies, the Ethiopian Pharmaceutical Association, universities’ schools of pharmacy, and private organizations from different regions. The findings of this inspection will be used to select the model sites. When successfully implemented, this program will contribute to the fight against substandard and falsified medicines and improve quality of care, thereby helping to improve health outcomes.

EFMHACA, along with PQM, established a technical working group to prepare guidance documents that facilitate medical device registration in Ethiopia. In Q3, a workshop entitled *Preparation of Guidance Documents on Medical Device Registration* was conducted. The guidance documents considered issues relating to implementation of the electronic regulatory information system and were adopted from Malaysia, Singapore, International Medical Device Regulatory Forum, and Association of Southeast Asian Nations Regulatory Harmonization guidance for medical devices. Representatives from the Medical Device Registration Team & Medicine Registration Team, PQM, and Jhpiego participated in the workshop. The workshop reviewed and incorporated best practices from other countries, as well as Ethiopia’s registration guideline, into the document. The presence of this document is expected to contribute to the quality assurance of medical devices in Ethiopia.

In Q3, PQM participated in the revision of three directives for inspection. The revised directives are Medicine and Medical Device Import Directive, Export and Wholesales Organization Control Directive, and Pharmaceutical Manufacturer GMP Inspection Directive. The directives are revised and ready for management approval. A workshop to review the Marketing Authorization directive was also conducted in Q3. Participants included medicine importers and wholesalers, staff from multinational pharmaceutical companies, and representatives of other government institutions. The stakeholders provided valuable comments that could enrich the document. After the workshop, further discussions were held with EFMHACA experts on ways to incorporate input from stakeholders. These directives will help enforce the requirements stated in the respective guidelines.

PQM provided mentoring on the clinical trial authorization conducted on SimpliciTB (Protocol No. NC-008 [B-Pa-M-Z]). The trial was an open-label partially randomized trial to evaluate the efficacy, safety, and tolerability of a 4-month treatment of bedaquiline + pretomanid + moxifloxacin + pyrazinamide (BPamZ) compared to a 6-month treatment of isoniazid + rifampicin + pyrazinamide + ethambutol (HRZE)/isoniazid + rifampicin (HR) (control) in adult participants with drug-sensitive smear-positive pulmonary tuberculosis (DS-TB) and a 6-month treatment of BPamZ in adult participants with drug-resistant, smear-positive pulmonary tuberculosis (DR-TB). The proposal was reviewed by PQM along with EFMHACA experts to ensure it meets all requirements for conducting clinical trials prior to approval. Review of the proposal is still in progress.

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

During this planning period, PQM assisted in reassessment of the EFMHACA laboratory by ANAB and maintenance of the already accredited test methods. Support was provided in revision of the Quality Manual as per the new ISO 17025:2017 standard; development and approval of confidentiality and impartiality policies; development of CAPA for the three minor nonconformances observed by ANAB during the April 2019 visit; and submission and follow-up of the CAPA with ANAB—after which all of the CAPAs submitted were found to be acceptable by ANAB and accreditation was reinstated until April 2021.

The laboratory completed participation in one titration proficiency test (PT) scheme in Q3, and the PT provider (CCG) found the result to be acceptable. Procurement of PT samples for the other test methods was completed, and the PT provider is shipping samples to the laboratory. Technical specifications were prepared in order to procure a conductivity meter and polarimeter. The polarimeter was delivered to EFMHACA, and the conductivity meter was shipped.

In Q3, the National Meteorology Institute of Ethiopia (NMI) trained about EFMHACA 40 staff from the main and branch laboratories on laboratory measurement uncertainty. Supervision was conducted at four branch laboratories, which helped to resolve some key issues identified during the visit. The laboratory in Dire-Dawa was unable to test antimalarial samples collected because of HPLC instrument malfunctioning (leakage and pressure drop). This problem was resolved by PQM mentors during the supportive supervision visit, thereby allowing the facility to provide routine testing services. The water distillation system at Mekelle branch laboratory was non-functional, so it was unable to provide key testing services for EFMHACA. PQM experts provided technical assistance to make it functional. In other branches, the team discussed the progress of the laboratories and helped to address bottlenecks associated with providing quality laboratory services to the population. Based on the findings at each branch, immediate action was taken to resolve some issues, while action plans were developed for those issues that require additional time and resources.

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

To help enhance branch laboratories' capability to conduct PMS, PQM provided laboratory supplies and reference standards during the supportive supervision; subsequently, testing of antimalarial samples was completed at the four branch EFMHACA Laboratories. This is the first time that the branch laboratories were able to commence full compendial PMS testing of selected antimalarial medicines on their own. A total of 73 samples, selected using a risk-based approach and consisting of artemether injection, primaquine phosphate tablet, chloroquine phosphate tablet, and chloroquine phosphate syrup samples, were collected and tested. All parameters stated in the compendial were tested to evaluate the quality of product samples collected from various sampling sites. The test results indicate no (zero) failure rate, signifying that the sample antimalarial products have all the desirable quality attributes, which is a major step in the prevention and treatment of diseases.

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

Sub IR 2.1 Quality-assured priority medicines produced locally increased

Following a request from EFMHACA, PQM assisted in a technical evaluation of a proposal submitted by VIN Bioproduct Limited, a pharmaceutical company that planned to open a production facility in Ethiopia to produce tetanus antitoxins (liquid), snake venom antiserum (Liquid, lyophilized), and rabies antiserum (liquid) at the new Kilinto Industrial Park. This evaluation was meant to serve as a QA tool to ensure that new pharmaceutical companies establishing manufacturing facilities fulfill the minimum current GMP requirements right from the start. This will greatly contribute to increased local production of quality-assured medicines.

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 PV system, PQM participated and made a presentation at the Pharmaco Vigilance Africa Annual Consortium meeting, where the country's PV roadmap was presented and discussed. PQM also helped to draft an article on PMS, PV, and clinical trials, which will be included in the new regulation that will be prepared in accordance with the new proclamation.

PQM continued to build the capacity of the national PV center to improve its performance. In Q3, PQM provided technical assistance in recording 110 ADE reports into the pharmacovigilance data management system. A total of 35 ADE reports were shared with WHO Uppsala Monitoring Centre. Feedback in the form of acknowledgment letters was provided to 26 healthcare providers who reported ADE on a regular basis. Of those 110 ADE reports, 35 were related to product defects. In connection to reports on product defects, further investigation was initiated through communication with the inspection directorate on 11 medicines. In Q3, regulatory action was taken on three of the

products. This is part of PQM's effort to build EFMHACA's capacity to use the routine PV system to detect and/or prevent the circulation of substandard and falsified medicines. The regulatory actions taken on products following the generation of evidence through the PV system augments PMS and inspection efforts, thereby enhancing EFMHACA's overall capability to ensuring patient safety and protect public health.

PQM supported EFMHACA in organizing to increase awareness about product quality defects among healthcare providers and program managers. The workshop began with an opening speech by the EFMHACA Deputy Director General and a keynote address by the PQM Chief of Party. A total of 37 participants drawn from EFMHACA branches, healthcare facilities, manufacturers, importers/exporters, and distributors attended the workshop. Participants received information on the national PV and ADR reporting system and how it is being used to monitor product defects. The role of healthcare providers in increasing both the number and quality of ADR reports was highlighted. The workshop emphasized how strengthening the ADR reporting system helps to monitor the circulation of poor-quality medicines and its values in saving lives. As part of encouraging good performance, healthcare providers who submitted the highest number of ADR reports were acknowledged in the workshop.

Sub-IR 3.2 Enforcement actions against falsified, substandard, and unapproved medical products increased EFMHACA has continued using the routine ADE reporting system as a mechanism to identify poor-quality medicines (product defects) and take enforcement actions. In Q3, EFMHACA recalled the following products found to be defective: disposable syringes, Z-Cold syrup (paracetamol 125 mg phenylephrine hydrochloride 5 mg + chlorpheniramine maleate 1 mg) and HCG rapid pregnancy test kits, following investigation of information received through a routine ADR reporting system. In fact, the manufacturer of the disposable syringe was asked to stop production until the root cause of the defect is identified and resolved. These actions, especially the removal of the pediatric paracetamol from the market, are expected to keep the Ethiopian public from being harmed. The action taken on the rapid pregnancy kits is also critical, as it protects mothers from getting false positive and false negative results. Since spontaneous ADE reporting occurs mostly at service delivery points, which are closest to patients, regulatory actions guided by product defect reports will have the highest potential for public health benefits. This practice, in conjunction with post-marketing quality surveillance and inspection, is expected to boost EFMHACA's capacity to detect and prevent substandard and falsified medicines from entering the Ethiopian market.

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

Activities under this objective were completed in previous quarters.

IV. Key Challenges

The reassignment of EFMHACA staff in other urgent and unforeseen activities has contributed to the delay of some planned PQM activities targeted for this quarter. Also, the current security situation in the country has played a role in postponing and rescheduling activities.

V. Lessons Learned

Following a request from EFMHACA a few years ago, PQM employed laboratory analysts for the four branch laboratories to kickstart the work. At that time, EFMHACA did not have the positions approved by the responsible government body (Civil Service Ministry) and could therefore not employ staff. EFMHACA promised to finalize the processes for approval of the positions and agreed to take over all staff. All the analysts were transferred to EFMHACA as of April 2019, which is an exemplary move by the regulatory agency to sustain progress made at the branch laboratories. Common understanding and consensus on expectations from each party at the outset has helped to make this transition successful.

Ghana

I. Quarter 3 Highlights

PQM continued to provide remote support to Entrance Pharmaceuticals Ltd as it addresses corrective actions toward improving its GMP compliance. The bioequivalence (BE) study protocol received institutional review board (IRB)/ethics committee (EC) review approval, and full approval for implementation of the study is now pending. A BE study is a statutory requirement for submission of artemether–lumefantrine tablet dossiers to WHO PQ.

The official Ghana FDA (GFDA) report on the uterotonics (oxytocin and ergometrine) post-market quality survey conducted in Q1 was released in Q3 and confirms the preliminary results shared previously. GFDA reported that all poor-quality medicines found in public facilities were recalled and removed from circulation.

GFDA conducted a rebranding event in April where the new official logo of the authority was unveiled. PQM was invited and recognized as a technical partner that has contributed to GFDA's successes over the years. The new logo was unveiled by the first lady of Ghana, along with other dignitaries from the country.

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 assisted GFDA to strengthen the medicines QA and QC systems. Activities have focused on strengthening GFDA's capacity in drug registration, medicines QC, and PMS. PQM has also recently provided technical assistance to ensure locally manufactured artemisinin-based combination therapies (ACTs) meet internationally acceptable quality standards.

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

There are several local pharmaceutical product manufacturers 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 3 Progress by Objective

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

The final results and report for the PMS of oxytocin injections and ergometrine injections conducted in Q1 were released by GFDA in Q3. The report confirmed the preliminary results discussed in Q2: the test results showed 41.2 percent (35/85) of oxytocin samples and 80.0 percent (4/5) of ergometrine samples tested did not meet assay specifications. Additionally, 62.9 percent (66/105) of oxytocin samples and 100 percent (11/11) of ergometrine samples were found to be unregistered. GFDA took regulatory action, including communicating with the Minister of Health to require that all public facilities/hospitals procure duly registered medicines, including uterotonics. All failed samples from public and private facilities were recalled in the previous quarter.

Results from this surveillance were discussed with partners from the USAID Global Health Supply Chain (GHSC) program implemented by Chemonics in Ghana. To further inform future regulatory enforcement for labeling and storage, PQM share with GFDA a joint statement issued by WHO/UNICEF/UNFPA in March 2019, which requires the procurement of quality-assured oxytocin that is labelled for storage at 2°C–8°C and kept cold at all points within the supply chain.

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

No activities this quarter. All activities for this objective have been completed.

Objective 3 – Strengthen facility inspection capacity of Ghana FDA

No activity this quarter. Training was completed in Q1.

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

In Q3, PQM continued to provide remote technical assistance to Entrance Pharmaceuticals Limited, including responses to technical questions as they arise. Entrance continues to address ongoing CAPA toward improving its GMP compliance. The BE study is a key outstanding item for Entrance before it submits its artemether–lumefantrine dossier. In Q3, the BE study protocol received IRB/EC approval; final approval from the Jordan FDA being awaited.

The BE study will be conducted by a CRO in Jordan, so approval of the protocol must be obtained from the Jordan FDA. The BE study reference and test samples were sent to the CRO in Q3.

Recognizing the unexpected delays in the approval of the BE protocol for study commencement, PQM requested an updated timeline from Entrance. Based on the new timeline shared with PQM, the dossier submission is now anticipated to occur in FY 2020 Q2. Since the PQM program period of performance ends in September 2019 and all PQM technical support must conclude by July 2019, PQM envisions providing as much technical support as is possible remotely through July 2019 to ensure Entrance is able to submit the dossier once the BE study is concluded and the report is made available next year.

Guinea

I. Quarter 3 Highlights

PQM completed the activities set in the work plan and closed out the project in Guinea.

PQM facilitated one round of PMS, including finalization and implementation of a national PMS protocol, and organized a dissemination workshop for the results of these activities. Following the workshop, PQM organized a closeout ceremony meeting. Mr. Souleymane Toure, the Minister of Health's Legal Advisor, chaired the workshop. The Deputy Director of the National Directorate of Pharmacy and Medicine (DNPM) presented an overview of PMS activities, highlighting their importance, while the representative of the National Medicines Quality Control Laboratory (LNCQM) presented the results of sampling and testing of medicines. PQM presented an overview of the program and key achievements, which included revising the national pharmaceutical law and strengthening the capacity of DNPM regulatory functions such as quality control, inspection, and PMS.

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 played a key role in strengthening the pharmaceutical system and the capacity of the national drug regulatory authority to assure quality in the supply chain through registration, inspection, and QC activities. Malaria is the primary cause of consultations, hospitalizations, and deaths in Guinea, particularly affecting 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 3 Progress by Objective

Objective 1 – Continue to strengthen the legal and regulatory framework to enable DNPM implementation of a comprehensive QA/QC mandate

To strengthen the DNPM inspectorate capacity, PQM trained 12 inspectors on current GMP inspection. This was the first training in current GMP that was ever received by DNPM inspectors. This activity was a priority for DNPM because it was among the activities in MOH's annual action plan. The 4-day training covered overviews of GMP inspection topics and included group work sessions. The training had several components that the inspectors can apply during inspection of wholesalers and distributors warehouses. Furthermore, the DNPM could build on this first training to develop a stronger inspectorate.

Objective 2 – Continue strengthening DNPL’s main functions including registration and launch post-marketing surveillance (PMS)

In collaboration with other stakeholders, including LNCQM and Health Programs, DNPM facilitated the finalization of the national PMS protocol and its implementation. Three teams carried out sample collection at three geographical axes going from Conakry to the borders with Liberia, Mali, and Senegal. The teams collected 333 samples from the public and private sectors and found that 1 amoxicillin sample lacked the API and 13 samples were found doubtful using Minilab™. Doubtful samples need confirmatory testing. One limitation was that the laboratory does not have the capacity to confirm these results using advanced analytical methods. However, it is worth noting that it took DNPM and LNCQM only 7 weeks to complete PMS activities from the adoption of the protocol to the presentation of the results to stakeholders. This was the first PMS activity carried out by DNPM at the national level.

During the workshop that PQM organized for sharing PMS results, the stakeholders provided feedback and recommendations to address the challenges identified and improve future PMS activities. The participants developed a workshop report and agreed on the following recommendations to be submitted to MOH:

- Strengthen LNCQM capacity to enable the laboratory to carry out the QC function.
- Ensure environmental control throughout the supply chain (mandate temperature and humidity control).
- Support sustainability of PMS activities and expand their scope.

IGAD

I. Quarter 3 Highlights

Q3 marked the successful conclusion of the Intergovernmental Authority on Development (IGAD)–Medicines Regulatory Harmonization (MRH) regional PMS activity that began in FY 2019 Q1. The survey focused on oxytocin injection, amoxicillin dispersible tablets, and amoxicillin suspension collected from select cross-border areas in the IGAD region. The survey revealed weaknesses in medicine registration capacity in the region and found samples of oxytocin injections that did not meet quality specifications.

In Q3, PQM collaborated with IGAD-MRH and the member state expert working group on PMS and PV to hold the results validation workshop, where details of the results obtained from the PMS survey were reviewed and validated. The report on the self-assessment on PV capacity in the region was also discussed and validated.

The PMS result dissemination meeting was held in Entebbe, where IGAD-MRH publicly shared the official report for the PMS survey. The result dissemination meeting was chaired by the head of the Uganda MRA as host country and with representatives from all IGAD member states in attendance. IGAD-MRH and PQM staff were also present.

II. IGAD Context

The IGAD region comprises eight countries in the horn of Africa region and includes Djibouti, Eritrea, Ethiopia, Kenya, Somalia, South Sudan, Sudan, and Uganda. The region experiences migration and cross-border mobility due to economic uncertainties and political conflicts, and cross-border mobile populations face major barriers in accessing 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, PQM will implement targeted interventions, including establishment of an expert working group (EWG) to identify PV/PMS document gaps, provide recommendations for implementation of PV/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) 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 3 Progress by Objective

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

No activities this quarter. All activities for this objective have been completed.

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 Q3, key activities implemented pertained to the PMS survey and the PV self-assessment. A major milestone was accomplished with the completion of the first regional PMS activity conducted by an MRH in sub-Saharan Africa, involving seven countries (Djibouti, Ethiopia, Kenya, Somalia, South Sudan, Sudan, and Uganda).

PMS Survey: With PQM support, EFMHACA laboratory completed the testing and obtained results for all samples collected during the regional IGAD cross-border survey (87 oxytocin injections, 37 amoxicillin dispersible tablets, and 29 amoxicillin suspensions). In collaboration with the IGAD-MRH secretariat, PQM organized a Results Validation Workshop with the IGAD EWG on PMS in Entebbe, Uganda, on June 17–18, 2019. Representatives from all seven member state MRAs participated in the workshop. PQM finalized a technical report on the survey and shared it with all member states and the IGAD-MRH secretariat.

Once the results were validated by the EWG, a result dissemination meeting was conducted the following day. Participants included the Uganda MRA Head, member state MRA representatives, the IGAD-MRH Director of Health and Social Development, staff from the secretariat, and the media.

The survey results did not find any substandard or falsified amoxicillin dispersible tablet or amoxicillin suspension products amongst the samples, as all tested amoxicillin samples met the quality specifications required by pharmacopeia for all tests performed. The survey found that 20.9 percent (18/86) of oxytocin samples did not meet quality specifications. The registration status of the samples collected also showed that only 27.8 percent of oxytocin products, 70.0 percent of amoxicillin dispersible tablet products, and 73.7 percent of amoxicillin suspension products were registered by the relevant MRAs of the region.

The failed samples highlight the quality concerns for oxytocin in the region, and the presence of unregistered medicines suggests weakness in the regulatory capacity within the region.

Following the dissemination of the results, the member state MRAs developed recommendations for next steps, including the following:

- Relevant regulatory action(s) should be taken by each MRA in the IGAD region based on the survey findings.
- A transparent information exchange system should be established among the IGAD MRAs to strengthen regulation of medicines in the region.
- All IGAD MRAs should have a PMS strategy upon which plans are developed.
- PMS plans should be risk-based, properly identifying products to be monitored after registration.
- MRH should have a regional generic PMS guideline to be adopted by all member states to allow for collaboration.
- Medicine evaluation, inspection, and registration systems should be strengthened.
- Collaboration among IGAD MRAs should be promoted, with the objectives of exchanging information on substandard and falsified products circulating in markets, lists of registered products, inspection outcomes, PMS plans, and outcomes of PMS activities.

PV Self-Assessment: In June 2018, with the work plan goal to identify gaps in PV capacity in the region, the IGAD EWG on PV/PMS was established. To facilitate the identification of PV capacity gaps by member countries, PQM developed a self-assessment questionnaire, which was shared with the member state representatives in the EWG. The self-assessment questionnaire was completed by member states and was collated at the October 2018 EWG meeting. PQM reviewed and consolidated the completed questionnaires into a report. In Q3, the EWG validated the PV self-assessment report at the results validation workshop. The report showed varied capacity exists to conduct PV

within the region and ranged from non-existent to limited, with some aspects of PV currently being implemented in some countries. The detailed report was finalized and provided to the IGAD secretariat and member states to help inform next steps in the development and capacity-building for pharmacovigilance in IGAD-MRH member state MRAs.

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

The IGAD-MRH secretariat has recruited a consultant to develop the regional health sector policy document. In accordance with the work plan, PQM is expected to provide a technical review of the pharmaceutical sector portion in the draft regional health sector policy to ensure the sector is adequately addressed. Based on recent communication, PQM expects to receive this draft document and complete the review by the end of July.

Kenya

I. Quarter 3 Highlights

In Q3, PQM conducted a Minilab™ training in preparation for the implementation of PMS of antimalarial medicines in 12 counties for 23 participants from national and county governments. Procurement of supplies for the PMS activity were initiated and is currently in the process of completion.

PQM also helped finalize the technical working group (TWG) terms of reference (TORs) and followed up on the nomination letters for the TWG members.

II. Kenya Context

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

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen the capacity of PPB functions and county government in quality assurance of medicines

Technical Working Group: In line with the planned work plan activity to revitalize the TWG for PMS activities, in Q3 PQM worked with the Pharmacy & Poison Board (PPB) staff to review and finalize the TORs for the TWG developed in the previous quarter. PQM worked with PPB staff to review the final draft of the TWG TORs after incorporation of the stakeholder’s comments and feedback. The document was shared with the PPB legal team for review and approval, which is anticipated next quarter.

Protocol Review: In preparation for the next (seventh) round of antimalarial PMS, PQM provided technical support and worked with PPB and other stakeholders (e.g., NQCL, Kenya Medical Supply Authority, and public health program representatives) to review the antimalarial PMS protocol and align it with activities to be conducted by 5 cluster teams in 12 counties. The next round of PMS will be conducted in these 12 counties.

Training: In Q3, PQM provided technical support in collaboration with the Kenya NQCL and facilitated a 5-day Minilab™ training, both theoretical and hands-on, at NQCL for 23 participants from national and county governments. PQM worked with PPB on the logistics for the training, which included invitation letters to participants and notifications to selected country governments and the Council of Governors. Training materials were prepared, and medicine samples were procured for training purposes.

In anticipation of the QC testing needed to analyze samples collected through the PMS activity, PQM met with the NQCL Director to discuss analytical the QC testing support that would be provided by the laboratory. PQM is working

to ensure a contract is in place that allows NQCL to provide the analytical testing in a timely manner once the samples are collected and available for testing.

Objective 2 – Promote medicines quality awareness and data sharing at the county level through monitoring and reporting of regulatory actions

No activity this quarter.

IV. Key Challenges

The timely delivery of Minilab™ supplies from the vendor was challenging, with a last-minute request for a special import permit prior to shipment. The order was placed in May and received in July. However, with supplies now received, PQM anticipates implementing the PMS activity in Q4.

Liberia

I. Quarter 3 Highlights

In Q3, all activities in Liberia were completed and the project closed out. The closeout event attracted key stakeholders, partners, government agencies, and USAID. At the event, the LMHRA CEO, Mr. David Suomo, highlighted LMHRA's key achievements and how PQM's support enabled the agency to adequately control the proliferation of substandard and falsified medicines in the country. He was particularly grateful to PQM and USAID for the support in building strong laboratory capacity for LMHRA. PQM donated multiple instruments, reference standards, reference books, and reagents and consumables throughout the life of the project. He lamented the unfortunate incident of the fire that gutted the laboratory, making it challenging for LMHRA to continue providing quality laboratory services for the population. He recognized PQM's additional support in helping to relocate the laboratory to its current location after the fire incident. For his part, the USAID Mission Director in Liberia, Dr. Anthony Chan, recognized the significant contribution of PQM in building strong regulatory systems in Liberia. He assured LMHRA and the government of Liberia about USAID and the U.S. Government's (USG) support in building strong health systems toward self-reliance in Liberia. He called on the Liberian government to demonstrate commitment in the ongoing USG support to the country by taking ownership of the investment to date. In closing, the PQM representative, Dr. Latifa El-Hadri, recounted the contributions of PQM from 2009 when there was a limited regulatory framework in the country to manage essential aspects of medicines quality to the population. With PQM guidance, a regulatory framework was developed and enacted into law to allow for the creation of LMHRA with a mandate to assure the quality of medicines and health products distributed in the country.

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 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 an LMHRA regulatory action and since then have become less prevalent. Although results from various MQM activities and subsequent regulatory actions have been encouraging, 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 medicines quality.

As part of the approved FY 2017 work plan, PQM provides technical assistance toward building the capacity of LMHRA's QC laboratory to attain 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 medicines quality.

III. Quarter 3 Progress by Objective

Objective 1 – Rebuilding capacity of LMHRA QC laboratory

In building the capacity of LMHRA's QC laboratory, PQM contracted the laboratory to undertake testing services for LMHRA as part of the PMS activity. The laboratory conducted physical and chemical analysis of all samples collected for the PMS activity. This is the sixth round of annual sample collection and testing, and the laboratory was able to conduct physicochemical tests on 600 collected samples, 85 percent of which were antimalarial medicines. The preliminary report indicated that nearly 14 percent of the antimalarials failed to comply with one or more regulatory requirements (e.g., country registration, proper labeling, expiry date, package inserts, manufacturer, disintegration rate, amount of active ingredients, and dissolution testing). Noncompliant products were collected and removed from circulation for further investigation.

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

No updates reported this quarter.

Objective 3 – Build LMHRA capacity to take appropriate regulatory actions

Following the outcome of the sixth round of annual sample collection and testing, LMHRA took action to remove and quarantine all products that were found noncompliant with the country's regulatory requirements country. This outcome was shared with key stakeholders in a dissemination meeting, which formed part of the PQM project closeout event.

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

Reported under objective 1.

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

Reported under objective 3.

IV. Key Challenges

Continuous stockouts of key reagents and consumables and the lack of instrument maintenance in the laboratory affect LMHRA's capacity to provide uninterrupted regulatory services as per WHO's nine functions of an SRA.

Mali

I. Quarter 3 Highlights

PQM closed out its project in Mali in a ceremony at the National Laboratory of Health (LNS). Dr Sécou Oumar Dembélé, Minister of Health and Public Hygiene Technical Advisor, chaired the ceremony, which was attended by 26 participants. PQM staff presented the program and its key achievements, lessons learned, and recommendations for the future. Pr. Benoit Koumare, Director General, presented in detail the support that the laboratory received through PQM and the impact on the institution. He highlighted the importance of the MQM program that PQM established in Mali to monitor the quality of antimalarial medicines available in the market and how PQM subsequently helped LNS and the Directorate of Pharmacy and Medicines carry out PMS activities. He stressed that the PMS program allowed active involvement of the Regional Directorate of Health in PMS activities and decentralization of some LNS quality control activities to the regions of Mali. In his closing remarks, Dr. Dembélé stressed the importance of USAID support to the MOH institutions through PQM and indicated that the end of the PQM program should be seen as the beginning of a new program and that MOH institutions need more support to strengthen their capacity. He pointed out that PQM helped strengthen MOH's capacity to control the quality and safety of medicines in Mali and raised awareness about the challenges that need to be addressed to assure the quality of medicines in the Malian market.

Mozambique

I. Quarter 3 Highlights

In Q3, PQM worked with the National Directorate of Pharmacy (DNF) PMS unit to conduct PMS for artemether–lumefantrine tablets in four provinces. Prior to implementation, staff from DNF and LNCQM were trained using a risk-based framework and tool to select products for sampling, as well as provinces and facilities with the highest risk to collect samples from for testing. The risk-based approach was also utilized for medicines quality testing: visual inspection is employed first, followed by Minilab™, and finally compendial testing.

The LNCQM space expansion rehabilitation was also completed. The laboratory layout and workflow were redesigned to meet international requirements.

DNF, USAID, and PQM had detailed discussions to plan for the conclusion of PQM's current activities. The transition plan jointly developed with DNF was discussed, and plans for the closeout event commenced.

II. Country Context

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

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 the required QC services. The assessment also identified a lack of PMS of medicines quality. In 2011, PQM and PD partnered to establish an MQM program that included training on screening medicines quality.

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

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

With more than 90 percent of medicines circulating in Mozambique being imported, the authorities are aware of the country's vulnerability and exposure to poor-quality medicines. This new legislature, including Article 4 that addresses quality, offers a great opportunity for PQM and other supporting partners to make long-lasting contributions to the country's efforts to strengthen medicines regulation and work toward eliminating substandard and falsified products.

III. Quarter 3 Progress by Objective

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

In Q3, the newly acquired “office in a container” was fully outfitted with water, electricity, and internet; the Laboratory Director and some staff moved into the new office space. The additional physical space next to the laboratory that LNCQM had been requesting from MOH was finally released, but the space was unsuitable. After approval was received, the rehabilitation work commenced and was completed in June 2019. PQM provided technical guidance and supported with the redesign of the laboratory to ensure the layout is aligned with international requirements.

In Q3, PQM supported translation and review of three standard operating procedures (SOPs): SOP for testing samples and reporting results; SOP for LNCQM out-of-specification (OOS); and SOP for verification of dissolution testing. PQM also procured and translated an ISO 17025:2017 compliant quality manual. In addition, PQM trained laboratory staff on GLP of pH measurement and re-evaluated and updated the LNCQM CAPA plan first developed in March 2018 after the LNCQM assessment.

PQM trained 13 participants (9 females and 4 males) on ISO 17025:2017. They learned and performed the following:

- Comparison of 2005 and 2017 ISO/IEC 17025
- Main changes to ISO/IEC 17025:2005
- New structure and emphasis for ISO/IEC 17025:2017

- New management system options
- Risk-based approach and implementation

PQM procured a Portuguese language version of the document outlining ISO 17025:2017 standards from the National Quality Institute in Portugal for LNCQM as a reference to prepare for the international accreditation the laboratory is seeking. To foster collaboration between INNOQ (the Mozambique national body for instrument calibration to ensure precision and accuracy of equipment measurements) and LNCQM, PQM visited INNOQ to discuss modalities for a better working relationship with LNCQM.

Objective 2 – Support and strengthen post-marketing surveillance

In Q3, PQM collaboration with DNF to conduct a 1-day training on the use of the medicine risk-based surveillance tool (MedRS) developed to simplify medicine sampling methods and help MRAs to consistently implement risk-based approaches. The training included how to develop a risk-based PMS protocol, sample collection, and screening using Minilab™. The 13 (4 male and 9 female) trained sample collectors from DNF and LNCQM also provided step-down training to the provincial staff who worked with them in the field during sample collection. Using the risk-based PMS approach and criteria, artemether–lumefantrine tablet was selected as the priority medicine to sample, and four provinces (Maputo city, Maputo province, Gaza, and Niassa) were selected as areas with the highest risk for sampling.

PQM procured Minilab™ reagents and supplies for the activities. PQM also supported logistics, including finalization and translation of the protocol and sample collection forms for the artemether–lumefantrine tablet sampling conducted in the four provinces. PQM facilitated creation of a WhatsApp group that helped communication and seamless co-ordination of the PMS activities during sample collection in the four provinces.

Objective 3 – Provide technical assistance to the Pharmaceutical Department

In Q3, to strengthen DNF regulatory capacity, PQM held one-on-one discussions with the DNF Director and heads of selected DNF divisions to discuss and find sustainable ways to continue and complete routine tasks and regulations. PQM motivated DNF and LNCQM to get approval for its price list with the department of finance and commence charging fees for their services. PQM met with the QA division head and discussed issues around QMS and the goals of attaining ISO 9001 for DNF and ISO 17025:2017 for LNCQM. PQM also met with DNF, LNCQM, and the USAID activity manager to discuss plans for PQM's end-of-project transition plan, closeout event, and dissemination of the recent risk-based PMS conducted. A tentative date for the closeout event was selected, and a DNF focal person was nominated to coordinate planning. To improve data availability for evidence-based regulatory action, PQM reiterated the importance of dissemination and motivated DNF to disseminate the last risk-based quality survey on artemether–lumefantrine in tandem with the closeout event to increase awareness on the consequences of poor-quality medicines in the health system. PQM continued to provide technical support to DNF's PMS team to continue performing activities unaided upon PQM's conclusion. To increase visibility and information-sharing with the public and stakeholders, PQM supported the one-off payment for the DNF webpage activation and subscription for 1 year.

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

Activities under this objective were completed in Q1.

IV. Key Challenges

PQM has identified the following as key challenges to implementation in Mozambique:

- No revenue generated by LNCQM to support operational costs.
- Inadequate government funding and insufficient revenue generated by DNF to support LNCQM's operations.
- Insufficient capacity of the local third-party calibration body (INNOQ) to calibrate all LNCQM equipment. Services are still sourced from outside the country.

V. Lessons Learned

To mitigate some of the key implementation challenges in Mozambique as outlined above, PQM has identified that efforts to attain country ownership and sustainability toward self-reliance will not be realized without strong financial and political commitment to strengthen medicines quality assurance systems.

In Q3, PQM also found that social media platforms (e.g., WhatsApp) can improve and ease communication and coordination of activities, especially during PMS.

Nigeria

I. Quarter 3 Highlights

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

- A pharmaceutical monitoring and evaluation (M&E) plan for NAFDAC was completed this quarter, and an electronic database (district health information software) was successfully deployed to enable improved data reporting for NAFDAC.
- NAFDAC took the lead on sustainability, as the proposition to increase product registration fees for MAHs submitted to the governing council by the NAFDAC Director General was approved by the governing council. This highlights an increase in NAFDAC's annual retention fee for registered products, which will be channeled for PV and PMS activities.
- PMS results of antimalarial and maternal and child health medicines were completed in Q3. The MNCH results showed a reduction in the failure rate for oxytocin compared to the last MNCH survey (from 74% to 38%). Results for sampled antimalarial medicines showed that 2.8 percent of samples failed QC testing.
- NAFDAC Kaduna and National Institute of Pharmaceutical Research and Development (NIPRD) laboratories maintained their accreditation status and upgraded to ISO/IEC 17025:2017.
- Technical assistance to two Nigerian manufacturers saw results this quarter. Emzor Pharmaceuticals resolved all identified CAPAs and received procurement requests for 2.1 million doses of the antimalarial sulfadoxine pyrimethamine by the Medical Export Group, an international distributor. Juhel Pharmaceuticals submitted its dossier for magnesium sulfate 50% w/v to the WHO PQ team for review.

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 of reducing malaria-associated mortality by 50 percent in Nigeria.

Through Maternal and Child Health funding, USAID/Nigeria is 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.

To accomplish NAFDAC's goals, PQM will continue to provide technical assistance to NAFDAC, MOH, the Pharmacists Council of Nigeria, NIPRD, and the National Malaria Elimination Program. In addition, there are pharmaceutical and nutraceutical manufacturers and other stakeholders whose activities directly impact system strengthening of NAFDAC and PQM-supported local manufacturers.

III. Quarter 3 Progress by Objective

Objective 1 – Strengthen national quality assurance and regulatory systems

PQM commenced support to NIPRD in FY 2017, when an extensive gap assessment at NIPRD was completed and a new roadmap with timelines was developed. NIPRD is the national center of excellence for research and development of phytomedicines, pharmaceutical and biological products, medicines, and diagnostics in Nigeria. Based on the roadmap, NIPRD commenced the process of equipment procurement, and PQM began technical

support to build the capacity and skills of key personnel ahead of accreditation of the laboratory. In FY 2018, the laboratory received accreditation for six test methods. In Q3, the laboratory maintained its accreditation status and upgraded to ISO/IEC 17025:2017; the achievement has the NIPRD laboratory among the few laboratories in Africa with the current accreditation status. NIPRD paid 80 percent of all costs associated with reaccreditation.

PQM Nigeria made a presentation on “Actualizing the potential of the Nigeria pharmaceutical manufacturing sector” at the inauguration of NIPRD’s Health Engagement Education, Access Discourse (HEEAD)-themed “Developing a Robust and Comprehensive Policy to Catalyze Pharma Industrial Development: Setting the agenda for the next level”. NIPRD-HEEAD is geared toward improving and developing the pharmaceutical sector. The inaugural NIPRD-HEEAD was attended by executives, legislative policymakers, researchers, multinationals, and major stakeholders in the pharmaceutical sector of the Nigerian economy. The issues deliberated at the event focused on how to improve and develop the pharmaceutical sector in Nigeria, with NIPRD as the nucleus for such reengineering.

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

NAFDAC takes the lead on sustainability

In FY 2016, PQM commenced building NAFDAC’s capacity to perform its PMS regulatory function, which aims to assess product quality in the market. This includes maintaining and monitoring the quality of marketed products throughout the distribution system and at all levels of the supply chain.

In FY 2017, a review of PMS findings from the survey carried out by NAFDAC, with PQM support, revealed quality issues at various levels of the supply chain and required appropriate regulatory actions.

In FY 2018, PQM’s emphasized supporting NAFDAC’s PMS unit to work with other agency directorates (e.g., ports inspection, enforcement, drug evaluation, and research and registration) to increase awareness on good storage and distribution practices amongst MAHs and stakeholders via platforms such as audience-targeted workshops. PQM liaised with NAFDAC’s PV/PMS directorate to discuss strategies for a sustainable funding stream for routine MQM to support PMS activities and regulatory actions.

The PV/PMS Director submitted a draft proposition to increase product registration fees for MAHs, subject to approval by the governing council. It highlighted an increase in NAFDAC’s annual retention fee for registered products, which will be channeled to fund PV/PMS activities. The document was approved by the NAFDAC governing council, published in the agency’s gazette, and made public to MAHs in Q3. This achievement serves as an executed exit plan for PQM.

Functional Monitoring, Evaluation and Learning system developed in NAFDAC

PQM supported the strengthening of NAFDAC’s M&E system through the development and implementation of an M&E plan, which will help NAFDAC assess and track the results of its pharmaceutical-related activities. The plan details key performance indicators, who is responsible for collecting them, what forms and tools will be used, and how the data will flow through NAFDAC. The plan also details what, when, how, and by whom the monitoring activities will be conducted, as well as how and when NAFDAC will evaluate its performance in pharmaceutical regulation. The plan helps improve NAFDAC’s focus on performance monitoring of service delivery and policy development in improving people’s lives through clearly articulated goals, targets, and methods of data collection and management. Fifteen NAFDAC M&E focal points were trained on the use of district health information software to improve data capture and availability of information related to the quality of medical products for effective decision-making.

The M&E plan is a fundamental complement to NAFDAC’s indigenous 5-year strategic plan. In addition to measuring implementation progress of the strategic plan, the M&E plan will help identify areas for improvement, explain why the 5-year strategy is or is not working, and suggest areas for corrective strategies.

NAFDAC Zonal laboratory Kaduna maintains accreditation status

NAFDAC Kaduna laboratory maintained accreditation for all existing tests methods, including microbiology test methods. The laboratory upgraded to ISO/IEC 17025:2017 accreditation status, the new requirement mandated for this accreditation going forward.

Institutional capacity for regulatory workforce sustainably improved

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

As a part of resolving CAPA identified during the assessment of all active pharmaceutical manufacturing facilities in Nigeria, 258 participants across the country were trained on various GMP courses. Training courses included

regulatory expectations in addressing nonconformance, benefits of a CAPA system, sources of quality data in QMS, and tools for investigating nonconformance (e.g., root cause analysis, cause and effect analysis). Several major observations from the assessment of the companies were used as case studies in proffering CAPA plans for the participants.

PQM facilitated a collaborative learning session for 20 NAFDAC laboratory quality management team members, technical managers, head of laboratories, and directors from the five regional NAFDAC QC laboratories. The planned key result of this activity was to further embed sustainability of all PQM achievements in the laboratories. As part of the resolutions made during the collaborative learning session, the NAFDAC QMS team and management will use a common document to maintain similar standards of practice across all laboratories. One of the medicine laboratories situated in the northeast region of the country, Maiduguri laboratory, greatly benefited from the learning sessions, as all QMS documents required toward achieving ISO 17025:2017 accreditation were developed during the learning session. The team drafted 40 SOPs, policies, and technical procedures during the workshop.

An additional 3-day training on monitoring SOPs were offered to 25 NAFDAC QMS staff. Training courses included process monitoring and learning, as well as development of an evaluation kit that will aid periodic QMS evaluation for NAFDAC. The developed evaluation kit will be deployed as soon as the necessary approvals are achieved.

An experience-sharing workshop on the recently concluded nationwide GMP inspection of pharmaceutical manufacturing facilities in Nigeria was conducted in Q3. The workshop provided the opportunity to improve regulators' expertise on inspection of local manufacturing facilities through the review of key SOPs required for GMP inspection and the GMP roadmap report.

Post-marketing surveillance results for MCH and Antimalarial medicines

PQM Nigeria focuses on building NAFDAC's capacity to perform PMS as a regulatory function, which is aimed at assessing product quality in the market. This includes monitoring the quality of marketed products throughout the levels of the supply chain. In FY 2018, NAFDAC conducted PMS of 11 maternal and child health medicines from several healthcare facilities and distribution and supply outlets in six states of the country: Federal Capital Territory (North-Central), Borno (North-East), Kano (North-West), Anambra (South-East), Rivers (South-South), and Lagos (South-West), respectively. Results by manufacturer label showed that 45.6 percent (902 of 1,975) of the collected samples were manufactured in Nigeria, while 21.3 percent (421 of 1,975) and 18.3 percent (363 of 1,975) of collected samples were manufactured in India and China, respectively. Below are disaggregated results according to type of medicine, results of analysis, and region of procurement for most failed samples.

Product	# samples tested	# samples passed	#samples failed	% failure	Region of procurement of most failed samples
Oxytocin	247	151	96	38	North-West, North-Central
Misoprostol	263	240	23	8.7	North-West
Chlorhexidine gel	112	99	13	11.6	North-West, South-South
Zinc dispersible tablets	201	171	30	15	North-Central, North-West
Oral rehydration salt	187	165	22	12	North-Central, North-West
Dextrose saline	125	121	4	3.2	North-West, North-Central
Normal saline 0.9%	119	114	5	4	North-West
Gentamicin injection	176	169	7	4	North-West, South East, South-South
Amoxicillin	150	115	35	23	South-South
Oral rehydration salt + zinc	240	116	24	10	Northern region
Water for injection	155	149	6	3.8	South-South, North-West, South-East

Results from this study will serve as evidence to carry out targeted interventions. They might also offer an opportunity for MOH to consider alternative options to strengthen cold chain capabilities for certain maternal health supplies, which will improve the integrity and quality of the supply chain system.

In Q3, laboratory analysis was concluded for the last round PMS of antimalarial medicines: 1,054 samples of antimalarial samples were procured in 7 states (Akwa Ibom, Ekiti, Jigawa, Kebbi, Nasarawa, Niger, Yobe). Results showed 3.1 percent of sampled medicines were not registered, while 51 percent had India as the country of origin. Also, 97.2 percent of sampled antimalarial medicines passed laboratory analysis, while 2.8 percent failed. Most failed samples were procured from the North-Central and North-East regions of the country. NAFDAC will disseminate all results to key stakeholders and commence regulatory actions to ensure unsafe medicines are not accessed by the public.

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

As part of building the capacity of local manufacturers, PQM provided technical support to eight local manufacturers in Q3. In addition, PQM continued providing targeted and product-specific support to one manufacturer toward production of quality-assured antimalarial sulfadoxine–pyrimethamine (SP) 500+25 mg tablet. Previously, the PQM GMP team audited Emzor Pharmaceuticals to assess its manufacturing practices for SP tablet. The audit concluded with a few critical observations, and Emzor Pharmaceuticals resolved all CAPA identified during the audit. Attaining production of quality-assured SP is big leap for the country, providing opportunities to procure quality-assured SP by international distributors, donors, and the Nigerian government. So far, Emzor has received procurement requests of 2.1 million doses of SP for delivery to the Medical Export Group, an international distributor. Also, because of technical assistance provided by PQM to overhaul the facilities' QMS, other product lines benefited from the strengthened system. In Q3, Emzor supplied 1.62 million doses of cotrimoxazole (960mg) tablets to the National Agency for Control of AIDS for various public health interventions in Nigeria.

In Q3, Juhel Pharmaceuticals, a PQM-supported manufacturer, submitted to the WHO PQ team a dossier for magnesium sulfate 50% w/v, which is used to treat preeclampsia/eclampsia. Having a locally produced, WHO-prequalified source of this product would ensure the availability of the quality-assured product on the local market and allow it to be procured globally. PQM also continued to support Juhel Pharmaceuticals as it monitors stability for oxytocin injection 10iu per 1mL, currently in its 5th month of stability study.

PQM continued to provide technical support to May and Baker to monitor the stability of reformulated artemether–lumefantrine. The stability study is in its 17th month.

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

In FY 2016, PQM collaborated with the Pharmacists' Council of Nigeria (PCN) to convene a committee of experts from different practice areas to review the QA aspect of the current training curriculum for both undergraduate and graduate pharmacy students. The curriculum review committee members held a series of well-articulated meetings. A comprehensive curriculum was developed, the Pharmaceutical Quality System (PQS) curriculum. In FY 2017, PQM commenced work with the faculties of Pharmacy in Nigerian Universities to help make their curricula more relevant to the needs of the pharmaceutical sector and build technical capacity to support regulatory science and manufacturing. Nnamdi Azikwe University was one of the universities that benefited from the collaboration, as the PQS curriculum has been adopted for use by the university. In Q3, the university shared its experiences with other universities in a workshop organized by PQM. Discussions during the panelist session were tailored toward improving the structure of the PQS curriculum based on implementation experience and other universities implementing the PQS curriculum.

The highlights of the workshop included:

- There is a need to improve the capacity of university faculty, which PQM can help with, as necessary.
- The course structure in terms of unit load should be carefully allotted such that the undergraduate level is not overburdened. A higher credit load should be allotted to the post-graduate level.
- Modalities for engagement of preceptors from industry and NAFDAC should be worked out by individual universities, such that it is mutually beneficial to both parties.

Next steps include the following:

- More schools of pharmacy will implement the PQS curriculum.
- There should be increased participation by preceptors from industry, NAFDAC, QA/QC practitioners, and experts from other aspects of the pharmacy practice related supply chain of drug products in content delivery/learning of the PQS curriculum.
- Experiential learning for faculty should be facilitated by participation in PQM projects such as factory inspections and audits, dossier review, and trainings with PQM-supported manufacturers and NAFDAC.
- In FY 2018, USP donated equipment to the faculty of pharmacy at Nnamdi Azikiwe University, including HPLC, Karl Fischer titrator, and weighing balances. In Q3, it became necessary to build the capacity of the faculty laboratory staff to install, use, and maintain the donated equipment. The training provided an additional platform to build the capacity and skills of students and lecturers. It was a collaborative learning process, as PQM-trained NAFDAC staff from Agulu laboratory provided technical assistance during the practical sessions. The faculty is expected to develop and maintain a planned preventive maintenance system for the equipment.

Rwanda

I. Quarter 3 Highlights

Activities in Rwanda resumed with the work plan goal of PQM providing technical assistance in the design of a PMS system. In March 2019, PQM provided technical assistance to begin the design of the PMS system with Rwanda FDA staff. PQM identified gaps in the regulatory framework, including regulatory provisions and guidelines. PQM identified the human and financial resources needed and developed a budget for a simulated PMS protocol and laboratory equipment. PQM also identified elements that ensure good governance, as well as means to evaluate PMS for continuous improvement.

As a next step, PQM will continue to work with Rwanda FDA to develop a PMS guideline in July. PQM began planning for this activity during Q3. The PMS guideline will detail how the authority will implement PMS activities, include adoption of a risk-based approach, and set the ground for development of PMS procedures by Rwanda FDA.

Senegal

I. Quarter 3 Highlights

Similar to Liberia, the Senegal country project concluded in June 2019. The closeout event was organized together with the final national campaign on medicines quality activity. The 2-day event attracted 41 participants drawn from different agencies in the country.

The campaign (forum) to combat illegal sales of medicines in Senegal was conducted over 2 days. PQM supported the organization of the campaign, which included many speakers from different areas of the health sector in Senegal. Among these speakers were medical doctors, veterinary doctors, pharmacists, scientists, researchers, market controllers, and custom services and law enforcement agents. The campaign was significant in that it attracted participants from Touba, a village near Dakar, that has a large illicit market of substandard and falsified medicines.

A total of 11 topics related to combating illegal sales of medicines in Senegal were presented, and then a follow-up plenary discussion was initiated. Among these 11 topics was the Laboratoire National de Contrôle des Médicaments (LNCM) presentation on the importance of PMS and the results of the testing of antimalarial medicines collected recently in Senegal. The PMS results should enable the government to take decisive actions. The PMS results and highlights of the campaign were summarized in a final report to MOH and campaign participants.

As part of the event, PQM presented on activities in Senegal to handover to Senegalese institutions to continue the work in combatting substandard and falsified medicines at the conclusion of PQM. PQM discussed the interventions in the area of PMS workshops, basic testing, and sampling procedures to monitor the quality of medicines. PQM also emphasized the awareness campaigns for health professionals and medicine providers that were initiated and supported in part by PQM, as well as the use of media promoted to educate people of Senegal around Dakar and Djourbel on the impact of illicit medical products. Other achievements of PQM in Senegal highlighted included the technical assistance provided to strengthen the medicines QA and QC systems.

Sierra Leone

I. Quarter 3 Highlights

The final assessment report is under management review and will be finalized and disseminated next quarter.

Asia



Bangladesh

I. Quarter 3 Highlights

PQM's activities in FY 2019 Q3 focused on the implementation of objectives 1, 2, 3, and 4 in the approved FY 2019 work plan. Q3 highlights include the following:

- PQM continued supporting DGDA's PMS committee to implement risk-based PMS. The field visit report to the sentinel sites was completed, and the risk-based PMS Guideline was updated and submitted to DGDA for adoption. DGDA's likely next steps are to acquire more Minilabs™ and increase the level of surveillance of post-market samples in more divisional districts.
- PQM continued to support the National Control Laboratory (NCL) to sustain its QMS and QA/QC systems. In Q3, PQM assisted NCL management to follow up on WHO peer review CAPAs. The CAPA plan for the WHO peer audit was submitted by NCL and approved by WHO. In Q3, 15 of 81 CAPAs were addressed. Two new SOPs were developed and implemented at NCL, and nine SOPs were revised.
- PQM undertook an assessment of the Chittagong Drug Testing Laboratory (cDTL) in June. The purpose was to outline gaps in ISO standards and share them with cDTL's management to improve systems, with an eventual application for ISO 17025:2017 accreditation.
- A training was held in June to build greater understanding of the WHO PQ process and dossier compilation for both DGDA and interested manufacturers, with a focus on anti-TB priority products. This introduction to WHO standards will contribute to manufacturers' dossier submissions for WHO PQ for anti-TB products, and eventually may increase the local and global supply of quality-assured anti-TB products.
- PQM completed a GMP assessment of the manufacturer ACI in April, focusing on the production of 4FDC, a first-line anti-TB product. The assessment will show gaps in the production and quality process that need to be corrected in preparation for a WHO PQ audit.
- In April, ACI informed PQM that it had packaging change approval from DGDA for its CHX 7.1% solution and had started the production process based on two local orders for the product. PQM provided the technical assistance that led to GMP compliance for this product and its availability in the local market. ACI is now in the UNICEF bidding process to market the product globally through UNICEF programs.

II. Country Context

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

III. Quarter 1 Progress by Objective

Objective 1: Provide technical assistance to the DGDA laboratory–NCL in Dhaka to achieve international ISO/IEC 17025:2017 accreditation or WHO PQ

In terms of laboratory capacity-building, PQM has been providing technical guidance to NCL to strengthen its QMS toward attaining compliance with international standards, and NCL recently was accredited for ISO/IEC 17025:2017. PQM is working to maintain this accreditation and move forward with the WHO PQ accreditation process.

In Q3, PQM followed up on the progress of the CAPA plan from the WHO peer audit that was conducted in February. PQM is also working with NCL to address the remaining CAPAs in the previous internal and external audits. With PQM assistance, NCL staff continued to develop SOPs to improve internal processes to sustain its ISO 17025:2017 standard and move forward with WHO PQ.

The following are some key accomplishments in Q3:

- For the WHO peer review audit, PQM supported NCL to address 15 of 81 CAPAs in Q3, and PQM is providing support to address the remaining CAPAs. Some CAPAs will not be able to be addressed within the timeframe of this project.

- PQM supported NCL to sustain its QMS and QA/QC systems. In Q3 PQM assisted with two new SOPs (developed and implemented) and nine SOPs that were revised.
- To sustain its recently achieved ISO accreditation status (October 2018) as well as to achieve WHO PQ, NCL will continue to perform PT/inter-laboratory testing (ILT) periodically. This will maintain NCL staff competency to perform the testing. In April, NCL successfully passed three PTs for its microbiology laboratory.
- To improve NCL operations, PQM conducted a training for five newly hired analysts and nine existing analysts and demonstrated laboratory operations, including laboratory safety, QMS, internal audit, CAPA management, SOP writing, and analytical methods and techniques. A total of 14 participants received this training with the objective of reinforcing the training SOP and building the capacity of NCL trainers.
- With Mission approval, on June 16–19, PQM undertook an assessment of cDTL. The purpose was to outline gaps in ISO standards and share them with management to apply for ISO 17025:2017. Attaining ISO would mean two laboratories in Bangladesh will have capacity to test according to international standards.

PQM staff assisted in developing SOPs, reviewing key documents, following up on CAPAs implementation, and calibrating equipment, as outlined below.

Items	Number of items completed
Approved and implemented new SOP through PQM review	2: (General procedure of HPLC; Handling of narcotic and psychotropic drugs)
Revision of SOPs	9: <ul style="list-style-type: none"> • Communication with all stakeholders of NCL • Control of records in NCL • Document archival management • Engineering maintenance system • Ensuring competent, impartiality, judgement and ops integrity • Management of lab glassware • Master document control • Receive, storage, distribution, and use of chemicals and reagents • Resolution of complaint and customer feedback
CAPA status in Q3 FY19:	
CAPA generated based on WHO peer review audit held in February 25–27 (85)	56 (44 in Q3, 12 in Q2); 29 under follow-up
Total remaining CAPA up to March 2019:	
CAPA from NCL Internal Audit – April 2019 (13)	8 completed in Q3 FY19; Under follow up : 05
CAPA from NCL Internal Audit – February 2019 (11)	9 (7 in Q3); 2 under follow-up
CAPA from NCL Internal Audit – October 28–30, 2018 (10)	09 (0 in Q3); 1 under follow-up
CAPA from NCL Internal Audit – March 2017 (28)	26 (0 in Q3); 2 under follow-up
CAPA from PQM assessment on November 2017 (13)	11 (0 in Q3) 2 pending follow-up
Internal Calibration performed by NCL	1. Mettler Toledo pH Meter (2) 2. Electronic balance (3) 3. Disintegration tester (2) 4. FTIR (1)
Validation performed by NCL	1. Glassware cleaning validation by HPLC

Objective 2: Provide technical assistance to local pharmaceutical manufacturers toward WHO prequalification for priority MNCH/FP and TB products

In April, ACI informed PQM that it had packaging change approval from DGDA for its CHX 7.1% solution and had started the production process based on two local orders for the product. PQM provided technical assistance that led to GMP compliance for this product and its availability in the local market. ACI provided the Director General of Family Planning with an order for the CHX 7.1% solution. ACI is now in the UNICEF bidding process to market the product globally through UNICEF programs. This is a strong achievement, as it would mean having CHX 7.1% solution available in the local market to prevent umbilical cord infection after birth.

In collaboration with DGDA, the Bangladesh Association of Pharmaceutical Industries selected seven manufacturers with the potential to produce anti-TB drugs. Among them, only ACI expressed interest in producing 4FDC, a first-line anti-TB product with intention of applying for WHO PQ. In April, PQM conducted a GMP gap assessment of ACI and will follow up with the manufacturer on the identified CAPAs. It is anticipated that this work will lay the foundation for an eventual audit for WHO PQ after PQM's current project is completed.

To build greater understanding of the WHO PQ process and dossier compilation for both DGDA and interested manufacturers, a training was held on June 17–20. PQM conducted the training with the objective of building awareness of the WHO PQ process as it applies to priority anti-TB products. A total of 5 DGDA staff and 17 representatives from local manufacturers participated in the training. This introduction to WHO PQ standards may contribute to manufacturers' dossier submissions to WHO PQ for anti-TB products, which could increase the local and global supply for quality-assured anti-TB medicines.

Objective 3: In collaboration with WHO, continue to provide technical assistance to strengthen DGDA's regulatory functions

The focus on enhancing DGDA's regulatory capacity in Q3 was mainly directed at improving the implementation of the PMS system. PQM also continued to support DGDA functions, providing guidance and follow-up on the CAPAs from the WHO assessment in September 2018.

PQM continued supporting DGDA's PMS committee to implement risk-based-PMS. The field visit report to the sentinel sites was completed, and the RB-PMS Guideline was updated and submitted to DGDA for adoption. DGDA has indicated that its next steps are to acquire more Minilabs™ and increase the level of surveillance of post-market samples in more divisional districts.

PQM continued to assist DGDA in addressing the CAPAs based on the WHO interim benchmarking assessment observations and recommendations by WHO assessor in September 2018. While no CAPAs were brought to closure in Q3, to date 41 CAPAs have been completed, strengthening DGDA's regulatory functions in marketing authorization, laboratory access and testing, clinical trial oversight, lot release, and regulatory inspection. PQM will continue to support DGDA to address its 23 remaining CAPAs in the project's final weeks of implementation.

Objective 4: To increase the visibility and relevance of quality assurance and quality control of medicines in support to National Health Programs with the main focus on MNCH, TB, and FP programs

PQM continues to facilitate the development of the National Quality Assurance Guidelines (NQAG) for medical products. In Q3, PQM continued responding to recommendations received from the team and committee members.

Summary of Trainings conducted in Q3 FY19

#	Training	Date	Laboratory Designation	Gender	Total Trained	Technical Areas
01	Cleaning validation of glassware	4/22/19	NCL	M4	4	ALS
02	Refresher training on data integrity	5/30/19	NCL	M5, F7	12	ALS
03	Training of newly hired analysts on laboratory operations and analytical methods	6/17–19/19	NCL	M10, F4	14	ALS
04	Training on preparation of CTD dossier per WHO standard	6/17–20/19	DGDA/ manufacturer	M15, F5	20	GMP
05	Training on QMS for cDTL staff	6/16–18/19	cDTL	M4, F1	5	QMS
	Total in Q3 FY19			M38, F17	55	ALS=30, QMS=5, GMP=20

IV. Key Challenges

- The main challenge in Q3 has been the change in leadership at DGDA. It has taken additional time to orient the new Director General on the project objectives and activities and to build the relationship and commitment to see the final project activities completed in a timely manner.

- One other challenge facing the project has been the slow recruitment of human resources at DGDA and NCL. The process of recruiting new staff involves MOH, the Ministry of Finance, and the Ministry of Administration, and the Public Service Commission, which results in a long submission and approval process.

V. Lessons Learned

As the project moves to a closure in the next quarter, the focus has been on sustainability. Much effort has gone into technical assistance to build systems within DGDA and NCL that can be maintained, such as engagement in the budgetary process, human resource development and recruitment, and equipment and resources to complete their activities. Thus, organizational development for both DGDA and NCL is essential to ensuring the quality of medicines in Bangladesh both now and in the future.

Indonesia

I. Quarter 3 Highlights

In Q3, PQM Indonesia's major activities/accomplishments were as follows:

- On May 6, the BPOM NQCL received the closing letter from WHO confirming it is compliant with WHO standards. This is a major achievement for the laboratory, as it will be recognized globally as a trusted QC laboratory. It is important with respect to public health in the country, since the data on medicines quality generated are more reliable and can be used for triggering regulatory actions as a result of the PMS program.
- To further support the provincial QC lab at Denpasar in complying with the WHO PQ standard, PQM conducted a mock audit on June 17–21 involving an international expert. Embodying PQM's Collaborative Learning Model, NQCL technical staff were actively involved in the mock audit. This is a positive sign that demonstrates that the valuable experience gained by BPOM NQCL staff during the WHO PQ audit was effectively transitioned to support the provincial QC laboratory in Denpasar. After finalizing the mock audit, the Denpasar laboratory will submit its laboratory information file (LIF) to the WHO PQ team for review. This will be the first non-national QC laboratory in the Association of Southeast Asian Nations region to embark on PQ.
- As a follow-on activity after the achievement of PT Kalbe Farma achieving WHO PQ for levofloxacin 500 mg tablets, PQM conducted a workshop to share knowledge and experience on the WHO PQ audit. Kalbe is now committed to developing a Quality Manual that will be adopted by all sister manufacturers under Kalbe's corporate structure, which is expected to boost implementation of international GMP standards across production sites.
- PQM facilitated a workshop on risk-based PMS on April 30 to strengthen and establish a more reliable and consistent strategy of national PMS. It was well-attended by participants from BPOM, BPOM DKI Jakarta, and relevant stakeholders from MOH (Directorate of Public Medicine Supply, National TB Program, National AIDS Program, and Sub Directorate of Malaria and Immunization). PQM and Provincial BBPOM DKI Jakarta shared the experience and cost-effectiveness of utilizing Minilab™, based on data obtained from the pilot project of field sampling and testing conducted in Jakarta and Jayapura.
- The risk-based PMS workshop was followed by a hands-on training on May 2 for relevant BPOM staff. The workshop introduced the MedRS tools that could be used to develop a sampling plan that takes into consideration factors such as geography, supply chain management, degree of urbanization, population density, distribution complexity, and prevalence of disease. While BPOM already has a PMS system in place, the knowledge gained during the workshop and training allowed BPOM to analyze and further refine its system and make it more effective.

II. Country Context

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

Since 2011, PQM has conducted activities to strengthen the QA/QC systems of medicines to treat TB and HIV/AIDS in Indonesia (with PEPFAR/HIV funding starting in FY 2014). PQM focused first on supporting selected local anti-TB medicines manufacturers to strengthen their QA/QC systems and GMP toward achieving WHO PQ status. Beginning

in 2013, PQM expanded its activities to build the capacity of BPOM, additional private manufacturers of anti-TB and anti-HIV medicines, and select local CROs for BE 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 3 Progress by Objective

Objective 1 – To strengthen Indonesia’s medicines quality assurance system by supporting the MOH and BPOM regulatory, inspection, post-marketing surveillance, 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

FY 2018 Carryover Activities

In the process of preparing to apply for WHO PQ, PQM provided technical assistance to the BBPOM Denpasar QC Laboratory to prepare its LIF document; revise and develop various technical procedures; evaluate the laboratory facility to ensure it meets the requirements; and conduct a mock audit on June 17–21 to prepare for WHO PQ inspection.

In Q3, PQM supported the BBPOM Denpasar QC laboratory to participate in Network of Official Medicines Control Laboratories (NOMCoL) ILT on dissolution testing of sulfamethoxazole and trimethoprim tablets. The test results and reports have been submitted for review, and the final report from the provider is expected in July 2019. BBPOM Denpasar participated in two NOMCoL ILTs and has had a 100 percent rate for successfully meeting ILT requirements since 2016.

FY 2019 Activities

Following WHO PQ audit activities, PQM provided technical assistance to the BPOM NQCL to develop a CAPA plan that was submitted on April 15 and subsequently accepted by the WHO PQ inspector. The official inspection closing letter was received by the BPOM NQCL on May 6. The draft of the WHO public inspection report has been finalized and was sent to WHO. The laboratory is waiting for the announcement and listing on the WHO PQ website.

To further address the need to increase the number of Indonesian laboratories capable of testing medicines quality for any third party, PQM Indonesia conducted an initial assessment of the chemistry QC laboratory of Fakultas Farmasi Universitas Indonesia on May 15. The laboratory was provided with assessment findings for improving their facility and QMS.

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

FY 2018 Carryover Activities

In Q3, PQM Indonesia provided technical assistance to PT Sanbe Farma/Caprifarmindo to finalize the levofloxacin 500 mg tablets product dossier for submission to WHO PQ and conducted the final product dossier assessment. PQM also supported Sanbe in facility/documentation review and a mock audit. On May 3, PQM provided training on CAPA management that was attended by 42 total participants (23 female, 19 male).

FY 2019 Activities

In Q3, PQM Indonesia provided support to review a total of 13 SOPs for manufacturers (8 QA-related SOPs and 5 supply chain control/warehousing-related SOPs).

PQM continued to provide technical assistance to PT Imedco Djaja and PT Pharos to support their commitment to local manufacture of priority anti-TB medicines rifampicin 150 mg/isoniazid 75 mg and moxifloxacin 400 mg. PQM conducted training at PT Imedco Djaja on two topics: GLP (on May 8, 2019, attended by 21 participants (16 female, 5 male)), and handling OOS (on May 9, attended by 18 participants (13 female, 5 male)). A follow-up visit to PT Pharos was conducted to discuss the progress of its product development of 2FDC, and to deliver training on CAPA management on June 13–14, which was attended by 39 participants (18 female, 21 male).

On April 26, PQM held a meeting with PT Kalbe Farma to discuss its plan to roll out the experience and knowledge of GMP based on its WHO PQ achievement to the sister companies under Kalbe's corporate structure. As a follow-up, on May 17, PQM facilitated a workshop for sharing the common findings obtained from the WHO PQ audit to all the manufacturers under Kalbe Corporate. Kalbe is now committed to developing a Corporate Quality Manual that will be adopted by all the manufacturers under Kalbe's group of companies, and this is expected to boost implementation of international GMP standards. Furthermore, PQM conducted a training on data integrity and handling of OOS, which was attended by 43 participants (28 female, 15 male).

As requested by USAID to assist the sub-directorate of HIV/AIDS, PQM conducted a meeting and a plant visit to PT Sampharindo Retroviral Indonesia (SRI)–Semarang. While the plant is not yet in operation, this manufacturer is planning to focus on producing quality antiretroviral medicines for both local and export markets with a dedicated facility.

Other GMP-related activities in Q3 included a training on data integrity for PT Equilab International on April 25, which was attended by 22 participants (18 female, 4 male). PQM provided training on data integrity for PT San Clin Eq on May 2, which was attended by 11 participants (6 female, 5 male).

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

On April 30, PQM Indonesia conducted a workshop and training on “Risk-based approaches to PMS in LMICs.” The objective of the workshop was to strengthen and establish a more reliable and consistent strategy for the national PMS system. The workshop was well-attended by participants from BPOM, BPOM DKI Jakarta, and relevant stakeholders from MOH (Directorate of Public Medicine Supply, National TB Program, National AIDS Program, and Sub Directorate of Malaria and Immunization). PQM and provincial BBPOM DKI Jakarta shared the experience and cost-effectiveness of utilizing Minilab™ based on data obtained from the pilot project of field sampling and testing conducted in Jakarta and Jayapura. The workshop was followed by a hands-on training on May 2 for 14 BPOM PMS staff (12 female and 2 male) to introduce the MedRS tool that could be used to develop an annual sampling plan that takes into consideration several aspects, such as, geography, supply chain management, degree of urbanization, population density, distribution complexity, and prevalence of disease. While BPOM already has a PMS system in place, the knowledge gained during the workshop and training allowed BPOM to compare and to further refine its current system to make it more effective.

Following the previous discussion on curriculum development with FF-UI, it was agreed to develop an optional curriculum for the professional pharmacist program with a public health perspective. The selected topic is supply chain management, specific to in pre-service and in-service training. Related to this, PQM has provided relevant documents on the method of Self-Initiative Supply Chain Management Strengthening (SI-SCM-S).

Related to the efforts to strengthen collaboration and knowledge in the professional community, PQM delivered a presentation on SI-SCM-S, a model to empower public health pharmacists, during a workshop conducted by the Public Health Pharmacist Association on April 26. PQM also provided support to the PSM/Chemonics antiretrovirals registration workshop on May 15–16 by assigning one of its staff as a moderator during the workshop and by liaising with selected manufacturers, speakers, and participants during workshop preparation.

Objective 4 – Monitoring and Evaluation for specific activities

In preparation for PQM Indonesia project closeout, PQM has finalized the draft Transition Plan and Recommendation documents and begun drafting the project final report.

The project closeout event for PQM Indonesia office is planned for July 23, as agreed upon with USAID. The terms of reference for the event were developed and shared with USAID and BPOM. The team discussed the event with BPOM's Bureau of Cooperation, and BPOM requested PQM to submit an activity report in Bahasa. The Bahasa activity report is currently being drafted.

IV. Key Challenges

Processing the official goods and services handover document (referred to as a BAST document) remained a challenge in Q3. To address some of the remaining issues raised by BPOM, a meeting between BPOM, the Ministry of Finance, USAID, and PQM Indonesia was held in May 2019. PQM Indonesia also met with the BPOM Director to

provide the additional information. PQM Indonesia expects to have the 2018 BAST signed by BPOM during the next quarter.

Myanmar

I. Quarter 3 Highlights

In Q3, PQM completed a survey of the quality of anti-TB medicines in selected geographical areas in Myanmar. A total of 217 samples were collected; 88 samples from 25 brands were selected for quality testing at the pharmaceutical chemistry laboratory of the Department Food and Drug Administration (DFDA) in Nay Pyi Taw. Of the 88 samples tested, 76 samples passed, while 12 did not meet quality specifications. The survey report has completed technical review and will be finalized before the end of July.

PQM provided technical guidance to the Mandalay pharmaceutical chemistry laboratory for its laboratory relocation, including the relocation plan, schedule, and resources. PQM also provided the laboratory with a document packet containing SOP models, relocation workflow, and best practices.

The Myanmar final report is currently being drafted, and a closeout event has been confirmed for July 31.

II. Country Context

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

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

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

III. Quarter 3 Progress by Objective

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

Activities under this objective were previously completed.

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

Activities under this objective were previously completed.

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

Technical guidance was provided to the Mandalay laboratory staff with the purpose of reviewing its relocation plan and ensuring there are no gaps in the process that would affect its ability to start preparing for ISO 17025 accreditation. PQM addressed the following items with the laboratory staff and provided corresponding documents:

- Relocation process
 - Planning, scheduling, and coordinating
 - Preparing the inventory and floor plans
 - Identifying regulatory documentation (calibration, qualification, and validation)
 - Disassembling the instruments (safe handling)
 - Managing transport and hazardous materials
 - Re-installation (water, power, and HVAC)
 - Performing qualification/validation
- Relocation timeline

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

Activities under this objective were previously completed.

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

Activities under this objective were previously completed.

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

Activities under this objective were previously completed.

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

Testing of the samples collected for the quality survey of anti-TB medicines in selected geographical areas in Myanmar was completed in Q3. In total, 217 samples were collected from 7 regions of the country. Of the 217 samples, 88 were selected for compendial testing at DFDA’s pharmaceutical chemistry laboratory.

Of the 88 samples tested, 12 samples failed. Among the failed samples, 11 were first-line anti-TB medicines and 1 was a second-line anti-TB medicine. All 11 first-line anti-TB medicines failed in the uniformity by weight testing, while the second line anti-TB medicine, a sample of levofloxacin, failed in the assay testing. The survey report has completed technical review and will be finalized before the end of July.

Pakistan

I. Quarter 3 Highlights

With PQM continued technical assistance, the Pakistan Drug Testing and Research Center (PDTRC) Lahore laboratory was prequalified by WHO in Q3. This is the first public sector laboratory—not only in Pakistan, but in southeast Asia—to be prequalified by WHO. Prequalification of the laboratory opened the opportunity to 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-market testing of pharmaceuticals. Also in Q3, with PQM support, Central Drug Laboratory (CDL) Karachi and Drug Testing Laboratory (DTL) Multan, submitted LIFs for WHO PQ.

With PQM support, in Q3 DRAP successfully passed a pre-audit assessment of ISO 9001:2015 by the Swiss certifying agency SGS. SGS found a few observations in QMS implementation at DRAP without any major or minor

nonconformances and recommended DRAP for ISO 9001:2015 certification. This is an important milestone for DRAP toward achieving WHO maturity level III. PQM continued supporting DRAP to reassess its WHO Global Benchmarking Tool (GBT) self-assessment scores based on the new WHO GBT version. With PQM's support, DRAP successfully submitted the revised WHO GBT self-assessment report to WHO, and an assessment visit is expected in October 2019.

II. Country Context

Chlorhexidine (CHX) is one of the 13 life-saving commodities identified by the UN Commission on Life-Saving Commodities for Women and Children. PQM is called to work alongside other implementation partners to help USAID achieve the objective of introducing quality-assured CHX in Pakistan. The collective effort would contribute to the Pakistani Government's effort to reduce the mortality (currently at 200,000 deaths/year, about 22 cases/hour) of newborns caused by cord infections that can be prevented by use of quality CHX gels.

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

III. Quarter 3 Progress by Objective

Objective 1 – (Corresponding to IR 2.1) Continue to provide technical assistance to selected manufacturers that received registration of CHX and to other potential MCH product manufacturers to improve their cGMP standards to qualify for WHO PQ, ERP, and local registration

In Q3, PQM continued to provide support to manufacturers of the following MCH products:

- **Amoxicillin DT:** M/s Macter International showed steady progress in Q3 and has completed 96 percent of the CAPAs. Only one point still needs to be addressed. The manufacturer prepared three formulation batches for initial trials. After achieving confidence in the stability of the formulation, in April the manufacturer developed two laboratory batches and one pilot scale batch using API from a U.S. FDA-approved manufacturer. The three batches developed with the new FDA-approved source were placed on 6-month stability studies to be completed in October 2019. The manufacturer is in the process of developing the Common Technical Document dossier for submission to WHO.
- **Zinc DT and zinc oral solution:** currently three manufacturers receive technical assistance from PQM for zinc DT production.

Following the WHO PQ team's inspection, M/s Pharmevo addressed all observations raised and submitted its final report. The manufacturer is currently awaiting a final response from WHO, anticipating that WHO PQ could potentially be awarded for zinc DT product in Q4.

M/s Atco Laboratories is in the process of manufacturing 1 laboratory scale batch of 25,000 zinc DT and 1 commercial batch of 220,000 tablets for the stability study after receiving approval from DRAP to proceed. The manufacturer also prepared a new formulation of its zinc oral solution that complies with the USP monograph, and a stability study will be conducted. PQM provided technical guidance to Atco on dossier compilation per WHO PQ guidelines.

Aspin Laboratories previously completed a 9-month stability study of its zinc DT product, and the manufacturer completed the dossier. In Q3, PQM provided technical review of the dossier and recommended changes prior to submission for WHO PQ.

- **Chlorhexidine 7.1% gel:** Two manufacturers, M/s Atco Laboratories and M/s Aspin Pharmaceuticals, have moved forward in attempting to become UNICEF suppliers for their locally approved products. UNICEF informed both manufacturers that the Expert Review Panel (ERP) will be conducted once the tender for

procurement is issued and its bid is received. M/s Aspin Pharmaceuticals is also expecting a forthcoming UNICEF audit.

Objective 2 – (Corresponding to IR 1.3) Strengthen the capacity of quality control laboratories to meet international standards

With PQM continued technical assistance, the PDTRC Lahore laboratory was prequalified by WHO in Q3. This is the first public sector laboratory—not only in Pakistan, but in Southeast Asia—to be prequalified by WHO. Prequalification of the laboratory opened the opportunity to 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-market testing of pharmaceuticals.

Also in Q3, the following additional Pakistan laboratories were supported:

- CDL Karachi submitted its laboratory information file for WHO PQ.
- PQM continued its technical assistance to DTL Rawalpindi on CAPA points for WHO PQ preparation and development of the LIF for WHO PQ. DTL Rawalpindi is expected to submit its LIF for WHO PQ in Q4, as the majority of CAPA points have been addressed.
- PQM continued its technical assistance to DTL Bahawalpur for WHO PQ preparation and development of LIF for WHO PQ. This technical assistance included revision of SOPs. It is expected that DTL Bahawalpur will submit its LIF for WHO PQ in Q4.
- PQM continued its technical support to the Federal Government Appellate Laboratory in Islamabad by reviewing newly developed SOPs, which include management of reference standards, waste management, document control, and risk management. PQM shared GLP guidelines from WHO to prepare other SOPs.
- PQM continued to provide technical support to DTL Multan on preparation for WHO PQ and followed up with WHO on the DTL Multan LIF evaluation that was submitted in Q3.
- PQM reviewed the finalized version of DTL Lahore's LIF for WHO PQ. Several observations were shared with the laboratory in light of PQM's discussion with the WHO LIF evaluator. The laboratory staff are working to address all observations and expected to submit the final version to WHO in Q4.
- PQM continued to provide technical support to DTL Faisalabad on preparation for WHO PQ and followed up with WHO on the DTL Faisalabad LIF evaluation that was submitted in Q2.

Objective 3 – (Corresponding to IR 1.1) Capacity building of DRAP Pharmaceutical Evaluations and Registration Division (PE&R) to improve its registration system to effectively evaluate all essential medicine products quality

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. With PQM support, in Q3 DRAP developed job descriptions, SOPs, key performance indicators, and process risks as per ISO clauses 4 to 10. Moreover, as per ISO requirements and DRAP internal procedure, the internal audit team was constituted and an internal audit of all 13 divisions was conducted. Based on internal audit team observations, CAPAs were taken.

In Q3, SGS Pakistan conducted an ISO 9001:2015 pre-audit of DRAP, followed by the final audit to verify QMS implementation as per ISO requirements. Based on the final audit, only a few observations were shared by the agency without any major or minor nonconformances.

PQM supported DRAP in reviewing, revising, adapting, and/or preparing several documents as per DRAP Institutional Developmental Plans under WHO GBT Level III compliance.

WHO's GBT is designed to assist regulators worldwide in evaluating the developmental status of their regulatory systems and related functions. In Q3, WHO shared the finding on DRAP's self-assessment report submitted last year through PQM support. PQM continued its support to DRAP to transform data from the previous tool to the new revised tool, and addressed the majority of WHO observations on previously submitted data. With PQM support new data have been submitted to the WHO SharePoint, along with necessary documentation for WHO assessment. The WHO team is expected to visit Pakistan in October 2019 to take samples before the final audit in November 2019.

Objective 4 – (Correspond to IR 1.5) 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. -

PQM collaborated with DRAP to develop a national framework for risk-based PMS, which was presented at a consultative meeting on May 31–June 1 in Islamabad. Meeting participants included the Secretaries of Provincial QC Boards, Chief Drug Inspectors of all provinces and administrative regions, Additional Director of DRAP QA< Division, and Additional Director Division of Pharmacy Services. Dr. Saif Ur Rehman Khattak, CDL Karachi Director, assisted PQM in presenting the national framework to participants. The meeting was interactive, and an open debate among participants will help refine the document.

To finalize the framework, a second meeting was held in on June 17–18 in Islamabad. The final draft of the national framework for Pakistan was presented to the respective participants for adoption. The provincial authorities were requested to nominate officials who attended the meeting on May 31–June 1 for the continuity and to facilitate adoption of the national framework. The authorities obliged by nominating the officials for the meeting that facilitate approval and adoption of the draft. The important feature of the meeting was a joint declaration by DRAP and the provinces declaring they would ensure implementation of the national framework and initiate all the required changes in rules and regulations as necessary.

Features of the framework included the following:

- DRAP will establish a PMS center office in the Directorate of QA and Laboratory Testing with the necessary structure and appropriate legal mandate to carry out activities related to PMS of medicines.
- The structure and legal mandate must support a coordination mechanism of the quality surveillance team with related DRAP departments, such as QC laboratories; safety surveillance and inspection and enforcement teams, and provincial health departments.
- An adequate annual budget must be provided to carry out the sampling and testing activity as per the approved protocol with specific objectives. The funds should be mobilized before beginning any sampling and testing activity.
- Necessary knowledge resources (e.g., software, national and international MOUs with research and regulatory institutes/organizations) will be considered for effective national PMS program.
- The PMS program should be managed by a committee that consists of representatives of DRAP, laboratories, provincial health departments, disease programs, and other relevant partners and stakeholders. The committee should be responsible for addressing issues around budget allocation and advocacy for the PMS program. The PMS committee also must establish the task force responsible for implementing PMS.
- DRAP will establish a web portal where stakeholders can upload their PMS data for accessibility by all stakeholders through their designated officials. The portal will be used to plan PMS activities and ensure that some level of effort can be reduced to enhance productivity.

As a next step, a training of selected drug inspectors from DRAP and each province will be conducted as a training of trainers in Q4 on the newly developed PMS national framework.

Eastern Europe & Central Asia



Kazakhstan

I. Quarter 3 Highlights

In the early part of Q3, 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 to strengthen its QMS in advance of the WHO PQ audit. PQM assisted the laboratory in preparation of the CAPA plan and corresponding documents addressing observations from the WHO PQ peer review visit conducted in FY 2018 Q4. The documents were submitted to the WHO PQ team.

In June 2019, the Karaganda laboratory was audited by the WHO PQ team, and the report is pending.

The laboratory was also audited by the local accrediting body, and it was certified as compliant with local ISO/IEC 17025 standards.

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 multidrug-resistant tuberculosis (MDR-TB) burden country; MDR-TB reached 26 percent among new cases and 58 percent among previously treated cases.

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

III. Quarter 3 Progress by Objective

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

In the early part of Q3, 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 to strengthen its QMS in advance of the WHO PQ audit. Particularly, PQM assisted the laboratory in preparation of the CAPA plan and corresponding documents addressing observations from the WHO PQ peer review visit conducted in FY 2018 Q4. The documents were submitted to for WHO PQ.

In June 2019, the Karaganda laboratory was audited by the WHO PQ team, and the report is pending.

The laboratory was also audited by the local accrediting body, and it was certified as compliant with local ISO/IEC 17025 standards.

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

In Q3, PQM provided remote support to Nobel Almaty Pharmaceutical Factory for its anti-TB product, levofloxacin. PQM provided additional recommendations on mitigation of risks for cross-contamination between products.

Uzbekistan

I. Quarter 3 Highlights

In Q3, the Agency for Development of Pharmaceutical Industry appointed dedicated QA specialists within the Testing Center of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment. PQM conducted a QA training for these members of the newly established QA unit.

In Q2, the Agency created a working group in the State Center for preparation of the Uzbek pharmaceutical inspectorate for PIC/S accession and development of the QMS requirements for pharmaceutical inspectorate. In Q3, PQM worked with the working group to complete a self-assessment based on the PIC/S indicators. As a result of this work, a roadmap with recommendations on the accession to PIC/S was developed, and the Agency for Development of Pharmaceutical Industry submitted it to the Cabinet of Ministers for further consideration and approval.

In April 2019, the president of the Republic of Uzbekistan issued Decree “Further measures for accelerated development of Pharmaceutical Industry in the Republic of Uzbekistan in 2019–2021.” The Decree includes some areas that PQM has advocated for in relation to strengthening the country’s medicines QA system. Complying with good practices, including GMP and GLP, will become mandatory for the corresponding entities beginning January 1, 2022. The Decree also requires the Agency for Development of Pharmaceutical Industry to collaborate with PIC/S and develop a roadmap for PIC/S accession. According to the Decree, funding will be allocated to develop the new compound of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment, including a new 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.

Medicines quality 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 3 Progress by Objective

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

In Q3, PQM continued to provide technical support to Nobel Pharmsanoat for its anti-TB product, levofloxacin. PQM discussed with the manufacturer the status of CAPAs from the risk assessment conducted in FY 2018 Q4.

Objective 2 – Strengthen the medicines quality control system

In Q2, PQM recommended the Agency for Development of Pharmaceutical Industry to establish a Quality Unit in the Testing Center of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment. In Q3 the State Center appointed dedicated QA specialists, who formed a Quality Unit. The Quality Unit included the quality manager and quality specialists from each department of the laboratory (physicochemical, microbiological, toxicological, and medical devices and equipment). The Quality Unit should oversee and manage the QMS for its medicines testing operations. In Q3, PQM conducted a 5-day training workshop on QMS evaluation and implementation to allow proper measurement and linkage to international quality standards. The training was focused on establishing the roles and responsibilities of QMS managers, aligning current QMS with the knowledge gained during the previous PQM trainings and re-enforcing the requirements of ISO/IEC 17025:2017. Under PQM's guidance, the participants discussed their own quality management documents, identified gaps in their QMS, and agreed about the ways to improve their system.

PQM provided technical assistance to the Quality Unit to develop a roadmap for the State Center to achieve compliance with ISO/IEC 17025:2017. The roadmap will be a guidance document for the State Center in terms of preparation for ISO/IEC 17025:2017 accreditation going forward.

In April 2019, the president of the Republic of Uzbekistan issued Decree "Further measures for accelerated development of Pharmaceutical Industry in the Republic of Uzbekistan in 2019–2021." The Decree includes some areas PQM was advocating for in relation to strengthening the medicines quality control system. The Decree makes obligatory compliance with GLP for all medicines QC laboratories beginning January 1, 2022. Also, according to the Decree, funding will be allocated to develop a new compound of the State Center of Expertise and Standardization of Medicines, Medical Devices and Medical Equipment, including a new medicines QC laboratory. PQM recommended applying for international ISO/IEC 17025:2017 accreditation after the Testing Center moves to this new building and improves its infrastructure.

In Q3, the semi-micro osmometer procured by PQM was delivered to the medicines QC laboratory.

Objective 3 – Strengthen GMP inspection system

In Q2, the Agency for Development of the Pharmaceutical industry formed a working group to prepare the Uzbek Pharmaceutical inspectorate for PIC/S accession and to develop the QMS requirements for the pharmaceutical inspectorate. According to the president's April 2019 Decree, national GMP certification of all local pharmaceutical manufacturers becomes mandatory beginning January 1, 2022. In addition, the Agency was requested to develop a plan of cooperation with PIC/S by June 1, 2019. This Decree plays a key role in preparation for PIC/S accession by Uzbekistan.

In Q3 PQM organized a follow-up visit focused on supporting completion of the self-assessment of the GMP inspection system according PIC/S indicators. During a 5-day discussion with the working group, each indicator to assess the current GMP inspection system was discussed, corresponding documents were reviewed, and gaps were identified. Steps on how to address those gaps, corresponding recommendations, and best practices were discussed. The PIC/S documents related to the GMP inspection regulatory system, QMS, and inspection performance were reviewed. As a result of this work, a roadmap for PIC/S accession has been developed and submitted to the Cabinet of Ministers for further consideration and approval.

Core Portfolio



Core MNCH

I. Quarter 3 Highlights

In Q3, with PQM's technical assistance and advocacy efforts, DRAP endorsed a procedure for registration of product dossiers in accordance with the WHO Collaborative Registration Procedure (CRP) process. This is an important milestone, as it will facilitate accelerated registration of quality-assured medicines (such as those that are WHO prequalified or SRA approved) in Pakistan. This would help to increase access to quality-assured public health medicines by patients in the country.

Also in Q3, PQM organized a workshop with GSK on "Increasing access to quality-assured essential medicines through technology transfer to local manufacturers: The Umbipro case study." The workshop focused on the concepts of technology transfer and provided detailed insight into the technology and manufacturing know-how for the manufacture of the Umbipro product. The workshop was followed up by one-on-one sessions with the participating manufacturers to address their specific concerns and confidential questions. The manufacturers now have access to information that is critical for developing and producing quality-assured chlorhexidine. It is expected that this will help increase the sources of quality-assured chlorhexidine in Africa and Asia.

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 3 Progress by Objective

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

In Q3, PQM provided technical assistance to manufacturers of the following MNCH products:

- **Magnesium sulfate FPP:** In Q3, PQM provided technical assistance to one manufacturer. The manufacturer is working on developing a CAPA plan based on the observations recommended by PQM. In addition, PQM is providing remote technical assistance to address the queries from WHO on the dossier. The additional data for both WHO GMP inspection and the dossier queries are expected to be received in the next quarter for PQM review.
- **Amoxicillin DT FPP:** During the last quarter, PQM conducted an onsite inspection of one manufacturer. In Q3, the GMP report was shared with the manufacturer, which is working to implement the CAPA on the cross-contamination observations due to adjacent beta-lactam manufacturing lines. The manufacturer has produced the pilot batch and is planning to produce scale up and validation batches in the next quarter. PQM will continue to provide technical support while the manufacturer is preparing the dossier for EAC submission.
- **Oxytocin FPP:** In March, PQM visited the manufacturer to follow up on the WHO audit and provide support for dossier preparation. The manufacturer produced validation batches for oxytocin injection and placed them under stability monitoring. The 6-month stability data will be available by July 2019.

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

In April, PQM participated in the 10th East African Community (EAC) joint assessment meeting in Entebbe, Uganda. The purpose of the trip was to provide technical guidance in assessing applications to register medicines in all EAC member states and revising the EAC Compendium of Guidelines for Medicines Evaluation and Registration. PQM contributed to the review of one new application and seven query responses. Three new documents were added to the compendium, and existing sections of the compendium were revised. The documents added included the quality information summary, EAC guideline on naming of medicinal products, and EAC policy/procedure for the API master file.

In Q3, with PQM's technical assistance and advocacy efforts, DRAP endorsed a procedure for registration of product dossiers in accordance with the WHO CRP process. This is an important milestone, as it will facilitate accelerated registration of quality-assured medicines (such as those that are WHO prequalified or SRA approved) in Pakistan. This will help increase access to quality-assured public health medicines by patients in the country. PQM continues to encourage the Indonesian manufacturer, Sanbe Farma, to register its high-priority MNCH medicine, oxytocin injection, in Pakistan via the WHO CRP mechanism, especially now that the procedure has been approved by DRAP.

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

In Q3, PQM continued working with GSK to help increase the availability of lifesaving quality-assured chlorhexidine via technology-sharing. Based on the information and documents provided by GSK, PQM developed the GSK Chlorhexidine Digluconate (7.1%) Gel Technology Transfer Report and made it available through free online access on the [PQM website](#).

PQM also organized a workshop with GSK on “Increasing access to quality-assured essential medicines through technology transfer to local manufacturers: The Umbipro case study.” The training workshop was conducted on May 20–22 in Ghana and was attended by 34 participants. The workshop focused on the concepts of technology transfer as delineated by the [WHO guidelines on transfer of technology in pharmaceutical manufacturing \(Annex 7\)](#) and provided detailed insight into the technology and manufacturing knowhow for the manufacture of the Umbipro product. The workshop was followed up by one-on-one sessions with the participating manufacturers to address their specific concerns and confidential questions. The manufacturers now have access to information that is critical for developing and producing quality-assured chlorhexidine. It is expected that this will help increase the sources of quality-assured chlorhexidine in Africa and Asia.

Core NTD

I. Quarter 3 Highlights

One praziquantel FPP manufacturer completed its bioequivalence study. The preliminary results suggest the study was successful. PQM continues to provide technical assistance to the manufacturer for preparation of dossier submission for WHO PQ in Q4.

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 expression of interest (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. This process allows manufacturers to partake in a rapid quality risk assessment of its product dossier and the level of GMP compliance at its manufacturing sites.

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

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

III. Quarter 3 Progress by Objective

Objective 1 – Increase availability to quality-assured NTD medicines

In Q3, 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. The manufacturer started supplying the API to a manufacturer currently working with PQM for praziquantel FPP.

PQM is also providing support to another manufacturer to prepare its responses to the WHO PQ assessment. In Q3, the manufacturer received feedback from WHO on its dossier and GMP desk review. With PQM support, the manufacturer completed the GMP desk review report. The manufacturer submitted the third round of API master file dossier responses and provided additional data to WHO.

- **Praziquantel FPP:** One of the two manufacturers began the BE study in April and completed the study in June. The final BE study report is under compilation by the CRO, and the draft report was expected to be received by PQM for review in July. As per the current information provided by the CRO, the BE study was successful. The dossier is under preparation, and the final version of the dossier without module 5 will be submitted for PQM review at the beginning of Q4. PQM will visit the manufacturer in July to provide assistance in finalizing the dossier for WHO PQ submission.

The second manufacturer has completed the BE study and sent the final BE report to PQM for review. Based on the report and as concluded by CRO, the test praziquantel batch failed to meet the acceptance criteria for BE requirement. The manufacturer is committed to continue working on the product and is currently investigating the reasons for the BE study failure.

- **Albendazole FPP:** PQM is providing technical support one manufacturer. The manufacturer's pilot BE study began on June 8 and was completed on June 22. The results of the BE study are expected to be received in July. The pivotal BE study protocol will be finalized once pilot study results are available and meet predetermined criteria. The manufacturer has completed the stability study, and 18 months of stability study data are available. The dossier is under preparation with PQM support.

Objective 2 – Technical support for bioequivalence study

In Q2, PQM continued technical assistance to two manufacturers of praziquantel FPP in support of BE study preparations. One manufacturer has successfully completed the bioequivalence study and will submit the final report in July. The preliminary results suggest that the BE study was successful. The second manufacturer completed the BE study, and the final report has been developed. However, that BE study was not successful. The manufacturer is investigating the reasons for failure of the study and plans to continue working on the product.

The pilot study for albendazole FPP has been completed. The report will be submitted to PQM in July. The pivotal BE study protocol will be finalized once pilot study results are available.

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

Approval was received from USAID to issue a subaward to Monash University to develop an interactive online GMP module through August 31, 2019. The agreement has since been signed by both Monash University and USP.

The Monash University team is developing templates and a user interface and has already provided sample design templates and branding for review by PQM and USP's Education Department. USP Education will oversee hosting of the developed modules on USP servers once complete.

PQM has also engaged a consultant to develop GMP case studies to be integrated into the online module. A total of seven case studies have been completed, reviewed by PQM, and forwarded to Monash for integration.

Monash University has provided its intended order of module development, and the first module is expected to be completed by the end of July.

Core TB

I. Quarter 3 Highlights

In Q3, the manufacturer of isoniazid API, which was engaged for PQM's technical assistance in Q2, submitted its API master file (APIMF) for PQM's review. PQM reviewed the draft and provided comments to the manufacturer. The manufacturer is in the process of developing the final APIMF for WHO submission. This is an important development; if the product is approved by WHO, there will be one more quality-assured source of isoniazid API on the market. This will help to mitigate a risk of shortage of the product, which occurred after one of the manufacturers of WHO prequalified isoniazid API stopped supplying the product.

II. Health Element Context

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

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

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

III. Quarter 3 Progress by Objective

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

In Q3, PQM provided technical assistance to manufacturers of the following TB products:

- **Clofazimine FPP:** PQM helped the manufacturer to draft the response for dossier submission to the Global Fund. In Q1, the product received ERP approval for 2 years. The manufacturer is preparing to provide additional data to WHO to address queries after the dossier review.
- **Clofazimine API:** PQM provided technical assistance to the manufacturer to draft the response for WHO PQ assessment queries. After submitting the responses to WHO in February, the manufacturer received the second-round queries on the APIMF, which is under WHO review after the manufacturer addressed two pending queries in May.

- **Rifapentine API:** In Q3, one manufacturer provided the first draft of its APIMF to PQM for review. The manufacturer is revising the APIMF to incorporate PQM's comments, and the revised draft will be available for PQM review in Q4.
- **Rifapentine FPP:** PQM was working with one manufacturer, but the manufacturer is unable to source quality-assured rifapentine API for product development, as there are currently no WHO-prequalified suppliers of rifapentine API. The project is currently stalled.
- **Kanamycin FPP:** The manufacturer revised the Quality Information Summary of the kanamycin dossier to address WHO queries, and the dossier is under review by WHO. The manufacturer is working to implement GMP CAPAs.
- **Isoniazid API:** In Q2, PQM visited the manufacturer to inspect the manufacturing site and determine the timeline for the APIMF submission to WHO. In Q3, PQM reviewed the APIMF draft and sent it back to the manufacturer. The manufacturer is in the process of developing the final APIMF for WHO submission.
- **Rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC):** One of the two manufacturers received BE protocol approval from the local regulatory and ethics committee, and the BE study is scheduled to begin in the next quarter. The manufacturer also received a GMP certificate from the local national regulatory authority. The second manufacturer is in the process of preparing its dossier, with the help of PQM. This manufacturer also received approval for the BE protocol from the local regulatory and ethics committee, and the BE study is scheduled to begin in the next quarter. The manufacturer is in process of compiling the dossier, with PQM support. In May, PQM visited both manufacturers to provide technical assistance in preparing the product dossiers.

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

Approval was received from USAID to issue a subaward to Monash University for development of an interactive online GMP module through August 31, 2019. The agreement has since been signed by both Monash University and USP.

The Monash University team is developing templates and a user interface and has already provided sample design templates and branding for review by PQM and USP's Education Department. USP Education will oversee hosting of the developed modules on USP servers once complete.

PQM has also engaged a consultant to develop GMP case studies to be integrated into the online module. A total of seven case studies have been completed, reviewed by PQM team, and forwarded to Monash for integration.

Monash University has provided its intended order of module development, and the first module is expected to be completed by the end of July.

Cross Bureau

I. Quarter 3 Highlights

- **MedRS:** Tool development has been completed, and it is being transferred to the USP platform that will host the tool when the PQM program concludes. The tool is expected to be available to countries' MRAs via the PQM website in August.
- **E-course:** After internal and USAID review of all modules, content is currently being uploaded to the Global Health eLearning Center (GHeLC) platform and will be available to the public at the GHeLC website in August.
- **Regulatory system country profiles:** Regulatory system profiles for Bangladesh, Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan were finalized and approved by the respective MRAs. Final versions were disseminated to the MRAs and USAID Missions in Ghana and Mozambique; the rest were sent to PQM country managers and representatives and will be disseminated in July. Nigeria's profile is still under review by NAFDAC.

- **Quality-assured medicines in UHC:** The “Importance of Medicine Quality in Achieving Universal Health Coverage: article was submitted to the WHO Bulletin on June 15. The first draft of a white paper on the same subject, which also includes regulatory aspects for ensuring the quality of medicines for UHC, is currently under review. Finalization and dissemination are expected by mid-August.

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 3 Progress by Objective

FY 18 Objective 2 – Provide technical leadership to regional networks of medicines quality assurance professionals

Activity 2.1: Support regional harmonization efforts to strengthen work sharing and mutual reliance within the RECs

PQM planned to participate in the “Expert Working Group Session to establish common tracking mechanism to monitor safety and quality of medicinal products” that was to be held in Rwanda on April 22–26. However, since this meeting did not take place, PQM will instead attend the “Expert Meeting to Review and Finalize EAC Strategic Plan on Post Market Surveillance of Medical Products” on August 19–21 in Dar Es Salaam, Tanzania.

FY 18 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

Questionnaires are being developed to assess utilization of risk-based approaches in dossier review, manufacturers’ GMP inspections, and PMS in Bangladesh and Indonesia. PQM will work with MRAs during a visit planned in Q4 to collect the data and establish a baseline for utilization of risk-based approaches in the selected regulatory functions. Due to end-of-project activities and other commitments of the MRAs in Ethiopia and Nigeria, the planned implementation in these countries could not take place.

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

Development of the web-based MedRS tool was completed, including a User Manual. In Q3, PQM worked with USP's IT department to transfer administration of the tool to USP servers. Webpage content was completed in early July, and the tool will be accessible to MRAs via the PQM website in August.

FY 18 Objective 4 – Development of e-Learning course on medicines quality assurance (FY 19 Objective 2)

All nine sessions of the e-Learning course on the importance of ensuring medical product quality for health systems strengthening have been completed and reviewed internally and by the USAID AOR team. The updated versions are being uploaded in the Global Health eLearning Center (GHeLC) platform, while additional interactive graphics are being developed in collaboration with K4H, a GHeLC partner. The final version in the GHeLC platform will be sent for external review by the second half of July, and the course expected to be published by mid-August.

FY 18 Objective 5 – Establish regulatory system country profiles

Country profiles for Bangladesh, Ghana, Ethiopia, Mozambique, Myanmar, and Pakistan have been completed and approved by the MRAs. Final formatted versions have been shared with the USAID AOR team and sent to PQM managers and country representatives for dissemination to country stakeholders (MRAs and USAID Missions). Profiles have already been disseminated in Ghana and Mozambique. Nigeria's profile is still under revision by NAFDAC. Upon approval from the countries' MRAs to post the profiles on the PQM website, they will be uploaded.

FY 18 Objective 6 – Provide guidance on the importance of medicines quality in Universal Health Coverage (UHC) schemes

The "Importance of Medicine Quality in Achieving Universal Health Coverage" article was submitted to the WHO Bulletin on June 15.

The first draft of the "Importance of Medicine Quality in Achieving Universal Health Coverage" white paper, including regulatory aspects for ensuring the quality of medicines for UHC, has been finalized and is currently under review. Finalization and dissemination are expected by mid-August.

FY 19 Objective 1 – Awareness of the importance of medicines quality in the global health community increased

PQM is waiting for an updated EAC program of activities to hold a meeting in Q4.

FY 19 Objective 2 – Development of e-Learning course on 'Strengthening Medical Products Quality Assurance Systems as an Essential Component of Health Systems Strengthening

See FY 2018 objective 4 above.

FY 19 Objective 3 – Close-out PQM Program

PQM held the end-of-project event, "Advancing Medicines Quality Assurance Systems in LMICs: Celebrating 10 Years of PQM Program Achievements," on June 27 in Arlington, Virginia. Keynote presentations were given by USP and PQM leadership and USAID's Director of the Office of Health Systems, Kelly Saldaña. The event included two panel discussions focused on "Increasing the Global Supply of Priority Public Health Medicines to Save Lives" and "Strengthening and Building Sustainable, Self-Reliant, Medicines Quality Assurance Systems in LMICs." Panelists included representatives from USAID, WHO, NAFDAC, an Indonesian manufacturer, and PQM. At the event, participants also had the opportunity to engage with knowledge fair stations showcasing key aspects of PQM work and approaches and tools developed.



Panelists discuss strengthening and building sustainable, self-reliant, medicines quality assurance systems in LMICs. from left: Timothy Nwogu (PQM Principal Program Manager), Alison Collins (Health Systems Advisor, Office of Health Systems, USAID Bureau for Global Health), Mojisola Adeyeye (Director General, NAFDAC), Victor Pribluda (PQM Principal Program Manager), and Hailu Tadeg (PQM Ethiopia Chief of Party)

Management Overview

In Q3, PQM presented three brown bag presentations/webinars hosted by USAID to support information sharing:

- **April 12, 2019:** The session detailed how NOMCoLs make essential contributions to expanding access to quality-assured medicines in LMICs and how a build–operate–transfer model for these networks better ensures long-term sustainability through regional ownership. NOMCoL–Sub-Saharan Africa was established in 2009 through PQM with USAID funding. Known today as the African Medicines Quality Forum (AMQF) and managed since 2017 by the New Partnership for Africa’s Development, the network is a powerful continental collaborative that helps NQCLs strengthen their capacity for medicines quality testing and supports countries in instituting programs that prevent substandard medicines from reaching consumers. As AMQF moves closer to self-reliance, it is providing keys lessons learned for fostering NOMCoLs in the Middle East and North Africa and the Asia–Pacific Regions.
- **May 29, 2019:** This webinar featured a discussion on how setting types of accreditation for medicines QC laboratories as an objective strengthens country-level programming for medicines QA in LMICs. Certification of compliance with ISO/IEC 17025 standards enables laboratories to demonstrate to stakeholders worldwide that they operate competently and generate valid test results; and WHO PQ makes such laboratories eligible for use by UN agencies. Key differences between ISO/IEC 17025 certification and WHO PQ were explored, and participants were able to consider how to prioritize or choose between the two when necessary.
- **June 25, 2019:** Three PQM Chiefs of Party from Bangladesh, Nigeria, and Pakistan discussed PQM’s multiyear history, exploring the journey of the PQM program in their respective countries. The presenters explained how interventions were designed to meet each country’s medical product QA system context and priorities, framing program achievements around challenges encountered and lessons learned. Emphasis was placed on outlining the continuous path toward country self-reliance in quality-assured medicines programming as a part of health systems strengthening.

Also in Q3, PQM Senior Director Jude Nwokike participated in a side event of the May 2019 World Health Assembly in Geneva, Switzerland, entitled, “A Right, Not a Luxury: Putting Quality Medicines & Diagnostics at the Heart of Quality Care.” The side event hosted a moderated panel discussion to drive home the importance of investing in quality-assured medicines and diagnostics as a foundational element of high-quality health systems and universal health coverage and chart a path toward greater investment and action. The event spotlighted the impact that poor-quality medicines have on patients, building trust in the health system, and achieving UHC.