

# Promoting the Quality of Medicines (PQM) Program

FY 2017 Second Quarter Report  
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### **About the Promoting the Quality of Medicines (PQM) Program**

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Agreement Officer's Representative Team	Mr. Bob Emrey, Lead Health Systems Specialist Ms. Elisabeth Ludeman, Senior Pharmaceutical Management Advisor Ms. Tobey Busch, Senior Pharmaceutical Management Advisor
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The Promoting the Quality of Medicines (PQM) program is a Cooperative Agreement between the United States Agency for International Development (USAID) and the United States Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to address critical pharmaceutical management challenges in developing 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 essential medicines for malaria, HIV/AIDS, tuberculosis, neglected tropical diseases, and maternal and child health.

As of December 2016, USAID supports PQM's work in 20 countries, two Regional Missions, one Cross Bureau program, and four core health programs.

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# Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance to build capacity of medicines regulatory authorities (MRAs) and quality assurance (QA) systems. PQM also provides technical support to manufacturers of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH). This report summarizes results achieved during the second quarter of FY17, from January 1 to March 31, 2017.

PQM's first result area is to strengthen medical products QA systems. Quality 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 work force capacity to helping implement regulations, guidelines, and operational procedures—PQM aims to reduce and eliminate substandard and falsified products that pose serious risks to patients' health and undermine global health and development efforts. A key accomplishment this quarter can be seen in Mozambique, where the Parliament unanimously passed a first reading of a bill on Medicines, Vaccines, Biological and Health Products for Human Use. This amends the original 1998 law (which lacked key regulatory provisions) to give the Pharmaceutical Department (PD) authority to improve medical products regulation to ensure their quality, safety, and efficacy. To accomplish this important milestone, PQM collaborated with the PD, key partners, and stakeholders to establish a technical working group that advocated revising the law to authorize the PD to perform key regulatory functions. As a next step following the final passing of the amendment, PQM will work with the PD to develop appropriate regulations and determine an action plan for implementation. This landmark regulation and its application by the PD will create an environment that promotes medical products quality and protects patients. In Ethiopia during Q2, Ethiopia's MRA (EFMHACA) took appropriate regulatory measures to address the problem of falsified quinine sulfate, which was identified following PQM-supported post-marketing surveillance (PMS). This finding was reported to the World Health Organization's (WHO) Rapid Alert system, and EFMHACA is further investigating to identify the route through which the product entered the country. To further strengthen PMS in Ethiopia, EFMHACA has instituted a new strategy that requires importers to cover the PMS-related costs for their affected products; this measure will help EFMHACA conduct PMS on a more routine basis, reduce financial constraints, and ultimately contribute to the sustainability of Ethiopia's PMS.

The second result area of PQM is to increase the supply of quality-assured priority medicines. A continuous supply of quality-assured products—particularly for essential priority medicines for TB, NTDs, MNCH—is necessary to address national health priorities and plans. PQM works with manufacturers to improve compliance with WHO standards and helps them develop and submit dossiers for certification by the WHO PQ of Medicines Program. WHO PQ and stringent regulatory authority approval ensure that medicines meet acceptable international standards for quality, safety, and efficacy, and can be purchased by procurement agencies. By increasing the number of suppliers and creating a competitive environment, PQM helps to shape the market for essential medicines and contributes to reducing their price. PQM provides technical assistance and guidance to manufacturers for the local production of medicines, which may decrease reliance on international donation and help establish a sustainable local supply with national resources. In Pakistan, PQM provides technical support to local manufacturers to improve and attain current good manufacturing practices for chlorhexidine (CHX) 7.1% gel. This combats the number of newborn deaths from umbilical cord infections, which is preventable by quality-assured CHX gel products. As a result of PQM's support, in Q2 two such products were approved for registration by the Drug Registration Board, marking the first time local CHX received government authorization for production. Sales by two local manufacturers will not only increase Pakistani utilization but will also allow for potential export to other Asian countries that also need quality-assured CHX 7.1% gel to combat infections and infant mortality.

The increased utilization of medical product quality information for decision-making is PQM's third result area. The collection, analysis, and use of data on medical products quality to support evidence-based decision-making is critical to reduce and eliminate 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. PQM works with local, national, and international partners to bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, inform decision-making, shape public policies on pharmaceuticals, and support the attainment of public health objectives.

Results in Nigeria this quarter highlight PQM's contributions towards use of information for decision making to eradicate falsified and substandard products. Through PMS in FY16, 159 samples of oxytocin injection, a vital product that controls hemorrhaging in mothers after childbirth, were collected and tested at the recently accredited Agulu regional laboratory. The comprehensive final laboratory analysis report showed that 74% of the samples collected failed. To discuss these alarming results, PQM requested and participated in a meeting organized by the Nigerian MRA (NAFDAC), where the Acting Director General expressed grave concerns with the high failure reported. She suggested that the failure may not be unconnected with the poor distribution channel in the country and went on to kick-start a brainstorming session to highlight possible root causes of the alarming failure of this product. PQM provided technical leadership during this meeting and supported with identification of feasible actions to address the problem. Some of the recommended solutions proposed included identifying and contacting the market authorization holders of oxytocin injection in Nigeria, as well as other relevant stakeholders for a dissemination meeting scheduled to take place before the end of next quarter, and for PQM to work jointly with NAFDAC to come up with a strategy to remove these ineffective medicine batches from the market to prevent access and use by vulnerable mothers after childbirth. This PMS information is crucial for allowing decision makers within regulatory authorities to ensure that proper actions are taken, based on evidence, to remove poor quality medical products from their markets and protect the lives of their citizens.

# Acronyms

ACT	Artemisinin-based combination therapy
AML	Antimalarial medicine
ANAB	ANSI-ASQ National Accreditation Board
API	Active pharmaceutical ingredient
BPOM	National Agency for Drug and Food Control [Indonesia]
CAMEG	Central Medical Store [Burkina Faso]
CAPA	Corrective Action and Preventive Action
CDCL	Central Drug Control Laboratory
CDL	Central Drug Testing Laboratory [Pakistan]
CHX	Chlorhexidine
CMO	Contract manufacturing organization
CRO	Clinical research organization
CTD	Common Technical Document
DER	Drug Evaluation and Research
DFDA	Department of Food and Drug Administration
DGDA	Directorate General of Drug Administration
DGPML	Director General of the Medicine Regulatory Authority
DMC	Directorate of Medicines Control [Burkina Faso]
DNME	National Directorate of Drugs and Equipment [Angola]
DPM	Directorate of Pharmacy and Medicine [Mali]
DRAP	Drug Regulatory Authority of Pakistan
DRB	Drug Registration Board [Pakistan]
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
EOI	Expression of Interest
EPCMD	Ending Preventable Child and Maternal Deaths
ERP	Expert review panel
FAA	Fixed amount award
FDA	Food and Drug Administration
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectroscopy
GCMS	Gas chromatography-mass spectrometry
GCMSMS	Advanced gas chromatography-mass spectrometry
GCP	Good Clinical Practices
GDF	Global Drug Facility
GDSP	Good Distribution and Storage Practices
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HNSP	Health, Nutrition Sector Program [Bangladesh]
HPLC	High performance liquid chromatography
ICPMS	Inductively coupled plasma-mass spectrometry
IGH	Inspector General of Health [Angola]
ILT	Inter-laboratory medicines testing
IPT	Isoniazid preventive therapy
LCMS	Liquid chromatography-mass spectrometry
LIF	Laboratory information file
LMHRA	Liberia Medicines and Health Products Regulatory Authority
LNCQM	Laboratório Nacional da Qualidade de Medicamentos [Mozambique]
LNS	National Laboratory of Health [Mali]
LNSP	National Laboratory of Public Health [Burkina Faso]

LSSC	Legal Services Support Center [Philippines]
M&E	Monitoring and evaluation
MDR-TB	Multidrug-resistant tuberculosis
MNCH	Maternal, newborn, and child health
MNHSR&C	Ministry of National Health Services, Regulations and Coordination [Pakistan]
MOH	Ministry of Health
MOP	Malaria Operational Plans
MQDB	Medicines Quality Database
MQM	Medicines quality monitoring
MRA	Medicines regulatory authority
mRDT	Malaria rapid diagnostic test
MRIS	Medicine Registration Information System [Ethiopia]
NAFDAC	National Agency for Food and Drug Administration and Control [Nigeria]
NASCOP	National AIDS & STI Control Programme
NCDPC	National Center for Disease Prevention and Control [Philippines]
NCEM	National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan
NEPAD	New Partnership for Africa's Development
NMCP	National Malaria Control Program [Angola]
NMI	National Metrology Institute [Ethiopia]
NPHLS	National Public Health Laboratory Services [Kenya]
NQCL	National quality control laboratory
NTD	Neglected tropical disease
PD	Pharmaceutical Department [Mozambique]
PE&R	Pharmaceutical Evaluation & Registration [Pakistan]
PMI	President's Malaria Initiative
PMS	Post-marketing surveillance
PNLP	National Malaria Control Program [Mali]
PPB	Pharmacy and Poisons Board [Kenya]
PQ	Prequalification
PQAD	Product Quality Assessment Directorate
PQM	Promoting the Quality of Medicines
PRSD	Product and Research Standards Development Division [Philippines]
PT	Proficiency test
PTB	Physikalisch-Technische Bundesanstalt
PTBB	Therapeutic Products National QC Laboratory of BPOM [Indonesia]
PTDRC	Pakistan Drugs Testing and Research Center
QA	Quality assurance
QC	Quality control
QMS	Quality management systems
RBEC	Regional Bioequivalence Center [Ethiopia]
TB	Tuberculosis
UNCoLSC	UN Commission on Life-Saving Commodities for Women and Children
UNIDO	United Nations Industrial Development Organization
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
WHO	World Health Organization
WWARN	World Wide Antimalarial Resistance Network

# Result Highlights



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

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## Overview of FY 2017 Second Quarter Achievements

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Medical products are instrumental to any health systems, 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 Promoting the Quality of Medicines (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-Intermediate Results and Key Highlights

#### 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 a sound pharmaceutical law, which provides the legal mandate for the creation of a national medicines regulatory authority (MRA). Working with in-country stakeholders at these levels, PQM helps to develop or revise policies and legislation by providing technical assistance to help MRAs develop guidelines and regulations—and to adopt internationally accepted standards of Good Regulatory Practices (GRP).

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

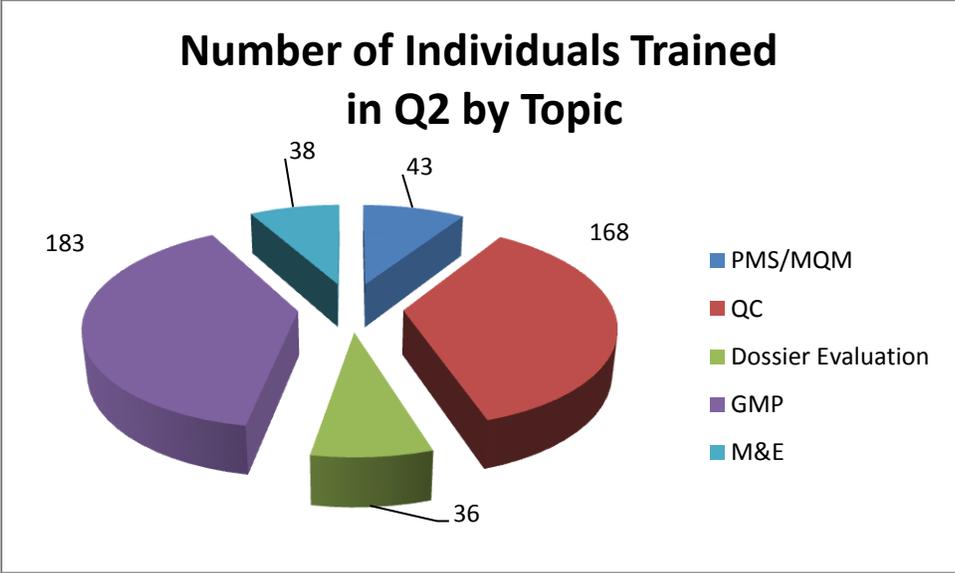
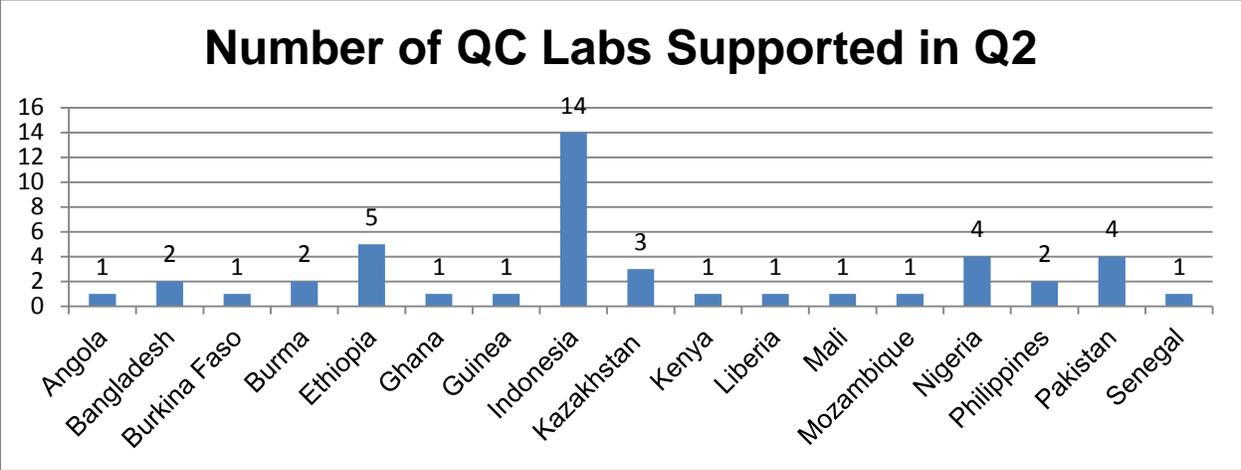
Among the key functions of an MRA, the registration of medical products and the inspection and licensing of manufacturing facilities are crucial processes designed to ensure that only quality-assured products enter the market. PQM works with MRAs to build strong institutional capacity and support registration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

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

MRAs, national procurement agencies, and international donors require reliable and accurate quality control (QC) of data 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 to help laboratories attain certifications of compliance with internationally recognized standards, such as ISO/IEC 17025:2005 and/or World Health Organization (WHO) prequalification (PQ).

#### Sub-IR 1.4 Institutional capacity for medical product quality assurance workforce sustainably improved

Building workforce capacity at central and decentralized institutions and facilities involved in maintaining operationally effective quality assurance systems is a core component of PQM's approach. PQM and USP experts work in collaboration with WHO's global, regional, and national offices to provide hands-on trainings focused on a wide range of good practice guidelines (GxP), particularly bioequivalence aspects of Good Clinical Practices (GCP), Good Review Practices (GRP), Good Manufacturing Practices (GMP), Good Laboratory Practices (GLP) including quality control testing procedures and laboratory equipment maintenance. Through support to pre-service and in-service training programs, train-the-trainers model, and support for the development of structures and processes necessary for effective quality management system, PQM builds sustainable in-country regulatory and quality assurance workforce.



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

Ensuring the quality of medical products throughout the supply chain presents challenges that extend beyond the registration and procurement processes. Substandard medicines may occur due to poor manufacturing practices or degradation 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 unregistered, substandard, and falsified 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 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.

A key accomplishment within this result area can be seen in Mozambique, where this quarter, the parliament unanimously passed a bill on Medicines, Vaccines, Biological and Health Products for Human Use. The bill amends the original law from 1998, which lacked key regulatory provisions. The ground-breaking bill gives the Pharmaceutical Department (PD) authority

to improve regulation of the medical products in the country to ensure their quality, safety, and efficacy. To accomplish this important milestone, PQM had collaborated with the Pharmaceutical Department and key partners and stakeholders to establish a technical working group that advocated for law revisions that would authorize the PD to perform key regulatory functions. As a next step following the final passing of the bill, PQM will work with the PD to develop appropriate regulations and determine an action plan for their implementation. This landmark bill and its application by the PD will create an environment that promote medical products quality and protect patients.

Also, during this quarter, Ethiopia's MRA (EFMHACA) took appropriate regulatory measures to address the problem of falsified quinine sulfate, which was identified following PQM-supported PMS. This finding was reported to the WHO Rapid Alert system, and EFMHACA is conducting further investigations to identify the route through which the product came into the country. To further strengthen PMS in Ethiopia, EFMHACA has instituted a new strategy to require importers to cover the PMS-related costs for their products. This measure will help EFMHACA conduct PMS on a more routine basis, will reduce some of the financial constraints experienced in the past, and ultimately contribute to Ethiopia's PMS being more sustainable.

In Bangladesh, a recommendation from a gap analysis conducted in April/May 2016 by PQM is to adjust and modify the organizational structure of the Directorate General of Drug Administration (DGDA) to align with its strategic vision and mission as part of its efforts to be a fully functional MRA in two to three years. Per DGDA's request, PQM helped review and provide initial inputs to the improved organogram of DGDA. In addition, PQM has completed expertise and skills mapping of key national control laboratory (NCL) staff positions, reviewing job descriptions, and suggesting improvement of organogram structure of the lab to align staff to better support DGDA's mandate and NCL functions.

## **IR2: Supply of Quality Assured Priority Medicines Increased**

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### **Overview of FY 2017 Second Quarter Achievements**

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A continuous supply of quality-assured products -- particularly for essential priority medicines for tuberculosis, neglected tropical diseases, and maternal, newborn, and child health (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 poor quality medicines. Further exacerbating supply challenges are 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 assistance ensures a steady supply of essential medicines of assured quality, safety, and efficacy, thus strengthening countries health systems to improve health outcomes.

### **Sub-Intermediate Results and Key Highlight**

#### **Sub-IR 2.1 Supply of 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 medicines, including those used to treat newborn infections, child and maternal health products. Local production may decrease reliance on international donation, and help establish a sustainable local supply. In addition, developing local manufacturing capacity and enhancing regulatory oversight can improve both national and regional capabilities for sustainable sourcing of quality-assured medicines.

#### **Sub-IR 2.2 Supply of quality assured priority medicines produced globally increased**

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

Number of Manufacturers Provided with Technical Assistance in Q2		
Countries/Core Programs	Number of Manufacturers	Types of Medicine
Core MNCH	6	Magnesium Sulfate injection, Amoxicillin dispersible tablets, Chlorhexidine gel, and Oxytocin prjection
Core NTD	5	Praziquantel API, FPP; Albendazole API
Core TB	9	Clofazimine API, Clofazimine FPP, Linezolid FPP, Gatifloxacin API, Gatifloxacin FPP, Rifampicin API, Rifapentine API, Rifapentine FPP, Kanamycin API
Ethiopia	9	Ethambutole, Ciprofloxacin, Zinc Sulfate, Doxycycline, and Chlorhexidine
Indonesia	5	FDC ARV, 2 FDC, 4 FDC TB, Levofloxacin 500mg
Kazakhstan	1	Levofloxacin, Moxifloxacin
Nigeria	11	Zinc/ORS, Chlorhexidine, Amoxicillin, Magnesium Sulphate, Artemether Lumefertrine, Pharmatex-Arthemether Lumefertrine, RUTF
Pakistan	4	Chlorhexidine

#### 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 Medicines Program or other stringent regulatory authority, manufacturers require access to clinical research organizations (CRO) to conduct bioequivalence (BE) studies. 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 BE studies. PQM prioritizes support to CROs that can provide reliable data for timely approval of priority essential medicines.

#### Sub-IR 2.4 Sources for quality assured API/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 drug. It also increases the risk for potential disruptions in supply if the manufacturer sustains any operational setbacks during production. PQM has witnessed companies that manufacture both the active pharmaceutical ingredient (API) and the finished pharmaceutical product (FPP) become the sole source of a quality-assured product on the market. Interrupting the supply of API to other FPP manufacturers allows for price increases in a monopolized FPP market. To prevent this, PQM works to identify API manufacturers that lack the capacity to produce FPPs but can ensure the API supply to multiple FPP manufacturers. This increases sources and competition within the market and helps reduce prices of essential medicines. Additionally, by developing multiple sources of quality-assured FPPs, the risk of global supply shortages is greatly reduced.

In Pakistan, thousands of newborn children die each year from umbilical cord infections, preventable by quality-assured chlorhexidine (CHX) gel products. To help improve the availability of quality-assured CHX, PQM provides technical support to local manufacturers to improve and attain current good manufacturing practices for CHX 7.1% gel. During the second quarter (Q2), as a result of this support, two such products were approved for registration by the Drug Registration Board, marking the first time local CHX received government authorization for production. The start of sales by two local manufacturers will result not only in increased Pakistani utilization, but also allow for potential exports to other Asian countries that also need quality-assured CHX 7.1% gel to combat infections and infant mortality.

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

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## Overview of FY 2017 Second Quarter Achievements

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The collection, analysis, and use of data on medical products quality to support evidence-based decision making is critical to reduce and eliminate substandard and falsified products. PQM's support the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data informs 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-Intermediate Results and Key Highlight

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

PQM assists national stakeholders with implementing medicines quality monitoring (MQM) programs to generate data on the quality of pharmaceuticals circulating in country. To increase the body of information generated by MQM activities in the countries, PQM advocates for priority essential medicines used in PMS programs to be included, including medicines used for MNCH, HIV/AIDS, and TB.

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

PQM is undertaking a series of additional initiatives to increase availability of data related to the quality of medical products, including working across regulatory functional areas; registration, licensing and inspection, and post-marketing surveillance 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 enforcement actions and remove these medicines from the market. PQM also shares information to alert stakeholders and the public of 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 of the dangers of substandard and falsified medicines – it provides the 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 allocation of resources for improving 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, and collaborates with local universities to develop quality assurance-related content for pharmaceutical curricula.

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

Results in Nigeria this quarter highlight PQM's contributions towards use of information for decision making to eradicate falsified and substandard products. Through PMS in FY16, 159 samples of oxytocin injection, a vital product that controls hemorrhaging in mothers after childbirth, were collected and tested at the recently accredited Agulu regional laboratory. The comprehensive final laboratory analysis report showed that 74% of the samples collected failed. To discuss these alarming results, PQM requested and participated in a meeting organized by the Nigerian MRA (NAFDAC), where the Acting Director General expressed grave concerns with the high failure reported. She suggested that the failure may not be unconnected with the poor distribution channel in the country and went on to kick-start a brainstorming session to highlight possible root causes of the alarming failure of this product. PQM provided technical leadership during this meeting and supported with identification of feasible actions to address the problem. Some of the recommended solutions proposed included identifying and contacting the market authorization holders of oxytocin injection in Nigeria, as well as other relevant stakeholders for a dissemination meeting scheduled to take place before the end of next quarter, and for PQM to work jointly with NAFDAC to come up with a strategy to remove these ineffective medicine batches from the market to prevent access and use by vulnerable mothers after childbirth. This PMS type information is crucial for allowing decision makers within regulatory authorities to ensure that proper actions are taken, based on evidence, to remove poor quality medical products from their markets and protect the lives of their citizens.

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### Select Data Points from FY 2017 Second Quarter

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Number of Individuals Trained in QA/QC related Topics	468
Number of QC Labs Supported	45
Number of Manufacturers Supported towards GMP Standards	50
Number of Active Sentinel Sites Supported for MQM Activities	197
Number of Samples Collected	93 (zinc & TB medicines)
Number of Regulatory Actions	3 - Ethiopia (Malaria), Liberia (Malaria), & Philippines (TB)
Number of QC Labs participated in PT and Passed	2 (PQAD of Ethiopia & Kaduna of Nigeria)
Number of QC Labs Accredited/Reaccredited	1 - Yaba Lab (Nigeria)
Number of QC Labs Expanded Scope of Accreditation	1 - Yaba lab (Nigeria) - multiple pharmaceutical testing scope expansion

# Africa



# Angola

## I. Quarter 2 Highlights

During this quarter, PQM continued to focus on strengthening the capacity of Angola's regulatory authority to monitor medicines quality in the country. To accomplish this goal, PQM has steadily strengthened the National Directorate of Drugs and Equipment (DNME) and Inspector General of Health (IGH) by providing key tools and training.

Building on two previous trainings, PQM conducted a third Minilab™ training in February 2017 for DNME and IGH staff from over eight provinces. The main objective of this training was to build the capacity and skills of the labs to carry out antimalarial QC screening from the various provinces and to assure that quality medicine is available to the general public. This event built upon previous trainings attended by several staff while also serving as an introductory training for staff in provinces who did not receive any prior training. PQM plans to roll out the official PMS before Q4.

## II. Country Context

Angola is a vast country sharing porous borders with the Democratic Republic of the Congo, Zambia, and Namibia, making Angola vulnerable to the threat of falsified and substandard medicines. This was evident in 2012 when large quantities of falsified Coartem® were seized by customs in Luanda.

To obtain a better understanding of the extent of the problem, the President's Malaria Initiative (PMI) in Angola sought PQM's technical assistance to conduct an antimalarial medicines (AMLs) quality study in private and public sectors in selected regions of Angola. This study was conducted in October 2015 and provided a snapshot of medicines quality to the National Malaria Control Program (NMCP) and its partners, which addressed concerns about the presence of falsified and substandard medicines in Angola.

PQM collected additional antimalarial medicines in July/August 2016 from six provinces to obtain information needed to design a post-marketing surveillance protocol for the country. The 2015 survey revealed that the proportion of failed samples for the specific products and in the specific locations was 50%. However, it is important to note that the results are not representative of the overall quality of medicines in Angola. This revealed that additional surveys and collections must be conducted to ascertain the extent of the problem. For the purposes of focused PMS, samples from major provinces of Angola will still need to be collected to conclusively target the areas where malaria is endemic, but the current evidence from Luanda suggests significant antimalarial quality issues may be present in other areas of the country.

## III. Quarter 2 Progress by Objective

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### **Objective 1 – Improve the policy, legislation, quality assurance, and regulatory guidelines and standard operating procedures (SOPs) of the Angolan MOH/DNME**

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In February 2017, PQM met with key DNME stakeholders to determine the legal structure of the Ministry of Health (MOH) and identify key gaps in the MRA's capacity to regulate medicines quality. It was confirmed that the Minister has not approved the decree that legalizes the functionality of the MRA, and there was no evidence that a formal registration of medicines was taking place. All of this information was reiterated by PQM to the key country stakeholders as critical to effectively improve the quality of medicines in the country. As PQM prepares to start official PMS in the country, regulatory actions may need to be taken to address any trends in poor-quality medicines observed during the monitoring exercise.

PQM met with a WHO country representative to discuss PQM's role, and support to DNME and the IGH, to promote collaboration and coordination of technical activities in the country. During the meeting, an agreement was reached for both partners to work with DNME and the IGH to identify and formally document gap areas each partner has the capacity and mandate to address. It was also agreed that PQM will follow up with the IGH, who indicated during the meeting in February 2017 that he will advocate to the Minister of Health to improve the regulatory functions of the MRA.

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## **Objective 2 – Develop and implement a sustainable medicines PMS quality monitoring program**

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During Q2, PQM completed Global Pharma Health Fund (GPHF) Minilab™ training for DNME and IGH staff in Luanda. The purpose of the training was to continue to build the capacity of the MOH and IGH to collect and screen AMLs with the Minilabs™. This marked the third training provided to the MOH by PQM. During the same trip in February 2017, PQM collected relevant pharmacy and health facility information that will aid in completing and finalizing the PMS protocol document. The MOH shipped the Minilabs™ to the provinces in preparation to start MQM exercise by the trained provincial staff once the protocol document is finalized and approved by DNME and the IGH. In total, PQM trained staff at 10 sentinel sites in preparation for the official PMS planned to start in Q3 of 2017.

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## **Objective 3 – Develop a basic quality control lab testing unit in Angola’s Ministry of Health to conduct an expanded sampling and testing of antimalarials**

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In February 2017 PQM, the head of DNME, and relevant stakeholders visited three spaces that could potentially serve as the basic QC laboratory for testing of antimalarials. PQM also provided expert guidance to the head of DNME on the number of staff needed to establish a QC and QA unit. Part of this guidance also included the type of qualifications necessary for staff to work in the respective units. PQM informed the head of DNME about the willingness of the USAID/Angola Mission to provide technical support through PQM to train recruited staff and help get the lab functional.

To ensure PQM’s investments in the lab are sustainable, PQM is also working to elicit a strong commitment of support from the Angolan government. PQM encouraged the IGH and the head of the MRA to meet with the Minister of Health to establish a budget, identify a specific location for the lab, and provide the necessary staff to make the lab effective. This is a prerequisite for PQM to get USAID Mission approval to move forward with this activity. A detailed proposal was provided to the head of the MRA and the IGH that will be used when meeting with the Minister of Health. PQM will provide an update on the outcome of this meeting.

During Q2, PQM hired an in-country consultant who will support PQM-approved activities with DNME and the IGH. The IGH and DNME key staff have been introduced to the consultant.

### **IV. Key Challenges**

Quickly clearing PQM equipment and materials through customs is one of the main challenges to achieving PQM’s goals in Angola. The country recently implemented new customs clearance requirements for shipping certain reagents and chemicals into the country. To address this challenge, PQM will retain Cargo Center, which was previously utilized in 2016 for clearing of Minilabs™ shipped to the Angolan MOH.

Another challenge to advancing the implementation of PQM’s FY17 work plan activities are MOH delays in approving and restoring identified lab space as well as hiring staff who will be trained by PQM to maintain a functional medicine QC lab. As noted, PQM is addressing this challenge by building a coalition of senior IGH and MRA officials to encourage the MOH to take action.

## **Benin**

### **I. Quarter 2 Highlights**

In Q2, PQM facilitated the installation and qualification of a new high performance liquid chromatography (HPLC) system that was donated to the NQCL. This activity was carried over from FY16.

An authorized distributor of the HPLC conducted the installation and qualification. This was also an opportunity to train staff on the performance qualification of the equipment. In addition, the lab staff received training on preventive maintenance of the HPLC.

A ceremony for the handover of the new HPLC was held at the lab. The Director of USAID/Benin, PMI Deputy Coordinator, PMI–Benin team, MOH Cabinet Director, and NQCL Director General were among the high-profile participants in the ceremony. Media coverage of this event included local television and newspapers.

## **II. Country Context**

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

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

## **III. Quarter 2 Progress by Objective**

The FY17 work plan is currently pending approval after revision.

# **Burkina Faso**

## **I. Quarter 2 Highlights**

In this quarter, PQM procured a spectrophotometer for the Directorate of Medicines Control (DMC) of the National Laboratory of Public Health (LNSP) and trained 12 DMC technical staff on the following:

- Good Documentation Practice
- Good Weighing Practice
- pH measurement
- Dissolution Performance Verification Test
- Ultraviolet-visible spectrophotometry
- HPLC

PQM facilitated a ceremony for the official handover of the spectrophotometer to LNSP. The hiring of a local consultant was initiated and is anticipated to be completed by the end of April.

## **II. Country Context**

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

PQM was selected by the USAID/Burkina Faso Mission to strengthen the capacity of the country's national MRA, Director General of the Medicine Regulatory Authority (DGPML), NQCL, LNSP, and other major pharmaceutical systems with the primary goal of improving its QA/QC of medicines.

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

### III. Quarter 2 Progress by Objective

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#### Objective 1 – Strengthen the capacity of the NQCL

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To support the DMC NQCL in its effort to implement its development plan, PQM procured a spectrophotometer and trained the lab staff on several analytical methods. This equipment was needed, as the existing spectrophotometer was very old and not performing properly.

During the training on different analytical methods and good practices, PQM and the lab staff had a chance to identify gaps in the way the lab conducts analytical work and discuss how to address them. At the end of the training, the lab staff was assigned to conduct the analytical work that they learned during the training and write a report documenting the lab work. The lab staff members were also tasked to develop new SOPs or revise existing ones to reflect current practices.

After interviewing four candidates, PQM selected a local consultant to support implementation of program activities in Burkina Faso and is in the process of finalizing the hire.

PQM facilitated a ceremony for official handover of the new spectrophotometer by the USAID Mission to the LNSP. The participants in the ceremony included the USAID/PMI team, MOH General Secretary represented by the DGPML, CAMEG Director General, National Malaria Control Program represented by its pharmacist, Director General of LNSP, and Directors of LNSP services. The participants in the ceremony had an opportunity to tour the lab and learn more about DMC activities. The event was well covered by the media, including national radio and television, two local print newspapers, and an online newspaper.

## Ethiopia

### I. Quarter 2 Highlights

During the second quarter, PQM continued to focus on strengthening the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA)—a critical partner in expanding access to quality medicines in Ethiopia, by providing ongoing support to the development of the Medicine Registration System (MRS). Based on PQM's recommendations, improvements were made to the system's authorization level to maintain confidentiality of users. PQM

also finalized and disseminated the Guidelines for Clinical Trial Authorization - the document is accessible on EFMHACA's website. In making the document readily available, EFMHACA is soliciting comments for improvement from the public.

PQM continues to strengthen the inspection system and achieve progress towards ISO 17020 accreditation of the inspection directorate of EFMHACA. To that end, PQM helped implement all the SOP procedures, guidelines, and other documents developed in previous quarters. To maintain its ISO 17025 accreditation and demonstrate its technical competency, EFMHACA's Product Quality Assessment Directorate (PQAD) laboratory passed proficiency tests (PT) that were assessed by an external evaluator of performance and competence in laboratory analytical tests. This progress puts EFMHACA inspection directorate on track to achieve ISO 17020 in the near future.

During this quarter, EFMHACA took appropriate regulatory measures to address the problem of falsified quinine sulfate, which was identified following PQM-supported PMS. This finding was reported to the WHO Rapid Alert system, and EFMHACA is conducting further investigations to identify the route through which the product came into the country. To further strengthen PMS in Ethiopia, EFMHACA has instituted a new strategy to require importers to cover the PMS-related costs for their products. This measure will help EFMHACA conduct PMS on a more routine basis, will reduce some of the financial constraints experienced in the past, and ultimately contribute to Ethiopia's PMS being more sustainable.

Lastly, to help develop the Addis Ababa University School of Pharmacy Standard Operating Procedure (AAU SoP), its workforce development initiatives, and technical competence in the use of laboratory equipment, PQM supported the maintenance and installation of refurbished laboratory equipment. This equipment will be used to help train a skilled workforce to support the emerging pharmaceutical sector in Ethiopia.

## II. Country Context

Ethiopia aspires to eliminate malaria from its mid and low lands in the east. While scaling up malaria control measures, the country will implement strategies to pave the way for a malaria-free Ethiopia by 2030.

AMLs are central to any effective strategy to reduce mortality related to malaria. Safe and effective AMLs are therefore essential to mitigate morbidity and reduce deaths. Assured quality also slows down the development of resistance to AMLs and enhances the perception of quality health care and treatment among healthcare professionals and patients. PMS conducted in 2015 showed 30% of the sampled medicines found to be unregistered out of 174 samples, and four of 83 samples of AMLs failed quality tests. This underscores the need to ensure the quality of AMLs to mitigate the possibility of resistance, treatment failure, and undesired health outcomes.

## III. Quarter 2 Progress by Objective

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### Objective 1 – Strengthen the performance of the medical products registration system of EFMHACA

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PQM provided technical support in the development of guidelines, troubleshooting of the Medicine Registration Information System (MRIS), and training of EFMHACA staff. Support also included the completion of the first draft of the strategy for enhanced marketing authorization.

Main accomplishments:

- Trained 10 EFMHACA staff on dossier assessment using EFMHACA funds while PQM provided technical resources. Unlike previous trainings, this training also involved hands-on sessions in addition to lectures.
- Conducted a workshop to review the Good Clinical Practice (GCP) guideline for clinical authorization. After undergoing several reviews, the GCP guideline is now complete and posted on EFMHACA's website to solicit comments for improvement from the public.
- Submitted first draft guidelines for registration of biological products to EFMHACA management for review. A stakeholder's workshop is planned next quarter to review these guidelines.
- Implemented improvements to the MRIS by addressing issues around the authorization level and confidentiality of user information.

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## **Objective 2 – Strengthen the inspection system of EFMHACA and regional/city administration authorities**

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PQM provided GMP technical assistance and on the job training to EFMHACA staff on the tools previously developed. Support was also provided to develop several SOPs necessary for the ISO 17020 accreditation. An ISO 17020 conformity assessment specifies requirements for the competence, impartiality, and consistency of inspectors.

Activities conducted during Q2 to address this objective included:

- Developed inspection manual and associated tools, including sections on the types of inspection at the regional city administration regulatory authorities, inspection checklists, and code of conduct for inspectors.
- Developed training materials for sterile products GMP inspection.
- Developed training materials for roll-out of basic GMP trainings for inspectors. This training material will also be used as training manual to support future internal trainings by EFMHACA.
- Provided technical assistance to implement guidelines developed for ISO17020 accreditation of the inspection directorate of EFMHACA. Support included training staff on 10 previously revised or developed SOPs reported in quarter one. PQM was also able to routinely monitor the use of the SOPs through its participation in weekly meetings conducted by the technical working group.

Progress toward ISO17020 accreditation continues to advance with the implementation of the developed SOPs. This stage is critical because it is the means by which the inspection system is standardized and improved toward meeting international standards. It also helps to increase the credibility of the inspections conducted by EFMHACA.

As a next step, an assessment on the implementation of different guidelines developed will be conducted. The assessment will help determine to what extent the guidelines are being applied and also identify challenges associated with their use. The development of the inspection manual will also continue during Q3.

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## **Objective 3 – Strengthen product quality testing system of EFMHACA and branch laboratories**

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During this quarter, with support from PQM, the PQAD laboratory received notification for ISO 17025 reaccreditation. PQM supported the surveillance assessment of the lab by ANSI-ASQ National Accreditation Board (ANAB) and provided technical assistance to respond to the Corrective Actions and Preventive Actions (CAPAs).

The following activities were implemented:

- Supported participation of EFMHACA PQAD Lab in proficiency test (PT) for eight test methods with SIGMA Aldrich RTC (PT provider). All of the PT results were acceptable.
- Identified calibration needs and initiated procurement of calibration equipment for the National Metrology Institute (NMI) that will enable the NMI to sustainably support the calibration needs of the EFMHACA laboratory.
- Coordinated discussions between Bahirdar University and EFMHACA to collaborate on testing foods and medicines. Such collaboration will help leverage resources among different government offices that play a role in medicine regulation in Ethiopia.
- Provided ongoing supervisory support to two branch laboratories in Bahirdar and Diredawa. The report from the labs indicates ongoing sample collection of antimalarial drugs from public and private outlets for PMS. The overall lab setup has improved, routine testing of inspected samples has started and is documented, internal supervisions is ongoing, and collaborative work with the regional health regulator is reported.

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## **Objective 4 – Support local medicine manufacturers to improve their GMP compliance**

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During this quarter, in collaboration with WHO and the United Nations Industrial Development Organization (UNIDO), PQM compiled the assessment reports on the GMP status of local pharmaceutical manufacturers. The report was shared with

each manufacturer, and the Corrective Action and Preventive Action (CAPA) report is being finalized. A follow-up visit was conducted with Addis Pharmaceuticals and East Africa Pharmaceuticals on their progress toward addressing the CAPAs. PQM continues to collaborate with WHO, UNIDO, Food, Beverage and Pharmaceuticals Development Institute (FBPDI), and EFMHACA with the goal to improve GMP compliance of local manufacturers and to ensure adequate follow-up on the CAPAs issued as a result of the two-round assessment.

Following the GMP knowledge gaps identified during the joint assessment, it was agreed that GMP training designed for staff of local manufacturers will be conducted next quarter. PQM will participate by providing trainers for GMP in accordance with the Terms of Reference (TOR) prepared by PQM and WHO. Another key activity beginning in April will be a mock audit of Cadila and follow-up on its Ethambutol dossiers submission.

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#### **Objective 5 – Strengthen the survey of quality of medicines circulating in the national market**

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PQM in collaboration with EFMHACA and other stakeholders has updated the MQM protocols, list of medicines, and areas of sample collection in preparation for the upcoming FY17 PMS of antimalarial medicines. PMS is expected to be conducted in quarter three.

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#### **Objective 6– Strengthen EFMHACA governance and management system**

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PQM is awaiting a decision on its previous recommendation to review the structure of EFMHACA. There is no update this quarter.

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#### **Objective 7– Provide technical assistance to the School of Pharmacy of the Addis Ababa University in workforce development in regulatory affairs**

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In collaboration with the AAU School of Pharmacy, PQM facilitated bringing a U.S. Food and Drug Administration (FDA)-based trainer to teach a course to students enrolled in the post-graduate program in Regulatory Affairs. The School has requested support for the development of additional modules, which include quality management systems (QMS) and audits, product registration and inspection, and regulatory science and compliance. PQM plans to prioritize these based on available funding. PQM will provide technical content and work in with other identified AAU School of Pharmacy partners to fully develop the curriculum.

This quarter, corrective maintenance and installation of laboratory instruments at the School was conducted by a PQM consultant to further support the workforce development initiative of the AAU School of Pharmacy.

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#### **Objective 8– Support the Regional Bioequivalence Center (RBEC) to be compliant with Good Laboratory Practices (GLP)**

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During this quarter, laboratory instruments and parts were procured for the support to RBEC, plans are also underway to secure a venue for experience sharing and training of RBEC staff and management.

#### **IV. Key Challenges**

As part of the Ethiopian government's initiatives, there have been reforms within MOH and EFMHACA that have adversely affected the implementation of activities as originally planned. EFMHACA staff have been in frequent meetings and engaged in other competing activities followed by the political unrest of the past few months. Another challenge was the delayed implementation of FY17 PMS due to insufficient time for the laboratory staff to perform tests of collected samples.

# Ghana

## I. Quarter 2 Highlights

In an effort to strengthen country-owned, sustainable PMS, PQM drafted a PMS protocol guideline and collected and tested 50 zinc samples at Ghana FDA for confirmatory testing. PQM and Ghana FDA agreed to a document that summarizes and highlights the USAID-funded support to Ghana FDA, FDA mandate and the importance of expanded accreditation. Additionally, PQM continues to strengthen the QMS of Ghana FDA by working with the lab for the upcoming ISO 17025 surveillance assessment of the laboratory services department.

## II. Country Context

The PQM program was funded by PMI in Ghana in FY08 to strengthen the QA of AMLs in the country. PMI Ghana has funded PQM to provide technical assistance and build capacity to improve efforts in ensuring medicines quality in the country. The program in Ghana has focused on support for the FDA by ensuring QC of medicines prior to registration and on PMS of the quality of AMLs in the marketplace. The antimalarial MQM program in Ghana has led to the identification of several falsified and substandard medicines; this has prompted Ghana FDA to recall several batches of AMLs from the market and to refer the illegal activities to law enforcement agencies. Based on the outcome of the antimalarial MQM over the years, Ghana FDA decided to enhance its PMS activities in 2013 by providing resources for the basic infrastructure to establish two additional sentinel sites, bringing the total to seven. The number of sampling cycles per round of the MQM was also increased to two.

## III. Quarter 2 Progress by Objective

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### Objective 1 – Expand MQM to country-owned sustainable post-marketing surveillance

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In January 2017, PQM met with the Deputy Chief Executive of the Ghana FDA drug registration and enforcement unit to discuss the PMS unit's current activities and plan for MQM for FY17. Since it was determined that there were no written and standardized PMS protocols, PQM drafted guidelines and is waiting on sentinel site information to finalize the protocol. In Q2, PQM also facilitated and procured reagents for the testing of 50 zinc samples that are now at the Ghana FDA drug physicochemical unit for confirmatory testing. The results of these samples will be available in Q3 for reporting. Additionally, PQM discussed the plan for antimalarial and uterotonics sampling and testing for Q3.

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### Objective 2 – Strengthen the capacity of medicine regulatory system to support regulatory actions against poor quality medicines

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PQM is collecting data on regulatory actions taken by FDA as a result of PQM-supported interventions. With a new Ghana FDA CEO appointed in March 2017, PQM has communicated USAID mission approved objectives and activities that the CEO should be involved with, such as the upcoming stakeholder forum and the document summarizing USAID support. The new CEO is very open and familiar with all PQM successes and activities with Ghana FDA and pledged her support to facilitate the accomplishment of USAID/ PQM's planned objectives and goals to strengthen the Ghana regulatory system.

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### Objective 2 – Strengthen Quality Assurance and Quality Control Systems through building the capacity of Ghana FDA's quality control systems and laboratories toward attaining or maintaining international standards of quality and practices

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In January 2017, PQM staff evaluated Ghana FDA's QMS progress and provided technical assistance to prepare the lab for the upcoming ISO 17025 surveillance assessment of the laboratory services department. PQM reviewed outstanding CAPA of the three accredited units (drug physicochemical, medical device, and pharmaceutical microbiology), internal audit reports, outstanding SOPs, and training records. Overall, PQM reviewed about 30 QMS documents and trained 15 Ghana FDA laboratory staff members to analyze and identify corrective actions through document review. Additionally, PQM met with the heads of accredited lab units and identified key lab supplies and consumables needed to continue to maintain their accreditation status. The procurement of those supplies was initiated in Q2 and should be in the lab before the planned audit in May 2017.

To get the lab prepared for the upcoming audit and to continue to strengthen their technical capacity, PQM has shipped procured laboratory items to the lab that includes weighing balances, reagents for testing, and lab consumables for the microbiology lab.

## Guinea

### I. Quarter 2 Highlights

PQM, in collaboration with the USAID-funded SIAPS program, conducted a workshop with key stakeholders in Conakry to resume reviewing and updating the pharmaceutical law. Discussions were benchmarked by WHO guidelines, internationally accepted practices, and experiences of other African countries. The main outcome of the meeting was consensus with key members of the law commission, and documentation of the table of contents of the future law, including the governance provisions.

### II. Country Context

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

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

To reduce disease burden, there is an immediate need to ensure reliable access to good-quality, safe, and efficacious essential medicines and to build up the country's QA/QC systems. The USAID/Guinea Mission selected the PQM program, implemented by USP, to assume this task. To accomplish this, PQM received funds from Maternal Child Health (MCH) and Family Planning (FP) to conduct a rapid assessment of Guinea's QA/QC systems and subsequently propose activities to address the major challenges.

### III. Quarter 2 Progress by Objective

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

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The Republic of Guinea has a pharmaceutical law (L-94/012/CTRN) and its corresponding decree (Decree No. 94/043/PRG/SGG) as the main regulatory documents concerning medicines and other health products. The revision of the law was deemed necessary by the authorities in the country because of recent developments and problems related to the proliferation of illicit markets for substandard and falsified medicines. The pharmaceutical market in Guinea faces major challenges at the level of regulations, practices, and pharmaceutical institutions. The Ebola epidemic of 2016 prompted Guinean authorities to review their health system, including medicines and health products regulations.

In FY16, PQM undertook a rapid review of the pharmaceutical law (L-94/012 and its Decree D-94/043). The analysis of L-94 was discussed with the commission, but it was not possible to bring together the members of the commission to review the law. In March 2016, PQM organized a two-day workshop in Conakry to commence review of the pharmaceutical law.

During this workshop, PQM experts worked with the members of the commission to reach the main consensus needed to start the full review of the law. The workshop resulted in a consensus and agreement on a participatory approach involving all key Guinean stakeholders. The national commission was supposed to continue working on the draft and share its work with key partners providing technical assistance in this area for review. Unfortunately, the commission has not done any additional work on the draft law since March 2016.

This quarter, in collaboration with the USAID-funded SIAPS program, PQM conducted a key stakeholder workshop in Conakry on March 27–31 to resume work on reviewing and updating the pharmaceutical law. Two PQM representatives and one SIAPS consultant joined efforts to effectively support the Guinean authorities. During the first two days of the highly participatory workshop, the team worked with key members of the law commission to agree on and document the table of contents of the future law, including the governance provisions. Discussions were benchmarked with WHO guidelines, internationally accepted practices, and experiences of other African countries. Some of the key agreements included:

- The first part of the law will focus on regulating medicines and other health products; the second part will focus on the practices.
- Key definitions and types of medicines will be identified and written.
- The law will address medicines, including veterinary products, other health products, and medical devices.
- MRA will be defined by the Minister of Health, and the support of the existing NQCL will be clearly defined in the law.
- MRA must be empowered by the law and regulations to cover all regulatory functions as defined by WHO, including its own inspection functions, which are up-to-date and covered by the MOH inspectorate general.

Cosmetics were listed, but consensus was not reached on whether or not the MRA will regulate them because limited resources required for different tests to assess medicines quality were also procured, shipped, and delivered to the LNCQM lab.

## Kenya

### I. Quarter 2 Highlights

PQM started working in Kenya in November 2009 by conducting an assessment of the QA/QC capacities of the country. This initial assessment was followed by meeting the key partners and stakeholders to prepare for the establishment of PQM MQM of AMLs in five selected sentinel sites. This PQM approach has focused on using Minilabs™ as a first identification method to ascertain for the quality of medicines.

PMS preparatory activities for malaria rapid diagnostic tests (mRDTs) were initiated this quarter with the NMCP, Malaria Reference Laboratory, and other key stakeholders. Malaria is one of the common parasitic diseases in Kenya, with a high mortality rate especially among children. Early diagnosis, followed by prompt and effective treatment, is the key to reducing malaria mortality and morbidity. RDTs that are not quality-assured can lead to mistreatment and waste of resources. In addition, the MRA has limited capacity for pre-approval evaluation for mRDTs; hence there is a need to strengthen PMS for diagnostics. Like other diagnostic tests, variations in the nature of the manufacturer, mode of transport, storage, and method of use may compromise the accuracy of mRDTs.

NMCP provided a list of mRDT commodities required for PMS and is currently developing the protocol for malaria-endemic counties in Kenya that will need to receive ethical approval before the testing can start. This will be the first such test in the country. Senegal Parasitology University experts are providing the training and technical assistance. Their support for quality testing of mRDTs exemplifies regional collaboration. This represents the first mRDT quality testing supported by PQM and builds on the WHO Stepwise Strengthening Laboratory Management towards Accreditation (SLMTA) process at the Malaria Reference Laboratory under the National Public Health Laboratory Services (NPHLS). The mRDT activities are based on FY 2016/2017 work plan.

Initial informal joint PMS discussions were held with NMCP, National HIV Program (NASCO), National TB Program, and Mission for Essential Drugs and Supplies (MEDS) to support one round of integrated PMS-MQM activities.

In February 2017, the PQM Kenya program hired a local consultant to assist and support the implementation of PQM activities in Kenya. His work has helped to fast-track activities at the country level.

A meeting is being planned for Q3 to discuss the joint PMS based on priorities from the various disease programs. The first round of malaria RDT PMS is also being planned.

## II. Country Context

USAID funding is provided for health systems strengthening interventions, including strengthening of the health workforce, the health information system, and supply chain management for HIV/AIDS, malaria, and family planning materials. In this context, PQM has been engaged to help strengthen the pharmaceutical regulatory system and to improve medicines quality. Kenya and other countries in Africa are 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 national regulatory authority to ensure that medicines are properly registered and tested, and take corrective regulatory actions related to substandard or falsified products and unlicensed pharmaceutical outlets.

PQM 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 2 Progress by Objective

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### Objective 1 – Strengthen PMS and integrate other essential medicines to existing MQM program at central and county levels

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The main activities conducted under this objective this quarter were:

- PQM built the capacity and skills of health workers at 11 new ports of entry to appropriately use and interpret results with Minilab™ for QC screening of imported medicines.
- To ensure consistency in approach and nationwide monitoring of quality of medicines in the country, the Pharmacy and Poisons Board (PPB) used its own funding to conduct Minilab™ training for county-level staff. This also is an indicator of country ownership and sustainability of medicine quality monitoring.
- PQM supported implementation of one round of integrated PMS–MQM activities, including at the 11 new ports of entry, and expanded coverage of medicines to include TB, HIV priority medicines, and AMLs previously collected.

As a follow-up to this activity, a joint PMS stakeholders meeting is planned for May 4, 2017, at PPB. Representatives from the National TB Program, NMCP, NASCO, MEDS, NQCL, Kenya Medical Supplies Authority (KEMSA), MOH, and select counties have been invited.

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### Objective 2 – Build the regulatory capacity of PPB by strengthening product registration

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No major activities or progress to report this quarter.

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### Objective 3 – Strengthen the quality control capacity of NQCL and support maintenance of ISO 17025 accreditation and WHO PQ

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No major activities or progress to report this quarter

A South African National Accreditation System (SANAS) accreditation assessment visit has been planned for June.

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**Objective 4 – Strengthen the quality control capacity of NQCL and support maintenance of ISO 17025 accreditation and WHO PQ**

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PQM continues to advocate that PPB leadership continue regulatory actions and public awareness efforts. This quarter, PQM noted some national and local press awareness information focused on adverse drug reactions, quality of medicines, and mobile-based applications for getting information about quality-assured medicines or pharmacy practitioners that were made available to consumers.

Sample documentation of PPB PMS advocacy and pharmacy practice activities and press articles included:

- Silent epidemic of ADR done by Daily Nation  
<http://www.nation.co.ke/health/MEDICINE-Killing-you-softly/3476990-3829988-3nmrxkz/index.html>
- Managing pharmaceutical risks in cross-border care by the deputy registrar of Kenya Mr Fred Siyoi  
<http://www.nation.co.ke/health/Managing-pharmaceutical-risks-in-cross-border-care/3476990-3830004-yrgsj1z/index.html>
- New app developed to improve access to quality care and safe medicine  
<https://www.linkedin.com/pulse/isikure-launched-kenya-facilitate-national-access-sabine-emmerich>

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**Objective 5 – Support the implementation of PQM activities in country and promote regional and international collaboration**

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In February 2017, PQM hired a local consultant to support the implementation of PQM activities in Kenya. Having an in-country presence helped to fast-track activities and allows PQM to be more engaged with country stakeholders.

## Liberia

### I. Quarter 2 Highlights

In 2016, the Liberia Medicines and Health Products Regulatory Authority (LMHRA) detected over 48 different batches of poor-quality medicines in the country's pharmaceutical supply chain that were imported into the country. Five of these medicines were brought into the country by importers registered with LMHRA. Three of the five medicines are AMLs. Preliminary investigations clearly suggest that these three AMLs were either poorly manufactured or falsified. This case and several other cases provide sufficient reason for LMHRA to conduct GMP inspection of the facilities of manufacturers of essential medicines being imported into Liberia outside the donor-funded procurement mechanisms. However, being a relatively new MRA, LMHRA lacks the technical capacity for GMP inspection of these international manufacturing facilities. There are no local medicine manufacturers in Liberia. Presently, the quality of all medicines entering Liberia is checked by LMHRA's NQCL.

While some capacity has been built within the NQCL to support product registration and marketing authorization, there are still challenges. In some cases, the NQCL is unable to provide evidence-based results due to the lack of needed equipment or reagents to carry out compendial testing to assess the quality of medicines imported into the country. PQM continues to provide technical assistance to support the NQCL. However, in addition to building the capacity of the laboratory, it is also important to strengthen other LMHRA regulatory functions, such as GMP facility inspections. To address the lack of capacity for GMP facility inspection, PQM conducted a five-day basic GMP workshop for 13 LMHRA inspectorate unit staff. The goal is to build capacity and basic skills needed to support GMP facility inspections. Additional training and hands-on facility visits will be needed in the near future to build this capacity.

Discussions on the proliferation of antimalarial monotherapy circulating in the Liberian market were elevated to the USAID Mission. Both LMHRA and the NMCP are involved in charting next steps. PQM also participated in the PMI FY17 Malaria Operational Plans (MOP) exercise.

## II. Country Context

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

Since 2011, PQM has provided technical assistance to strengthen post-marketing surveillance in Liberia through Medicines Quality Monitoring (MQM) for antimalarial medicines and encouraged the LMHRA to take appropriate regulatory actions. Through these MQM activities, several antimalarial medicines including quinine and chloroquine were removed from circulation. Monotherapies, once widely available but subsequently banned through regulatory action by the LMHRA, has made these products less prevalent. Results from various MQM activities and subsequent regulatory actions have been encouraging; however, the data continues to show that falsified and substandard medicines are still a major concern in Liberia.

In Liberia PQM is focused on:

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

As part of the approved 2016 work plan, PQM provides technical assistance to build the QC capacity of the existing LMHRA QCL toward ISO 17025 accreditation, strengthen and expand the monitoring of the quality of AMLs, promote regulatory actions for falsified and substandard medicines, and increase awareness of quality medicines.

## III. Quarter 2 Progress by Objective

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### Objective 1 – Continue building the QA capacities of LMHRA in registration and inspection

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During Q1, it was observed and reported that two AMLs imported from India were either poorly manufactured or falsified. In FY15 and FY16, cases of substandard AMLs were observed. To build the LMHRA inspectorate unit's capacity to support the GMP inspection of manufacturing facilities, in Q2 PQM provided training on basic GMP concepts to 13 LMHRA inspectors. Preparation for the second phase of the GMP training, which will be hands-on training, is expected to begin in Q3. After the second phase of the training, LMHRA inspectors will be equipped with inspection skills and able to check basic GMP compliance indicators of manufacturers exporting AMLs to Liberia. A reduction or elimination of importation of substandard AMLs into Liberia due to improved GMP compliance inspection capacity will contribute to improved treatment outcomes in Liberia and reduce the aggravation of risk of drug resistance by poor quality medicines.

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### Objective 2 – Continue strengthening the quality control of LMHRA QC Lab toward ISO 17025 accreditation

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During this quarter, the QC Manager—joined by two analysts trained at USP Ghana—continued to make improvements to the laboratory. During this quarter, eight analysts participated in three different in-house advanced compendial training sessions between January and March 2017. The purpose of the training was to build laboratory staff capacity and skills to carry out various tests for medicines quality verification. Topics covered included good laboratory practices (GLP), Karl Fischer, and Fourier transform infrared spectroscopy (FTIR) method. More advanced training is expected to be rolled out on FTIR and other selected laboratory equipment.

As the technical capacity of QCL personnel improve, LMHRA is making steady progress toward its readiness for ISO 17025 accreditation. An ISO 17025 accreditation will assure that the QCL is able to assess medicines quality at an internationally acceptable standard, thus allowing the lab to support all Global Fund medicines (including antimalarial and HIV medicines) to be tested in Liberia for a fee. This will positively impact the quality of AMLs in the public sector and generate needed revenue for LMHRA to sustain its activities.

In Q1, PQM arranged a meeting with Mr. David Sumo, head of LMHRA, to leverage World Bank funds received by LMHRA. In this quarter, this meeting bared the fruit of using the World Bank through MOH with \$487,950 to procure key equipment

(e.g., FTIR, HPLC, UV spectrophotometer) for QC tests at the NQCL. The procurement process is currently ongoing within the MOH. This generous contribution provides a major boost to LMHRA's preparation toward ISO accreditation.

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### **Objective 3 – Build the capacity of LMHRA on the Post Marketing Surveillance Program for the monitoring of the quality of antimalarial medicines**

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During this quarter, PQM staff met with LMHRA, NMCP, and USAID regarding re-enforcing the monotherapy ban and PMS. Highlights of PQM achievements for this activity included:

- Submission by NMCP of a list of antimalarial monotherapies to be banned
- Submission of draft letter for enforcing monotherapy ban to the MOH., Revision of PMS budget which includes plans for public awareness activities that will support the removal of monotherapies .
- Revision of PMS budget that includes public awareness activities for removal of monotherapy
- Concept note drafted demonstrating the importance of integrating PMS into NMCP's monitoring and evaluation (M&E) program. This concept note is expected to be considered during the Global Fund grant preparation.

PQM plans to write a letter of no objection to allow LMHRA/NMCP to use the available funds (Monotherapy Research Funding) for PMS.

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### **Objective 4 – Promote regulatory actions and raising awareness about poor quality medicine in country and at regional levels:**

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During this quarter, PQM staff participated in a five-day MOP exercise in Monrovia. During the meeting A presentation giving an overview of PQM activities in Liberia was made to malaria stakeholders (including PMI, NMCP, Centers for Disease Control and Prevention [CDC], MOH) and other partners. The presentation highlighted implemented activities, geographical coverage, achievements to date, challenges, and planned activities for FY18. One of the main areas of emphasis during the meeting was the need for ISO accreditation of the LMHRA QC Lab. PQM's priority areas were corroborated by LMHRA during the PMI meeting with stakeholders. Also during this meeting, PQM requested additional funding to support newly identified priority areas for PQM's FY17 work plan for Liberia.

During the next quarter, PQM will arrange discussions between LMHRA, NMCP, Global Fund and PMI about the need for additional funds to leverage PQM activities in Liberia.

#### **Key Challenges**

- Insufficient lab space could hinder efforts to get the lab ISO accredited. There are discussions with other donors (e.g., Global Fund, World Bank) to fund a better lab with additional space.

## **Mali**

### **I. Quarter 2 Highlights**

In this quarter, PQM support has focused on strengthening the technical and managerial capacity of the National Laboratory of Health (LNS) of Mali. PQM trained six staff, including three new staff members, from Medicine Quality Control services of LNS on analytical methods and GLP. SOPs related to the scope of the training were developed. PQM continues to work with LNS to develop the lab strategic plan. The lab trainings covered the following topics: Laboratory safety, GLP, Good Documentation Practice, Good Weighing Practice, pH meter, HPLC, Spectrophotometer performance verification, Dissolution performance verification test.

PQM worked with LNS, the National Malaria Control Program (PNLP), and the Directorate of Pharmacy and Medicine (DPM) to develop a sampling plan for antimalarial MQM activities.

## **II. Country Context**

MQM activities had been delayed due to the lack of staff capable of coordinating these activities with the Regional Health Directorates or to conduct the sampling and testing in the field. More skilled staff are necessary both at the regional level and at LNS. Strengthening DPM's capacity and generating evidence-based data for DPM to take regulatory actions against substandard or fake medicines are urgently needed, and implementing MQM activities will help achieve that.

## **III. Quarter 2 Progress by Objective**

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### **Objective 1 – Strengthen the Capacity of the National Quality Control Laboratory in Mali**

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PQM continues to strengthen LNS analytical, managerial, and human resource capacity and to assist the lab in developing its strategic plan.

One of the challenges that LNS has faced is the high turnover of its staff at Medicine Quality Control services (MQCS). Based on recommendations coming out of the workshop for disseminating antimalarial QC monitoring activities, and with approval from the Ministry of Health and Public Hygiene, LNS hired three new staff members for MQCS. PQM tailored several training sessions for MQCS staff based on their evaluation of LNS.

PQM trained six LNS staff how to test the antimalarial artemether/lumefantrine HPLC, replacing testing methods that were neither current nor standard. These staff members also received training in GLP, including Good Documentation Practice and Good Weighing Practice as well as laboratory safety and pH, and had the opportunity to apply these practices during hands-on training on HPLC. The same staffers also received training in HPLC qualification and preventive maintenance, and on how to qualify lab timers. The training allows LNS staff to keep the HPLC systems in good working condition. PQM provided spare parts and supplies needed to carry out qualification and preventive maintenance of HPLC systems, which has been a challenge for NQCLs.

PQM also provided a hands-on training session for LNS lab staff that focused on performance verification testing of spectrophotometer and dissolution tester. PQM focused on HPLC, spectrophotometry, and dissolution because they were identified for lab accreditation. The lab staff developed SOPs for training they received.

In Q2, PQM hired a full-time local technical consultant, who participated in PQM training. He is helping to ensure the lab staff applies the acquired skills, follow GLPs and is also assisting lab staff in drafting new SOPs.

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### **Objective 2 – Strengthen Post Marketing Surveillance of Antimalarial medicines in Mali**

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To prepare for the upcoming round of sampling and testing of AMLs, PQM assisted LNS in developing a sampling plan in coordination with PNLP and DPM. PQM gathered information on all registered antimalarials and identified all the outlets in the areas where LNS will potentially collect samples. The areas selected are the District of Bamako and the regions of Koulikoro, Mopti, Segou, and Sikasso. The sampling was expected to start on April 24, 2017.

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### **Objective 3 – Facilitate studies on the efficacy and resistance of antimalarial medicines**

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PQM worked with the Laboratory of Applied Molecular Biology on a fixed amount award (FAA) document. They drafted the scope of work, milestones, and budget. The FAA documents will be submitted to the Agreement Officer's Representative (AOR) for review and approval before the end of April.

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### **Objective 4 – Strengthen the capacity of the Directorate of Pharmacy and Medicine (DPM)**

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Based on recommendations from a December 2016 workshop to share PMS data with the National Commission against Illicit Sell of Medicines, the DPM revised its action plan and resubmitted it to the Ministry of Health and Public Hygiene for approval. PQM will assess DPM in early May.

### III. Key Challenges

A lengthy process to establish an FAA with local partners has delayed antimalarials quality surveillance.

## Mozambique

### I. Quarter 2 Highlights

The Laboratório Nacional da Qualidade de Medicamentos (LNCQM) is working to obtain ISO 17025 accreditation. PQM continues to provide pertinent equipment, reagents, and lab consumables that allow the lab to function properly and analyze medicines. PMS protocols were revised based on the data collected from years of conducting PMS in the country; PQM will collaborate with the in-country partners to start the locally driven PMS. This quarter, the parliament unanimously passed first reading of a bill on Medicines, Vaccines, Biological and Health Products for Human Use. The bill amends the original law from 1998, which lacked key regulatory provisions. The bill gives the PD authority to improve regulation of the medical products in the country to ensure quality, safety, and efficacy.

### II. Country Context

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

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

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

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

### III. Quarter 2 Progress by Objective

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

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PQM continues to strengthen LNCQM's technical capacity to prepare for ISO 17025 by providing pertinent equipment, reagents, and lab consumables that allow the lab to function properly and analyze medicines. During Q2, PQM supported and completed an overhaul of the electrical system in the lab to ensure a more stable electrical supply. Frequent fluctuations in electricity may damage equipment and affect productivity levels in the lab, since some equipment cannot be used without electricity. The electrical overhaul included installation of a stabilizer and a new electrical box and outlets in the lab.

In February, the second HPLC (equipment for identifying and quantifying individual components in a medicine to detect poor quality) was installed, as was the new dissolution system (equipment that detects how the medicine is released in the body and helps to establish its safety and effectiveness) that PQM had procured in Q1.

To continue to prepare the lab for ISO 17025 accreditation, PQM has ordered a set of proficiency tests to determine the performance of the lab for specific tests and measurements to be delivered to the lab in Q3. This will be the second round of PT tests for the lab to complete. The aim is to ensure the lab has the requisite technical capability to assess the quality of medicine employing a specific test methodology and can demonstrate continuous good performance as compared to

standards. The test results will be reported in Q3. During Q2, laboratory equipment required for different tests to assess medicines quality were also procured, shipped, and delivered to the LNCQM lab.

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### **Objective 2 – Support and strengthen post-marketing surveillance**

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To continue to improve PMS to monitor the quality and safety of medicines in Mozambique, PQM has comparatively analyzed the data collected from previous years of conducting PMS in the country and applied the lessons learned to improve the sampling protocols. In Q2, PQM drafted revised protocols incorporating lessons learned that will be shared with the lab in April 2017. PQM plans to work collaboratively with in-country partners to train and supervise sampling and testing in Q3, including a site visit to the main port of entries for sample collection. The sampling plan will include uterotonics and family planning medicines during Q3 2017. The need to monitor the quality of uterotonics available to the general population, especially oxytocin, an essential MNCH commodity used in the treatment of PPH, is urgent, especially given recent PQM-supported studies in Ghana and Nigeria showing significant failures (68% and 74%, respectively).

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### **Objective 3 – Provide technical assistance to the Pharmaceutical Department (PD)**

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PQM provides technical assistance to the PD to improve its functionality. In March, the parliament unanimously passed a first reading of a bill on Medicines, Vaccines, Biological and Health Products for Human Use. The bill amends the original law from 1998, which lacked key regulatory provisions. The bill gives the PD authority to improve regulation of the medical products in the country to ensure quality, safety, and efficacy. Since 2016, PQM supported the country's effort to revise the law and established a technical working group that provided guidance on regulations and law revisions that would authorize the PD to perform key regulatory functions. As a next step following the final passing of the bill, PQM will work with the PD to determine an action plan for implementation.

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

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In February 2017, PQM, the LNCQM lab director, and the LNCQM QC unit head visited Portugal's regulatory authority, INFARMED. The purpose of this visit was to initiate future collaboration between the two agencies. INFARMED has an ISO 17025 accredited lab with a large scope of accreditation and is familiar with Mozambique's regulatory authority and its challenges. The trip is intended to initiate a train-the-trainer collaboration that will help improve the capacity of the Mozambique lab and PD. During the visit, INFARMED gave an overview training session on ISO 17025 requirements to two LNCQM staff members, provided training on how to properly write SOPs, and provided staff with QMS documentation in Portuguese. The group also discussed QC and QA training and made a plan for INFARMED to travel to Mozambique to assist PQM to train lab staff on QMS topics and help establish key SOPs.

## **IV. Key Challenges**

During Q1, LNCQM experienced challenges with Internet services, making communication and correspondence with the lab delayed and sporadic. Since PQM requires the Internet to make upgrades and updates, PQM is working with LNCQM/PD to try to find solutions to this problem. In Q2, quotes were received from two providers, and the winning provider plans to overhaul the lab's outdated Wi-Fi system and install a new modem. In Q2, PQM completed due diligence and began drafting a contract with the company.

PQM confirmed that the monthly cost to main Internet services will be covered by MOH.

## **Nigeria**

### **I. Quarter 2 Highlights**

PQM provides technical assistance to strengthen the quality assurance systems of the National Agency for Food and Drug Administration and Control (NAFDAC), the Nigeria MRA, as well as to support manufacture of quality-assured primary essential medicines for malaria and MNCH.

PQM's first aim is to strengthen national regulatory systems. In pursuit of this goal, PQM provides technical assistance to strengthen pharmaceutical policies, legislation, and regulations to address critical QA topics and enhance the ability of the MRA to execute policy. An integral component of the MRA is its NQCL; PQM strives to raise laboratory standards through capacity building of personnel and other interventions to achieve the desired goal. Highlights under the first result area during the quarter include:

- Yaba laboratory received official notification from ANAB for a successful reaccreditation for ISO 17025:2005 for multiple pharmaceutical testing.
- Yaba laboratory also received official notification for multiple pharmaceutical testing scope expansion from 7 to 10.
- PQM provided technical assistance to Kaduna Laboratory, which has been recommended for accreditation.

As part of sustainability plans, PQM identified a local calibration body that is ISO 17025 accredited. NAFDAC has since begun the process of signing a memorandum of understanding (MOU) with the calibration company. Considering the number of NAFDAC laboratories that need equipment calibration, this development will be more cost effective than past practice, which entailed paying significant sums for calibration services from firms outside of West Africa. It is worth noting that all laboratories seeking accreditation or reaccreditation must ensure that all equipment is calibrated annually or biannually.

Improvement in capacity for sustainable PMS of medical products is a critical result for Nigeria. Regulatory authority field staff are trained in sampling and testing methods, while national laboratories handle samples requiring advanced confirmatory testing. This quarter, 21 NAFDAC staff were trained by PQM in sampling and testing methods. They were also trained in online data capture and analysis software used during the sampling exercise.

The FY17 round PMS of antimalarial drugs in Nigeria was carried out successfully in the six geopolitical zones. Five regional laboratories handled Minilab™ tests of the sampled antimalarial products, and results are expected by next quarter. In FY16, 166 samples of misoprostol, 163 samples of magnesium sulfate, 148 samples of calcium gluconate, and 159 samples of oxytocin were analyzed. The results of all MNCH samples except for oxytocin were shared in a previous report (FY16 Q4). The comprehensive final oxytocin laboratory analysis report was received from the recently accredited Agulu regional laboratory and the result showed that 74% of the samples tested failed. While the sampling results are not necessarily representative of the burden of poor quality oxytocin in the country, NAFDAC organized a meeting to discuss the cause of these findings. The FY17 round of PMS of MNCH medicines will commence next quarter, its scope tailored to include identification of issues responsible for the high failure rate of oxytocin and possible solutions.

Increasing the supply of quality medicines, the second result area, encompasses PQM's broad technical assistance for the manufacturing of quality-assured priority essential medicines. PQM provides support to manufacturers to attain stringent international GMP standards necessary for the supply of quality medicines. Significant accomplishments for this quarter include the development of a new zinc sulfate dispersible tablet formulation by Emzor pharmaceuticals with the support of PQM Nigeria. This breakthrough creates a pathway for the local manufacturer to commence full-scale production. Trials indicated positive outcomes for critical quality attributes. As part of capacity building, a workshop on data integrity was conducted for 115 participants from five local manufacturers. In addition, 25 participants were trained in dossier compilation in Common Technical Document (CTD) format to help prepare for upcoming dossier compilation of priority products and subsequent implementation of interventions.

PQM's third result area is the use of information on medical products for decision making. Results in this quarter highlight PQM's contributions to eradicate falsified and substandard products. PQM participated in a meeting organized by NAFDAC to discuss the report on the PMS results of oxytocin injection in Nigeria. The Acting Director General expressed grave concerns with the high number of failed samples reported and went on to kick-start a brainstorming session to highlight possible root causes and recommended actions. Recommendations included identifying and contacting the market authorization holders of oxytocin injections in Nigeria, as well as other relevant stakeholders for a dissemination meeting scheduled to take place before the end of next quarter.

To improve data reporting and capturing of outcomes of NADFAC interventions, 38 NAFDAC staff across all the directorates were trained on fundamentals of M&E. The training was organized to develop competency for good data

collection and reporting that showcases the public health interventions of the agency and sets the pace to close gaps in NAFDAC's M&E system.

## II. Country Context

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

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

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

## III. Quarter 2 Progress by Objective

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### **Objective 1 – Continue to provide technical assistance to selected manufacturers with strong interest and commitment to locally producing products of interest (Zinc/ORS, CHX, Amoxicillin DT, Artemether/Lumefantrine, oxytocin injection, magnesium sulphate injection, and Ready to Use Therapeutic Foods (RUTF) in compliance with international quality standards**

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PQM delivers broad technical assistance to local manufacturers to address GMP and other quality-related concerns. By doing so, PQM increases access to a steady supply of essential medicines of assured quality, safety, and efficacy, thus improving local health systems. Technical assistance is provided throughout the application process for Stringent Regulatory Authority, or local National Regulatory Authority approval, from early initiatives to the final submission of the application or dossier.

#### **Progress with Emzor on zinc sulphate dispersible tablet**

This quarter marked significant progress with the development of new zinc sulfate dispersible tablet formulation by Emzor Pharmaceuticals with the support of PQM. Trials indicated positive outcomes for critical quality attributes. This will create a pathway for the local manufacturer to commence full-scale production. PQM provided technical assistance to the local manufacturer in developing a standard procedure for writing, administering, and training, as well as protocols for requalification of the heating ventilation air conditioning system. This resulted in successful requalification of the system (a critical utility in pharmaceutical manufacturing), making the standards for the manufacturing environment compliant to ISO class 8 for clean room standards. This forms part of the building blocks in making the facility compliant with GMP. With the formulation success, further scale-up production trials and stability batches will commence next quarter.

#### **PQM supported local manufacture - Drugfield- to resolve UNICEF audit observations**

In FY16, UNICEF conducted a GMP inspection of the Drugfield with the intention of purchasing chlorhexidine for program intervention. Thirty-five CAPAs were identified by UNICEF. In the last two quarters, PQM has provided technical assistance to the local manufacturer to resolve the identified CAPAs and develop QMS documents. To verify the resolution of CAPAs this quarter, PQM conducted a mock audit of the facility. Results confirmed CAPAs have been resolved. The next step is for the local manufacturer to send the final CAPA report to UNICEF.

PQM supported another local manufacturer, Tuyil Pharmaceuticals, to review the three-month accelerated stability report for chlorhexidine gluconate gel. The report indicated that the medicine stability was within specification.

Additionally, technical assistance was provided to the local manufacturer in the development of the site master file, out of specification SOP, risk management SOP, handling of incident SOP, stability study protocol, and calibration master plan. Next steps for the local manufacturer include:

- Continuing with the stability studies
- Continue to support improvement of quality management system in the facility

#### **PQM continues support to potential manufacturer of RUTF in Northern Nigeria**

Last quarter, DANADAMS Pharmaceutical, a local manufacturer with strong interest in the local production of Ready-to-Use Therapeutic Food (RUTF), reached out to PQM to join PQM-supported manufacturers. PQM provided technical assistance for the design of the new RUTF facility and modification of the existing pharmaceutical facility to meet GMP standards. This quarter, the PQM team completed evaluation of the facility drawing, and the local manufacturer has received cost estimates for facility reconstruction that is current GMP (cGMP) compliant. The document has been submitted to the Bank of Industry, a financial lending institution. If successful, the northern region of the country will have another cGMP pharmaceutical manufacturing facility that will produce quality-assured RUTF, used to decrease child morbidity and mortality attributable to malnutrition.

#### **PQM continues support to FIDSON Healthcare, a potential oral rehydration salts manufacturer to meet cGMP**

PQM responded to a request for technical assistance from a local manufacturer, Fidson Healthcare, with high interest in improving the production of oral rehydration salts and strong prospects for locally manufacturing anti-TB medicines in Nigeria. PQM conducted a complete walkthrough of the facility and reviewed 13 QMS documents, which showed some deficiencies. The next step for this local manufacturer include:

- Technical assistance to develop relevant QMS documents.
- Onsite training on key aspects of cGMP, including good documentation practices, risk management, CAPA and deviation management, annual product review, and cleaning validation.

Other activities this quarter included the successful completion of the magnesium sulfate injection accelerated stability report and all scheduled equipment calibration. Next steps for the local manufacturer include compiling data for the dossier and continuing with the real-time stability studies. PQM also began providing technical support to CHI pharmaceuticals to review product quality data for dossier compilation in Common Technical Document format for artemether/lumefantrine. Another local manufacturer, May & Baker, has sent in some data for dossier compilation. When they complete the dossier, the two local manufacturers will resubmit an improved dossier to the local MRA.

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### **Objective 2 – Strengthen regulatory quality assurance and quality control systems through building the capacity of NAFDAC's quality control laboratories to attain international standards of quality and practices**

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PQM builds the capacity of NQCLs to improve laboratory standards through hands-on training and technical assistance. Internationally recognized standards, such as ISO accreditation and/or WHO PQ, are just one possible result of this increased capacity. ISO accreditation signifies that a laboratory is technically proficient to produce consistently valid results. Regulatory agencies and medicines manufacturers typically accept test results only from accredited labs. WHO PQ aims to increase the supply of quality priority medicines by applying unified standards of acceptable quality, safety, risk, and efficacy to guide procurement decisions of UN agencies and other entities involved in procuring bulk medicines.

#### **NAFDAC Central Drug Control Laboratory (CDCL) Yaba gets reaccredited**

Last quarter, PQM conducted a mock audit of the Yaba laboratory with the aim of identifying deficiencies and opportunities for improvement in preparation for the ISO/IEC 17025:2005 reaccreditation by ANAB. All identified gaps during the mock audit were resolved. ANAB conducted the laboratory assessment this quarter, and NAFDAC Yaba in Lagos received official notification from ANAB for a successful reaccreditation for ISO 17025:2005 for multiple pharmaceutical testing and scope expansion from seven to 10. The multiple pharmaceutical testing methods include HPLC, ultraviolet visible spectroscopy, pH measurement, dissolution, loss on drying, Karl Fischer water content determination, uniformity of dosage form (weight variation and content uniformity), FTIR spectroscopy, melting point, and volumetric titration.

#### **NAFDAC Kaduna Area Laboratory recommended for accreditation**

This quarter, Kaduna regional laboratory passed 11 proficiency tests as a result of technical assistance from PQM, a critical requirement for laboratories seeking ISO 17025 accreditation. Additionally, 28 laboratory staff (13 women, 15 men) were trained in auditor–auditee etiquette, refresher training on measurement of uncertainty, and handling of out-

of-specification tests in preparation for the ISO 17025 accreditation. All relevant equipment to support the laboratory accreditation was duly calibrated in line with the calibration schedule for existing equipment and was completed. PQM conducted a mock audit of the Kaduna laboratory with the aim of identifying deficiencies and opportunities for improvement (OFI). Support was provided to the laboratory to close up identified nonconformances. ANAB audited the laboratory, and only four minor observations and two OFI were observed. The laboratory has been recommended for accreditation. It will be first of its kind in the northern region of the country and will provide the guarantee that almost 100% of all NAFDAC's drug quality tests are conducted in line with global best practices. Official notification of accreditation is expected after all observations are resolved by next quarter.

**PQM increases the building blocks for sustainability**

As part of sustainability plans for all achievements in various laboratories, PQM identified a calibration company in West Africa with ISO 17025:2005 accreditation. This development was communicated to NAFDAC, which has since commenced the process of signing an MOU with the calibration company. Considering the number of NAFDAC laboratories, this development will prove highly cost effective in NAFDAC's efforts to sustain PQM's work on equipment calibration. Previously, significant funds were expended on engaging calibration bodies from other countries outside of West Africa. It is worth noting that all laboratories seeking accreditation or reaccreditation will have to ensure that all equipment is calibrated annually or biannually.

Additionally, NAFDAC signed an MOU with a reference standard supplier granting a discount of 75% on all purchases. This will greatly aid making primary reference standards readily available for all accredited laboratory analysis. This development will also fast-track the registration process of medical products and sustain PMS of medicines.

NAFDAC management has completed the installation of new equipment for Kaduna regional laboratory. This equipment includes HPLC, gas chromatography-mass spectrometry (GCMS), advanced gas chromatography-mass spectrometry (GCMSMS), liquid chromatography-mass spectrometry (LCMS) and inductively coupled plasma-mass spectrometry (ICPMS). The listed equipment will enhance research, QC testing, and possible ISO accreditation scope expansion in the nearest future.

To further strengthen the human resources capacity in the laboratories, NAFDAC deployed 14 new staff to two laboratories (10 to Kaduna lab and four to Agulu lab).

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**Objective 3 – Strengthen NAFDAC's registration unit (R&R) capacity to manage registration information IR: Medical products quality assurance systems strengthened Sub IR: Registration, inspection and licensing functions of medicine regulatory agencies sustainably improved (Pre-market)**

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**Assessment of NAFDAC registration directorate completed**

PQM collaborated with NAFDAC's Registration and Regulation Directorate to ascertain the need to develop a medicines registration information management system that creates the necessary procedures for improved efficiency in product registration processes. This activity should have commenced in Q1 but experienced delay in the recruitment process of the identified consultant to conduct the assessment. This quarter, PQM completed the assessment of existing capabilities of the registration unit's information system and its impact to other directorates in achieving an improved product registration process in NAFDAC.

PQM engaged all NAFDAC technical units and various stakeholders, including the Pharmaceutical Council of Nigeria, Federal MOH, and Pharmaceutical Manufacturers Group of Manufacturers Association of Nigeria. The assessment report and recommendations are expected by next quarter. The recommendations will form the foundation for system-strengthening building blocks for an automated and improved product registration and monitoring system that will reduce lead time (average time span between application, submission, and date of issuance of the registration certificate) for registering a pharmaceutical product.

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**Objective 4 – Strengthen NAFDAC Drug Evaluation and Research (DER) Directorate capacity for inspections and Dossier Evaluation**

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DER is committed to the development and continued improvement of its quality management system to ensure a robust and effective inspectorate that will guarantee safe, effective, and good-quality medicines. Since 2009, the unit has used inspection guidelines that do not present parameters that can benchmark contemporary situations in the country. To continue strengthening NAFDAC's regulatory systems through a review of the inspection guidelines that

support processes related to GMP, dossier evaluation, and good storage and distribution practices, 46 SOPs and the existing guideline were received from the agency for review. Next steps after the guideline review are to facilitate implementation of the reviewed guideline through at least one round of inspection to three different PQM-supported local manufacturers by the NAFDAC inspection directorate.

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### Objective 5 – Strengthen NAFDAC’s PMS directorate capabilities

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PQM Nigeria focuses on building NAFDAC’s capacity to perform its PMS regulatory function, which is aimed at assessing product quality in the market. This includes maintaining and monitoring the quality of marketed products throughout their shelf life and at all levels of the supply chain. Twenty-one NAFDAC staff were trained in sampling and testing methods. They were also trained on online data capture and analysis software that was used during the sampling exercise. This software will further reduce poor data entry and fast-track accurate data analysis. The FY17 round of PMS of antimalarial drugs in Nigeria was carried out successfully in the six geopolitical zones. Five NAFDAC regional laboratories handled Minilab™ and confirmatory tests of the sampled antimalarial products. Comprehensive results are expected by next quarter.

In the FY16 round of PMS for MNCH, 166 samples of misoprostol, 163 samples of magnesium sulfate, 148 samples of calcium gluconate, and 159 samples of oxytocin were analyzed. Below is a table demonstrating results by facility type.

**Table 1: Tabular representation of FY16 Nigeria PMS results by facility type**

Facility	Magnesium Sulfate			Calcium Gluconate			Misoprostol			Oxytocin		
	FAIL	PASS	% Failure	FAIL	PASS	% Failure	FAIL	PASS	% Failure	FAIL	PASS	% Failure
Primary Health Center	0	29	0	3	26	10	12	16	43	19	11	63
State Hospital Store	1	15	6	1	7	13	5	5	50	7	3	70
Federal Medical Center	0	11	0	0	9	0	0	5	0	5	3	63
Mid Wife Clinic	2	31	6	5	20	20	10	17	37	25	6	81
Pharmacy	1	52	2	1	63	2	22	41	35	40	17	70
Patent Medicine Store	0	21	0	0	13	0	7	26	21	22	1	96

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### Objective 6 – Strengthen human capacity and program effectiveness of key regulatory agencies, local manufacturers and local PQM staff

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PQM serves as a global technical leader in medicines QA and as an advocate for medicines quality in collaboration with a number of partners. Technical leadership entails contributing to an expanding body of knowledge on pharmaceutical quality-related health systems research, as well as developing and disseminating innovative and efficient quality testing techniques and approaches. Advocacy efforts involve the promotion of quality medicines and eradication of falsified and substandard products, forged through collaboration with diverse partners at local, national, and international levels, as well as visibility in external information outlets.

To improve data reporting and capturing of outcomes of interventions in NAFDAC, 38 NAFDAC staff (27 males, 11 females) across all the directorates were trained on M&E fundamentals. The training was structured to develop competency for good data collection and reporting that showcases the public health interventions of the agency and set the pace to close up gaps in the M&E system of the agency. As part of PQM's sustainability strategy, the training cost was shared with NAFDAC. A post-training knowledge assessment showed that 83% of the participants increased their knowledge on the subject matter. In addition, a capacity-building workshop was conducted on data integrity for 115 participants (71 males, 44 females) from five local manufacturers (CHI Pharmaceuticals, May & Baker, Daily Need, Fidson Healthcare, Drug field Pharmaceuticals) by the PQM team. Twenty-five participants (10 males, 15 females) were trained in Dossier Compilation in CTD format to help prepare for upcoming dossier compilation of priority products and subsequent implementation of interventions. Thirty participants (21 males, nine females) from a PQM-supported local manufacturer (Tuyil) were trained on key GMP topics: pharmaceutical quality system, good documentation practices, data integrity, dossier compilation, writing of SOPs, maintenance and cleaning of punches and dies, importance of line clearance to avoid cross contamination during production.

PQM participated in a meeting organized by NAFDAC to discuss the report on PMS results of oxytocin injection in Nigeria. The meeting commenced with a speech from NAFDAC's Acting Director General. She appreciated the presence of PQM Nigeria and also expressed delight in the survey of antimalarial conducted in FY14 and FY16. In her remarks, she stated that in order to save lives it is essential to preserve the availability of quality-assured oxytocin injection primarily used on vulnerable groups in the country's population. She mentioned that NAFDAC was becoming more scientific, thus the need for data is key to help make informed decisions. She informed the audience that, as part of sustainability, the agency had concluded an MOU with the country's Bank of Industry and that the sum of N42 million naira (\$133,000 USD) has been released for the procurement of new HPLC equipment for the laboratories.

She expressed serious concerns with the high oxytocin failure rate reported. She went on to kick-start a brainstorming session to highlight possible root causes of the alarming report and recommended actions. Among the recommendations is the need to review and monitor the distribution channel/status of Marketing Authorization Holders (MAHs) and take regulatory actions as appropriate; revisit the needs to establish drug marts at various locations in the country; regular training and enlightenment programs for MAHs and stakeholders on the importance of good distribution practices; review basics of identifying stability related issues (discoloration, turbidity); and identify sources of low-cost cooling technologies. In the next quarter, PQM will support NAFDAC as it intends to identify and contact the MAHs of oxytocin injection in Nigeria and other relevant stakeholders for a dissemination meeting scheduled to take place before the end of April 2017.

## SENEGAL

### I. Quarter 2 Highlights

During this quarter, PQM engaged with the Senegal partners on two main activities: (1) mock audit and assessment of the NQCL (LNCM) QMS according to ISO 17025 requirements, and (2) assessment of LNCM laboratory equipment and follow-up on maintenance and installation of equipment. These activities are aimed at building the capacity of the national laboratory to attain either WHO PQ or ISO 17025 Accreditation.

### II. Country Context

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

In collaboration with the regulatory authority (DPM) in August 2015, PQM organized an Inter-Ministerial Workshop on Reinforcing Regulatory Actions Against Counterfeit and Substandard Medicines that included illicit markets. The main objective of the workshop was to develop a road map with an enforceable action plan detailing how to join efforts

among (DPM) and enforcing entities. One of the recommendations included the organization of an operation called “Coup de Point” to eradicate at least one illicit market in Senegal in addition to the one in Dakar that had been removed in 2012. As of April 2016, PQM has done strategic planning on how to execute this activity jointly with inter-ministerial committee (IMC) members. Delays in receiving PMI funds pushed PQM to execute this activity in late 2016.

As part of strengthening LNCM QC capacities, in 2014 PQM performed an audit of the lab that revealed the following problems that need to be addressed: inadequate QMS; inability of skilled lab staff to maintain their roles and responsibilities in the lab due to university work commitments; lack of motivation, which led to staff members not fulfilling their assigned duties; insufficient technical capacity of the lab staff to conduct QC testing of medicines according to compendial methods, a part of ISO 17025 and WHO PQ requirements; delays in procuring lab equipment; lack of equipment maintenance and services leading to non-calibrated analytical balances and improper use of verification and calibration tools; lack of regular employees, as opposed to contractual staff, which led to high turnover; periodic turnover or restructuring, which has hindered progress toward ISO 17025; and the need for five additional full-time, trained, qualified staff in the physical chemistry group.

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

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

### **III. Quarter 2 Progress by Objective**

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#### **Objective 1– Assist the NQCL toward attaining WHO prequalification or ISO 17025**

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PQM trained select staff members on advanced maintenance of lab equipment and tested their capacities by providing an evaluation of their maintenance skills for major lab equipment. The PQM team also met with the LNCM and DPM directors to complete the pending FAA documents, discussed the status of LNCM and DPM strategic planning, and shared the implementation plan for the remaining activities for the lab and DPM.

# Asia



# Bangladesh

## I. Quarter 2 Highlights

PQM's activities during the second quarter of 2017 were focused on the implementation and support of Objectives 2 and 4 of our approved work plan. This quarter highlights are:

- Capacity-building trainings were delivered on QMS; Good Practices in Pharmaceutical Quality Control, Hygiene, Protection and Safety, and Good Documentation Practices. These trainings were held at the national control laboratory (NCL) in Dhaka and supported the training of 23 (19 male, three female) laboratory managers and laboratory analysts.
- A training of trainers was conducted on the Proper Use of Pharmacopeias and Analytical Techniques, which was also held at the NCL in Dhaka. PQM sponsored the participation of two laboratory staff from Chittagong as well, for a total of 27 laboratory analysts (17 male, 10 female).
- Five members of PQM's technical team from USP's Rockville headquarters facilitated the trainings and provided onboarding support for newly hired, national technical staff.
- Considerable effort went into developing, reviewing, and consulting with Management Sciences for Health (MSH)/Systems for Improved Access to Pharmaceuticals and Services (SIAPS) and WHO to finalize the Directorate General of Drug Administration's (DGDA) Five-Year Strategic Plan and FY17 Action Plan. This was done through remote communication and face-to-face meetings held this quarter with SIAPS and other stakeholders in Bangladesh. Both plans are very important, as they serve as the foundation for the areas of priority work and a timeline for DGDA in developing an implementation plan. The plans also serve as guides and means for budgetary support to move forward in the process of accreditation as a fully functional regulatory agency.
- PQM explored complementary sources of funding to support procurement of the essential lab equipment/instruments needed to outfit the NCL.
- Updated and coordinated with the USAID Country Mission, providing inputs into the Bangladesh 4th Health, Nutrition Sector Program (HNSP) and the Operational Plan to strengthen DGDA. DGDA's current funding is insufficient to upgrade the NCL facility, which needs critical lab equipment to improve its testing capability.

In addition, this quarter PQM focused on staffing the Bangladesh Field Office, where the senior operations manager, technical manager, and one of two QA/QC specialists were hired and onboarded in March 2017. During the quarter, the recruitment of the Chief of Party (COP) intensified, with shortlisting of candidates, and at time of report writing a final candidate recruited. Two additional staff—the QMS specialist and the Senior QA/QC specialist—will start their roles on April 17, 2017. Registration of the USP-PQM Field Office is also progressing, with submission anticipated in mid-April to the Director General of NGO Affairs Bureau, under the Prime Minister's office.

PQM has also made significant progress in finding a field office location that meets with the predefined criteria, such as security and safety, logistic access convenience, and cost considerations. The negotiation and contractual arrangement with the landlord has been progressing. In the meantime, PQM was able to negotiate with the DGDA leadership and secure three temporary work stations within the DGDA building for its local staff. Additionally, another two work stations have been secured at the NCL for PQM national staff who are working daily at the NCL to improve quality standards. PQM expects that, in the next quarter, the staffing and registration of the USP-PQM Field Office will be a priority, as this will allow for more timely coordination and delivery of technical assistance and therefore project implementation. Follow-up on the CAPA for the NCL will continue for several months to move forward toward compliance with international standards such as ISO/IEC 17025, which is targeted for the end of 2018. In addition, assessment of manufacturers will be done locally with support from the USP-PQM technical team, and a final selection of manufacturers will be completed to support the production of essential medicines, including priority training needs for the most qualified manufacturers.

## II. Country/ Context

PQM's goal in Bangladesh is to strengthen the institutional capacity for sustainable regulatory and QA/QC systems that meet international standards. To achieve this goal, PQM has developed strategic objectives based on a PQM gap analysis conducted in April/May 2016 and discussions and consultations with the USAID country mission, DGDA, Management Sciences for Health (MSH)/SIAPS, and other relevant partners/stakeholders.

PQM is partnering with SIAPS to strengthen selected DGDA regulatory functions in line with extensive discussions and consultations between the two programs teams and in alignment with guidance from the AOR and the USAID Country Mission. For those areas in Objectives 3 and (especially) 4 where SIAPS has been working, including product registration (dossier format and registration software), GMP training, and PMS, PQM will provide technical support to SIAPS, which takes a leading role in providing technical assistance to DGDA. In consultation with USAID, PQM and SIAPS will continue to work on transitioning these areas of work to PQM before the end of SIAPS program in September 2017. For those areas where SIAPS does not provide assistance, PQM will provide direct technical assistance in collaboration with relevant partner(s) to DGDA and other relevant clients.

## III. Quarter 2 Progress by Objective

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### **Objective 1 – Conduct a well-designed gap analysis on regulatory related to the quality assurance and quality control systems, develop FY17 work plan, and take part in the peer review work plan meeting**

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There are four activities under this objective, and all were completed prior to Q2.

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### **Objective 2 – PQM to provide direct support to DGDA National Control Lab (NCL) in Dhaka and Drug Testing Lab (DTC) in Chittagong toward achieving international ISO/IEC 17025:2005 accreditation or WHO PQ**

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PQM has been providing technical guidance/inputs to NCL to strengthen its QMS. The activities for this quarter included:

- Following up on the progress with implementation of CAPA from the gap analysis and recommendations provided by PQM.
  - Evidence that progress and completion of some of the 42 CAPA items identified in the planning phase with a defined completion timeline has gradually been achieved.
  - The PQM QMS team reviewed progress and provided feedback and guidance to NCL for additional revision and improvement of quality processes (five staff: one female, four male).
- PQM continues to work with the NCL QA team to finalize its quality manual, assist in SOPs development and training, and conduct onsite verification of its CAPA progress in their daily work. PQM provided specific training and capacity building to NCL in the following areas this quarter:
  - Conducted practical observations and five-day training on Good Practices for Pharmaceutical Quality Control Laboratory, Chemical Hygiene, Laboratory Safety, and Good Document Practices for 20 NCL technical staff/analysts (17 male, three female) and three Central Drugs Testing laboratory (DTL) staff (two male, one female) from February 28 to March 9, 2017.
  - Conducted hands-on training on strengthening pharmaceutical analytical techniques: HPLC, Infrared, Dissolution, and Performance Verification Testing for 25 NCL analysts (16 male, nine female) and two DTL analysts (one male, one female) from March 20 to 30, 2017.
  - Conducted expertise and skills mapping of key NCL staff positions, reviewed job descriptions, and suggested improvement of the lab's organogram structure to align staff to better support DGDA's mandate and NCL functions from March 5 to 9, 2017. To support the delivery of trainings, three new staff were onboarded in Q2, including the senior operations manager, the technical manager, and one of the QA/QC specialists.

In Q3, two more staff will join the Field Office team, including the QMS specialist and senior QA/QC specialist. They will be onboarded in April 2017 and receive orientation training to bring them up to speed on PQM processes, activities to date and

introduction to key stakeholders. Recruitment of the COP is underway; an approval decision is expected from the Mission in April 2017.

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### **Objective 3 – PQM collaborates with SIAPS to improve the GMP compliance of local pharmaceutical manufacturers toward WHO Pre-qualification Program for priority MCH/FP products**

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PQM drafted a questionnaire to collect general information from manufacturers about their capacity, list of products, GMP compliance maturity, and interest in moving toward international standards production of essential medicines. The questionnaire will be distributed to local pharmaceutical companies producing MNCH/reproductive health and TB medicines with assistance from DGDA and the Bangladesh Association of Pharmaceutical Industry. PQM initiated discussion with DGDA for its support to gather this information from the industry. In Q3, PQM will conduct one training course, possibly in collaboration with SIAPS on advanced GMP inspection for DGDA inspectors (Activity 3.3). This will be held in Dhaka, with 20 to 25 participants from the Licensing and Inspection Division of DGDA and the drug super-attendants from the provincial level.

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### **Objective 4 – PQM to provide technical support to SIAPS in strengthening the DGDA's regulatory functions**

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In Q2, PQM and DGDA Directors and Assistant Directors agreed on approaches and key activities for implementation that will support key functions of DGDA. This was accomplished via a series of remote phone calls and face-to-face meetings throughout February and March 2017. To develop and finalize DGDA's Five-Year Strategic Plan 2017–2021 and FY 17 Action Plan, meetings were held this quarter with SIAPS and other stakeholders in Bangladesh on December 21, 2016, March 5, 2017, and March 25, 2017. Both plans are very important in developing the activities that DGDA will implement, and determining means for budgetary support to move forward in the process of accreditation as a fully functional regulatory agency.

PQM also identified—subject to changes/adjustments as deemed necessary—the technical and financial resources to support implementation of these plans. One recommendation in the gap analysis conducted in April/May 2016 by PQM is to adjust and modify the organizational structure of DGDA to align with its strategic vision and mission as part of its efforts to be a fully functional MRA in two to three years. Per DGDA's request, PQM helped review and provide initial inputs to the improved organogram of DGDA. In addition, PQM has completed expertise and skills mapping of key NCL staff positions, reviewing job descriptions, and suggesting improvement of organogram structure of the lab to align staff to better support DGDA's mandate and NCL functions (Activity 4.1).

One barrier facing NCL in progressing toward international standard ISO/IEC 17025 is the lack of critical laboratory equipment, including (but not limited to) an HPLC system with auto-sampler, dissolution tester, Karl Fischer, friability tester, disintegration tester, analytical microbalance, UV-Vis spectrophotometer, vacuum oven, reference weigh, and mechanical calibration kit. PQM staff, DGDA, and NCL management have created a priority list of equipment/instruments to acquire, and have discussed other possible sources of funds for their purchase, installation, and operationalization in the laboratory.

Continuing in Q3, PQM will focus on providing inputs to the finalization of DGDA's Five-Year Strategic Plan 2017–2021 and FY 17 Action Plan (Activity 4.1.1); continue to seek out complementary sources of funding to support implementation of the Five-Year Strategic Plan (Activity 4.1.1); and collaborate with WHO to suggest revision to DGDA's staffing structure, including staff roles, responsibilities, staff capacities, to attain a level of personnel that provides for an advanced regulatory platform (Activity 4.1.2). PQM will work closely with DGDA and consult with the USAID Mission and other partners to pursue additional sources of funding (e.g., Global Fund) for the purchase of critical lab equipment/instruments for NCL.

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### **Objective 5 – Increase visibility and relevance of QA/QC in support to National Health Programs**

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PQM staff have met and initiated discussions to implement one activity in Q3 under Objective 5, which is to “develop and adapt a QA policy and QA mechanism on medicines in the priority health programs.” The national technical manager will be working with DGDA to determine the improvements needed to encourage political will to adopt an overarching policy. In addition, the PQM Operations Department has been active in establishing operations locally in Bangladesh. This includes the following activities:

- Engaged local legal counsel to support the registration process. At this time, registration documents have been prepared and are under review by local legal counsel for anticipated submission in early April 2017.

- Engaged a professional employment organization (PEO) to hire national staff and administer payroll, benefits, lease of office space, and monthly payments.
- Recruited national staff, including senior operations manager, technical manager, QC specialist, senior QA/QC specialist, and QMS specialist; currently supporting the recruitment of the COP.
- Located office space in Dhaka; working to finalize the lease agreement.
- Secured temporary office space in DGDA for three to four staff and in NCL for two to three analytical staff.
- Explored the option of hiring a local accounting firm to manage local finances and payments to suppliers for procurement needs and implementation of activities.

#### IV. Key Challenges

The recruitment of the COP has been a challenging endeavor, given the difficulty in finding suitable candidates that meet the USAID Mission's expectations. Twenty applications were received (11 national and four expatriates), and two (one national and one expatriate) were proposed to the Mission for concurrence.

The program has had difficulty with customs clearance and duties in Bangladesh; it has been very challenging to ship supplies (essential analytical reference standards, chemicals, training supplies, and reference materials) to Bangladesh due to clearance from customs, as well as the costs incurred in shipping them from the United States.

Coaching and mentoring local technical staff to be trainers/technical providers is also challenging, as the staff are transitioning from an industrial setting to a regulatory environment. Thus, additional coaching and mentoring are required to make the transition. PQM has implemented a plan to shorten this transition period and to ensure that national technical staff fully engage with the project clients, thereby supporting the delivery of technical assistance as outlined in the work plan.

The Field Office registration has been progressing, but the process is complicated and requires a great deal of communication with local legal counsel to meet the requirements for submission:

- It has taken some time to locate a permanent office location that is both professional and addresses security standards; contractual arrangements for the lease will also require review by PQM's legal department, as well as additional coordination with the PEO, who will be the signatory on the lease.
- Safety and security remain a concern for USP-PQM technical staff while providing technical assistance in Bangladesh; the security situation is being monitored closely by the Global Security Director.

## Burma

### I. Quarter 2 Highlights

ISO 17025:2005 accreditation of Burma's Department of Food and Drug Administration (DFDA) has been a key priority for both PQM and DFDA since the beginning of PQM's technical assistance to the country. The breakthrough came during the first quarter of FY17 when the lab was finally accredited by ANAB. That news was disseminated the following quarter to program stakeholders and the general public. The following are highlights of key activities for Q2:

- A January 10 press conference on ISO 17025 marked the accreditation of DFDA Nay Pyi Taw laboratory. Ms. Karen Cavanaugh, Director of USAID's Office of Public Health (OPH) in Burma, handed over the accreditation certificate to Dr. Than Htut, the Director General of DFDA.
- PQM participated in a symposium entitled "ISO 17025 Accreditation of DFDA's Laboratories: Road to International Recognition," held during the Burmese National Research Congress on January 11.

- PQM provided training on titrimetry (a QC test used to determine the unknown concentration of an identified chemical substance) to DFDA lab analysts from Nay Pyi Taw, Yangon, and Mandalay labs as part of the continuous improvement of the technical capacity of national laboratories.
- Dr. Khin Chit, DFDA Deputy Director General and PQM's point of contact in Burma, was one of the six awardees selected by the U.S. Embassy/USAID for the first ever "Women of Change" award ceremony to recognize highly valued women who actively contribute to positive changes in Burma.

## II. Country Context

Malaria is one of the key public health burdens in Burma, with the spread of drug resistance posing a major challenge to the country, especially in the border areas. The combined effort of international donors and Burmese authorities has reduced malaria morbidity and mortality significantly. However, the prevalence of poor-quality medicines in the country not only threatens the effort to contain resistant malaria but also wastes resources needed to fight the disease.

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

In order to modernize DFDA and develop strong QA systems for Burma, key functions (e.g., product registration, licensing, supply chain inspection, and PMS systems) must be strengthened alongside with pharmaceutical legislation (e.g., National Drug Policy and National Drug Law). PQM is working closely with DFDA to identify gaps in the current regulatory system and target technical assistance to specific areas of need. PQM's technical assistance is building DFDA's capacity to make more good-quality medicines available, which should help Burma eliminate malaria by 2030, one of the National Malaria Control Program objectives.

## II. Quarter 2 Progress by Objective

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### **Objective 1 – Strengthen the capacity of DFDA laboratories in Nay Pyi Taw and Mandalay, in preparation for ISO 17025 accreditation**

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DFDA Nay Pyi Taw Pharmaceutical Chemistry Laboratory was successfully accredited by ANAB for ISO17025:2005 (an internationally recognized standard for competence of testing and calibration laboratories) in December 2016. During Q2, PQM and DFDA announced the news through a press conference and held a symposium for key stakeholders and the general public. Representatives from DFDA, USAID, PQM, and the UN Office for Project Services attended the press conference, which was held at DFDA headquarters at Nay Pyi Taw.

During the event, Ms. Karen Cavanaugh, Director of USAID OPH, presented the ANAB accreditation certificate to Dr. Than Htut, Director General of DFDA. Accreditation recognizes the lab internationally as competent to carry out tests and calibrations to detect poor-quality medicines. It will also help protect the public from the use of substandard and falsified medicines that hamper achievement of positive treatment outcomes.

DFDA hosted a symposium on "ISO 17025 Accreditation of DFDA Labs: Road to International Recognition" during the Burmese National Research Congress on January 11, 2017. The symposium, chaired by Ms. Cavanaugh and Dr. Htut, was attended by personnel from various government ministries, UN organizations, INGOs, the pharmaceutical industry, and the general public. PQM was represented by one of five symposium speakers, delivering a presentation on the overview of ISO 17025 accreditation.

The U.S. Embassy and the USAID Mission in Burma presented the "Woman of Change" award to Dr. Khin Chit, Deputy Director General of DFDA and PQM's focal person in the country, for her leadership and commitment during ISO 17025 accreditation of the DFDA laboratory. Dr. Chit was one of six outstanding women to receive the award for the year 2016. PQM attended the award ceremony and celebrated Dr. Chit's achievement with DFDA Leadership, the U.S. Embassy, USAID Mission staff, and her family at the U.S. Ambassador's residence on March 16, 2017.

PQM conducted training on titrimetry on March 11–20, 2017, at DFDA Nay Pyi Taw laboratory. Participants included 26 attendees from DFDA Nay Pyi Taw, Mandalay, and Yangon laboratories. Training emphasized calibration of equipment and hands-on software training. Titrimetry application training will be conducted in subsequent training.



Ms. Karen Cavanaugh, Director of USAID's Office of Public Health (OPH) in Burma, handed over the accreditation certificate to Dr. Than Htut, the Director General of DFDA.

#### IV. Key Challenges

Delayed receipt of FY 17 program funds from the Mission was the major challenge for PQM. The delay impacted PQM implementation timelines for program activities in Q2. Time-sensitive activities such as providing technical assistance to DFDA to design and layout plans for new lab construction projects in Mandalay and Nay Pyi Taw were delayed, and the construction continued without proper lab design. This will inevitably result in reconfiguration of some parts of the building and improper layout of the lab (such as the location of staircases). It is recommended that forward funding be made available for such time-sensitive activities to properly maximize available in-country resources.

## Indonesia

### I. Quarter 2 Highlights

PQM convened the FY17 administrative coordination meeting with all relevant National Agency for Drug and Food Control (BPOM) divisions on work plan proposals and administrative issues to finalize the PQM program with the government of Indonesia. These activities are required as part of the formal agreements for PQM to implement the program. Activities are currently under review with approval expected soon.

PQM participated in the international Joint External Monitoring Mission for TB and HIV, which included the MOH, WHO experts on HIV and TB, NGOs, and academia. PQM was part of the procurement and supply chain group, looking at a number of gaps in both policy and practice regarding TB and HIV control, including the need to scale up isoniazid preventive therapy (IPT) in HIV patients, as well as addressing regimen changes for first- and second-line TB. High-level

recommendations were made to the MOH, including advocacy to ensure TB and HIV medicines quality as an integral component of the overall disease control strategy. In addition, the Minister of Health signed a new regulation designating TB as a notifiable disease in Indonesia.

In preparation for dossier submission to WHO (expected in Q4 2017), QC and analytical method training were provided to private manufacturers Kalbe Farma and Sanbe Farma/Caprifarmindo. The analytical training for the QC laboratories is recognized as a crucial component in the management of GMP activities in Indonesia, as both of these manufacturers are having difficulties with some of the required tests (residual solvent analysis by GC). PQM is assisting the manufacturers with a number of issues the QC labs are facing, in addition to GMP.

## II. Country/Health Element 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 FY14). PQM focused first on supporting selected local 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 capacity of BPOM, additional private manufacturers of TB and HIV medicines, and select local CRO for BE studies, to improve their QA/QC systems.

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

## III. Quarter 2 Progress by Objective

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

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During Q2, the PQM Indonesia Field Office began procurement activities to support \$2 million of equipment for the provincial BPOM QC laboratories through a direct Global Fund contract. This activity supports capacity building for 11 provincial BPOM institutions to work together with provincial and district health offices to monitor the quality of medicines in government storage facilities through the supply chain, focusing on TB and HIV medicines. PQM is providing the technical assistance and coordination through the USAID program with equipment supplementation from the Global Fund grants to build overall QC capacity.

PQM also oversaw the installation and operation qualification of Dionex Ion Chromatography instruments at the National Reference Standards laboratory, Therapeutic Products National QC Laboratory of BPOM (PTBB) laboratory, and Jayapura, Papua, provincial laboratory in following up from the first Global Fund contract to support second-line TB medicines testing. PQM plans to conduct ion chromatography (IC) training for these labs, to ensure that the analysts can properly analyze kanamycin and other important medicines on this Global Fund-provided equipment.

With Global Fund financial support, PQM is also assisting in procuring roughly \$200,000 worth of upgraded laboratory software for the PTBB lab. PQM continues to review laboratory information file (LIF) documentation in preparation for the PTBB laboratory to submit to WHO for PQ during this calendar year. Upcoming activities include:

- Ion chromatography training in NQCL and Jayapura lab at the end of April or May.

- Coordination and preparation for a “BPOM-MOH Joint Sampling” workshop, including discussion of SOPs and requesting provincial BPOM institutions’ information on equipment specifications for procurement of lab supplies.
- Environment control equipment installation at the PTBB laboratory in the context of WHO PQ.
- QMS training focusing on internal audits in May.
- Continued development of a Frequently Asked Questions master list on QC analytical methods for National and Provincial QC Laboratory analysts.
- Continued technical assistance for LIF submission to WHO for PQ of the BPOM PTBB laboratory.

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

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Follow-up onsite technical assistance visits were conducted at both Kalbe Farma and Sanbe Farma as part of the WHO PQ projects for levofloxacin. WHO PQ gap analyses were conducted, with a year-end deadline for submission of the product dossier to WHO for both manufacturers. CAPA verification was performed, as was analytical training on selected topics for the QC laboratories for Sanbe and Kalbe. In accordance with the project plan, PQM plans to assist the microbiology lab and perform mock audits prior to WHO audits.

During Q2, PQM helped Kimia Farma with its GMP recertification process, as well as with its potential restart of a WHO PQ program for TB medicines. Additionally, based on concerns about recent failures of ARV products circulating in the government sector, PQM will continue to work with Kimia Farma on its HIV medicines manufacturing and to support its QC lab.

Upcoming activities:

- Conduct follow-up visits to Kalbe Farma to discuss WHO PQ progress.
- Conduct a follow-up visit to PT Phapros-Semarang to deliver safety glasses for QC laboratory and training on Good Documentation Practices (GDocP) and Data Integrity (DI).
- Provide Levaquin comparator products to Kalbe Farma for comparative dissolution study in pilot scale.

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**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 and FARMALKES to ensure quality and production is in line with procurement policy/new treatment guidelines**

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PQM convened coordination workshops with the line ministry BPOM on FY16 activity finalization and the proposed FY17 approved work plan activities. The technical changes during FY17 include shifts to strengthen the BPOM GMP inspectorate and build capacity for better inspections and technical competence, and include discussions on long-term sustainability for the Indonesian government’s reference standards program for provincial laboratories.

PQM participated in the international Joint External Monitoring Mission for TB and HIV, which included the MOH and global experts on HIV and TB from WHO, NGOs, and academia. PQM was part of the procurement and supply chain group, looking at a number of gaps in both policy and practice regarding TB and HIV control, including the need to scale up IPT in HIV patients, as well as addressing regimen changes for first- and second-line TB. High-level recommendations were made to the MOH, including advocacy for ensuring the quality of TB and HIV medicines as an integral component of the overall disease control strategy. In addition, the MOH signed a new regulation that identifies TB as a notifiable disease in Indonesia.

During Q2, PQM supported Litbang (the National Institute for Health Research and Development) to socialize a research protocol on the distribution, availability, and medical services for medicines and vaccines under the auspices of rolling out

Universal Health Coverage by 2019 (Badan Penyelenggara Jaminan Sosial). This workshop brought together stakeholders from MOH, BPOM, and academia and was recognized as an important step in ensuring quality, safety, and efficacy of medicines. This first research program will focus on vaccines, stemming from the 2016 fake vaccines scandal in which public and private sector procurement of falsified vaccines created mistrust in the health system and exposed large gaps in the overall monitoring of vaccine quality, as well as the need for better selection practices. PQM will continue to support these initiatives, with the aim of also including solid dosage form medicines during the next research project by Litbang.

Upcoming activities:

- Joint sampling and testing coordination workshop with the Provincial Health Office (TB program, Pharmaceutical Officer) and BPOM from 11 Provinces.
- Stakeholder workshop with manufacturers, MOH, BPOM, other stakeholders for new TB regimen and to ensure availability of quality-assured medicines.
- Discussion with Association of Indonesian Pharmacists (IAI) on upcoming IAI Annual Scientific Seminar and support IAI for the development of Pharmaceutical Practices SOPs in Hospitals in West Java.

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#### **Objective 4 – To support the overall management and functions of the PQM Indonesia field office, including reporting, monitoring and evaluation, logistics, and staff development**

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PQM Indonesia continued to make significant progress on the design of the new field office in Mega Kuningan. PQM plans to conduct construction vendor selection at the beginning of Q3, with a planned move-in date of June 2017. The operations team is implementing new accounting software, Quickbooks, for the field office and is rolling out the activity-level accounting system. The field office also continues to identify candidates for the open positions of QC Specialist, M&E Specialist, Accountant, and Project Coordinator. In support of PQM Indonesia and overall activities in Asia, during Q2 PQM also hosted Dr. Emily Kaine, the Senior Vice President for the USP's Global Public Health (GPH) Division, and the Country Planning and Operations Director, Lindsey Clawson, during Q2 in support of PQM Indonesia and overall activities in Asia. Discussions included planning meetings with BPOM ahead of the planned visit by the Chairwoman of BPOM to USP's headquarters in Rockville, MD.

Planning for communications materials included initial discussions with graphic designers in support of rolling out planned communications media for the PQM Indonesia office.

Progress was made toward securing work permits (IMTA/KITAS) for the expatriate COP in Indonesia. The USAID program was finalizing the technical agreement with BPOM under the assistance agreement between the U.S. Government and Government of Indonesia.

## **IV. Key Challenges**

Slow progress in finalizing the USAID-BPOM technical agreement has delayed some activities implementation by PQM. In addition, the PQM COP is still waiting final granting of the official IMTA/KITAS visas based on the first registration process of the USAID agreements with the government. The renewal of these documents should be much faster. The move to a new office has placed significant additional work burdens on the operations team, as the move requires significant procurement, planning, designing, and logistics support. The PQM Indonesia office is still facing considerable challenges in identifying qualified and technically competent candidates to fill the open positions, some of which have been open for a year and a half. The current staff is overstretched with FY16 and FY17 activities; Global Fund procurement; and ongoing and increasing reporting requirements by the government of Indonesia, donors, headquarters, and others.

# **Pakistan**

## **I. Quarter 2 Highlights**

PQM provided technical support to local manufacturers to improve and attain current GMP for chlorhexidine 7.1% gel, which reduces umbilical cord infections, a cause of neonatal death. As a result of this support, two such products

were approved for registration by the Drug Registration Board (DRB). The start of sales by two local manufacturers (M/s Atco Laboratories and M/s Aspin Pharmaceuticals) will result not only in increased Pakistani utilization but also potential exports to Asian countries that need CHX 7.1% gel to combat umbilical cord infections and infant mortality.

PQM support also led to the development of a stable formulation of the product that will be produced by the four target manufacturers in the country. PQM contributions included guidance to the manufacturers to improve GMP, help preparing required data for submission to the Drug Regulatory Authority of Pakistan (DRAP), and follow-up with DRAP's Pharmaceutical Evaluation Cell to ensure timely evaluations.

PQM continues to work with DRAP and the main laboratory under DRAP's oversight—Central Drug Testing Laboratory (CDL)—to improve its QMS. Main highlights for this quarter include support to CDL to develop SOPs, QMS documents and implementation of CAPA recommendations; support to Pakistan Drugs Testing and Research Center (PTDRC) to evaluate CAPA implementation progress, and preparation of a plan of action to build capacity of DRAP's licensing division.

This quarter, PQM continued to support the Division of Pharmaceutical Evaluation & Registration (PE&R) to prepare a series of trainings for the CTD that DRAP will utilize to improve its registration system. Main activities included an assessment of the Division of Licensing's regulatory system and preparation of an action plan for improving PE&R's registration system.

PQM provided technical support to DRAP and provincial health authorities to establish an inter-laboratory medicines testing (ILT) network among QC laboratories in Pakistan on selected finished products. PQM also supported the establishment of a monitoring system for PMS with special focus on chlorhexidine 7.1% gel products to ensure effective and robust monitoring of quality of products in the supply and distribution chains.

In January 2017, PQM visited Islamabad and met with the PQM Activity Manager of USAID Country Mission, WHO, UNICEF and the DRAP CEO and management staff. PQM shared its progress in Pakistan, as well as plans in the areas of MNCH and family planning products. A special meeting was held with the Federal Secretary, Ministry of National Health Services, Regulations and Coordination (MNHSR&C) and his team, where both the USAID Mission and the DRAP CEO were present. During the meeting, the PQM team discussed the PQM program in detail, including the challenges regarding potential delay in pricing of chlorhexidine 7.1% gel as part of the marketing authorization process; this is important in light of the approval of the first chlorhexidine product (Atco Laboratories) by the DRB. The Secretary expressed commitment to support the progress of PQM program in Pakistan.

The PQM team also met with the prime recipient of the Global Fund, MNHSR&C, and discussed the funding need to procure essential equipment required by Federal Appellate Lab at the National Institute of Health (NIH); this is the most important laboratory in QA and QC of products produced locally and imported into Pakistan.

## **II. Country Context**

Under the 18th amendment to the Drugs Act of 1976, the federal government provides the provinces with regulatory authority over their provincial jurisdictions. In the exercise of these powers, the Provincial Government of Punjab made certain amendments to the Drugs Act of 1976 that are now being implemented in that province. These amendments have included the imposition of harsh sentences and fines for violators of the provisions—both imprisonment and significant fines imposed on the pharmaceutical industry. As a result, retail pharmacies and wholesale dealers closed down their businesses for a few days, which affected patients adversely because private sector pharmacies are the first point of care contact for many people in Pakistan; this act brought the government to the negotiating table. However, the consultation between government and industry is at a stalemate; thus, the industry is planning to go on strike throughout the country for an indefinite period. The fear in the industry is that if the law remains in its current form, it will be extremely difficult for the industry to continue working in the country.

Interestingly, provincial drug inspectors are also reluctant to work under the new law because it imposes equally harsh punishments for the drug inspectors if they are found to have violated the code of ethics. In response, the provincial government has announced plans to outsource the enforcement to private organizations. Such organizations will be responsible for post-marketing surveillance and quality control at the level of pharmaceutical manufacturers situated in their jurisdiction.

There have been some reports of unregistered cardiac stents sold at exorbitant prices, prompting a suo moto action in response by the Supreme Court of Pakistan. This has created governmental interest, resulting in increased pressure on DRAP to further examine the pricing mechanism for medical devices that were being registered as drugs. This will likely result in some changes to regulations related to medical devices.

### III. Quarter 2 Progress by Objective

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

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PQM continues to provide technical assistance to chlorhexidine 7.1 gel manufacturers in Pakistan to improve their manufacturing practices to meet international quality standards. As a result of this support, in Q2 the DRB approved for registration two chlorhexidine gel products (manufactured by M/s Atco Laboratories and M/s Aspin Pharmaceuticals); it also accepted stability data from two potential manufacturers of chlorhexidine gel (M/s Akhai Pharmaceutical, and M/s Zafa Pharmaceuticals). This signifies good progress toward increasing the quality-assured chlorhexidine 7.1 gel market size in Pakistan and potentially other countries in Asia through export. This would reduce neonatal mortality due to umbilical cord infections.

PQM assessed Aspin Pharmaceuticals' capacity to meet international standards for manufacturing chlorhexidine gel. The final report that specifies all CAPA for implementation to meet good manufacturing practices will be submitted to the manufacturer in Q3. PQM also conducted a pre-assessment of M/s Shazoo Zaka and Pacific Pharmaceuticals (producers of MNCH and TB products) as a prerequisite to a comprehensive GMP assessment planned for April 2017.

PQM conducted follow-up visits to three manufacturers—M/s Zafa Pharmaceuticals, M/s Akhai Pharmaceutical, and M/s Atco Laboratories—to assess the implementation of recommended CAPA and to identify areas where they need PQM support to address corrective actions.

PQM provided technical assistance to two potential manufacturers of chlorhexidine 7.1% gel to prepare stability data requirements as specified by the DRB.

In Q3, PQM will provide ongoing assistance to MNCH products manufacturers and to potential manufacturers of chlorhexidine 7.1% gel. PQM will also continue its support to manufacturers in Karachi (M/s Akhai Pharmaceutical, M/s Zafa Pharmaceuticals, and M/s Aspin Pharmaceuticals) for full implementation of CAPA. In addition, PQM will conduct an assessment of both Pacific Pharmaceutical and Shazoo Zaka Pharmaceutical to identify CAPA recommendations for complying with international good manufacturing practices.

DRAP has decided to implement the CTD format, instead of using the existing Form-5, for the medicine registration application. After receiving approval from the USAID Mission, PQM will hold a series of hands-on trainings on CTD for DRAP assessors/evaluators and the pharmaceutical industry to build skills in compiling and completing information in CTD format. The planned locations for these trainings are Lahore, Islamabad, and Karachi. The first training is planned for May 2017 in Lahore and will be led by PQM's Senior GMP Specialist, who has expertise in the subject area.

#### **Objective 2 – Strengthen Regulatory, Quality Assurance and Quality Control Systems through building the capacity of DRAP's quality control systems and laboratories toward attaining international standards of quality and practices**

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Capacity building of DRAP is a long-term objective, and PQM is moving in the right direction to improve the standard of regulatory systems of the national regulatory authority. CDL is the main laboratory under DRAP's oversight, and PQM is working with CDL to improve its QMS and thereby obtain both ISO:17025 accreditation and WHO PQ. CDL has already signed the Complementary Reference Standards (CRS) program agreement, and some critical Reference Standards have been ordered to enable the laboratory to participate in ILT.

During Q2, PQM continued to work with DRAP's Licensing Division to assess its regulatory system using the National Regulatory Authority Assessment Tool developed by WHO. This tool helps to strengthen, expand, and maintain GMP by aligning strategic directions and revising plans as deemed necessary. The assessment led to the preparation of a plan of action to build the division's capacity.

PQM also continued to provide support to CDL for CAPA implementation and development of SOPs and other required QMS documents. Newly inducted CDL Assistant Directors were also trained on good laboratory practices and compendial analyses. PQM continued to assist in QA of chlorhexidine gel imported by USAID-supported chlorhexidine, providing test results of the consignment that was received from Lomus Pharmaceuticals in Nepal.

During a follow-up visit to PTDRRC, PQM conducted a detailed evaluation of progress with implementation of CAPA recommendations. The laboratory was also advised on further improvements to undertake to meet its development plan.

PQM conducted a detailed evaluation of the Planning Commission 1 of the Federal Appellate Laboratory at NIH. As a follow-up to this assessment, PQM initiated discussion with the MNHSR&C, the prime Global Fund recipient under health systems strengthening, to explore a possible avenue to receive funding support for the laboratory. If successful, the funding will be used to procure needed equipment to upgrade the Federal Appellate Laboratory so it can meet its obligation to achieve international standards for QA and QC of medicines in the country.

For Objective 2, the main activity in Q3 will be PQM's follow-up visit to PTDRRC. This visit will assess progress and recommend further improvements (if any) or could enable PQM to recommend sending a request to WHO based on no further improvement required, after which WHO will make its own onsite assessment to determine readiness for WHO PQ.

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

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Building the capacity of DRAP's PE&R is a long-term process and is likely to continue until an integrated regulatory information system is in place. The initial achievement is the master plan, and the next step will be training both DRAP staff and manufacturers on the adoption of CTD as an application format to register medicines. This is part of PQM's effort to build DRAP's database of products registered in the country through application of a recognized international standard for registrations.

PQM has been working with PE&R to prepare a series of trainings for the CTD that DRAP will utilize to improve its registration system and also on data standards for regulatory information management. During Q2, PQM:

- Conducted an assessment of the Division of Licensing's regulatory system and developed a plan for building the capacity of the division.
- Coordinated with PE&R staff to prepare a plan of action for improving its registration system.

The major activity in Q3 will be to hold the series of trainings on CTD adoption—both for DRAP officials and for manufacturers that will prepare applications using the CTD format. Altogether three training sessions for the pharmaceutical industry will be held, starting from early May 2017. The training sessions are likely to cover about 400 regulatory professionals from the pharmaceutical industry in three areas: Islamabad, Karachi, and Lahore.

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

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Currently there is a volatile situation in the Province of Punjab, which was caused by the Government of Punjab's amendments to the Drugs Act of 1976; in response, the provincial government plans to outsource the inspectorates and QC laboratories. As a result, activities involving the inspectorates have been postponed. Nevertheless, PQM implemented some activities, including:

- Technical support to DRAP and provincial health authorities to establish an ILT network among QC laboratories in Pakistan on selected finished products. In order to achieve the plan on the ILT network, DRAP will need to organize a provincial conference to develop ownership of the network and establish the components of the plan.
- Support for the establishment of a monitoring system for post-marketing surveillance program with special focus on chlorhexidine 7.1% gel products to ensure effective and robust monitoring of quality of products in the supply and distribution chains.

Thus far, PTDRC in Punjab and DTL in Quetta have completed ILT network and submitted their reports.

The plan originally was to conduct a series of trainings on PMS during Q2 for the drug inspectors of all the provinces, starting with the Province of Baluchistan; however, due to safety and security issues, they are now planned for Q3.

In Q3, a series of PMS trainings from April to September 2017 are planned. These PMS training events will cover all provinces and have the primary objective of training all provincial inspectors with the help of local trainers (trained through the training-of-trainers methodology) and facilitated by PQM national consultants.

Also in Q3, a plan will be submitted for DRAP to hold a stakeholders meeting to initiate an ILT network, with the aim of establishing an integrated QC system in Pakistan.

#### **IV. Key Challenges**

The two key challenges that remain are registering the field office and securing access to multiple entry visas for PQM's program and technical team. Relations with DRAP are improving (see Q1 Report comments); however, bureaucratic hurdles are still present and pose a challenge in seeing quick progress on activities that require DRAP participation and coordination.

The position taken by the Government of Punjab has had a destabilizing effect on the overall regulatory system, and has also undermined the status of DRAP as the principal regulator in Pakistan. The USAID Mission and PQM need to leverage influence to correct the situation by holding a senior-level stakeholders' meeting. This should be arranged at the earliest, where the top-ranking officials of federal and provincial health officials can participate. The primary objective of the meeting will be to have these authorities understand the importance of an integrated and centralized regulatory system that will enable the control of substandard/falsified/spurious medicines.

## **Philippines**

### **I. Quarter 2 Highlights**

Building on work done in Q1 by PQM staff and analysts from the Philippines FDA to collect samples from the Island of Mindoro, four manufacturers of TB drugs were identified for potential violations of Philippines FDA regulations. While the samples passed quality testing, they were submitted for investigation due to suspected label issues and were subsequently found to be unregistered.

There is an ongoing investigation in the case. PQM is working closely with the FDA's Legal Services Support Center (LSSC) and Product and Research Standards Development Division (PRSD), providing technical assistance as needed.

### **II. Country/Health Element Context**

With a vision to foster a TB-free Philippines, the National Center for Disease Prevention and Control (NCDPC) of the Department of Health led the 2010–2016 Philippine Plan of Action to Control TB (PhilPACT). This plan was formulated as the roadmap towards the MDGs for the country to reduce TB prevalence and mortality by half from 1990 baseline figures. The plan encourages bringing the case detection rate to 85% of all incident cases and treatment success rate to at least 90% by 2016.

### III. Quarter 2 Progress by Objective

#### Objective 1 – Strengthen the regulatory system of the Philippines Food and Drug Administration

PQM is supporting FDA's mission of ensuring the safety, efficacy, purity, and quality of products through effective implementation of the national regulatory framework consistent with international best practices. One effort is to enhance the inspectorate through various trainings to increase efficiency and effectiveness. The overall goal is to align with the international level of standards for Good Distribution and Storage Practices (GDSP), Administrative No. 2013-0027 "Adoption and Implementation of the WHO Annex 5 Guide to GDP for Pharmaceutical Products" and Annex 9 Guide to GDSP for Pharmaceuticals that were issued by the FDA on October 2, 2013.

#### Objective 2 – Strengthening the capacity of FDA Common Services Laboratories (Alabang, Cebu, and Davao Testing and QA Laboratory)

Strengthened enforcement through intensified PMS is one of FDA's strategic thrusts. In 2016, there were 35,039 drug establishments and 23,623 drug products registered/notified with FDA. A total of 33,940 entities (establishments and products) were inspected by the FDA through the regional field offices; 7.58% of the inspection resulted in the issuance of notices and reports of violation. Through its LSSC, FDA reported 2,438 violations and complaints and resolved 2,310 cases in 2016.

PQM collaborated with FDA to develop an updated PMS strategy to build a more effective PMS system and improve FDA's capacity to monitor and evaluate TB products in the country.

PQM successfully established an MQM program for first-line TB medicines (ethambutol, isoniazid, pyrazinamide, and rifampicin) and their fixed-dose combination formulations at eight sentinel sites in the Philippines. The sample collection and quality testing of TB medicines provides evidence-based data on the quality of medicines available in the market. Philippines FDA relies, in part, on the information obtained from PQM to identify and take action against poor-quality TB medicines. A total of 143 TB medicines samples were collected from January to March 2017. Currently, the samples are being tested for quality measures. The testing results data from Q2 will be released by April 30, 2017.

**Table 2: Tabular representation of Philippines Medicine Quality Monitoring for TB Drugs FY17**

<b>Medicine Quality Monitoring for TB Drugs FY17 (Collected and Tested Samples using the Minilab™ Kit)</b>		
<b>Sentinel Site</b>	<b>Q1 (Oct – Dec 2016)</b>	<b>Q2 (Jan – Mar 2017)</b>
Bicol	49	0
Calabarzon	13	61
Cebu	21	10
Davao	23	6
Iloilo	13	27
La Union	0	17
Pampanga	0	0
Zamboanga	8	22
<b>Total (collected):</b>	<b>127</b>	<b>143</b>
<b>Passed (tested)</b>	127	To be determined
<b>Failed (tested)</b>	0	To be determined
<b>No. of samples submitted to FDA Laboratories for Confirmatory Analysis/ Quality Testing</b>		
<b>Passed</b>	9	To be determined
<b>Failed</b>	0	To be determined

PQM is also developing a PSA video to increase public awareness of good-quality TB medicines.

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**Objective 3: Intensified MQM with improved sampling and testing methodologies, and a sustainable PMS program**

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No progress to report this quarter.

# Eastern Europe & Central Asia



# Kazakhstan

## I. Quarter 2 Highlights

During Q2, PQM made major progress in implementation of FY17 work plan activities:

- Three medicines QC laboratories supported by PQM started revision of QMS documents based on PQM recommendations. PQM reviewed the revised documents and provided feedback and recommendations for improvement. Also based on PQM recommendations, the laboratories started cross-audit of QMS.
- PQM conducted training for Nobel Pharmaceutical Factory to improve their theoretical knowledge and develop practical skills needed for assuring and sustaining GMP compliance by the company.

The current work will prepare the supported laboratories for PQM's follow-up assessment, which will take place in Q3.

## II. Country Context

The Republic of Kazakhstan is situated in Central Asia and Europe. It is the ninth largest country in the world, covering an area of 2,727,300 km. The country has a population of 17.29 million.

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

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

Kazakhstan has a well-established national MRA, the Kazakhstan FDA. Medicines regulation in Kazakhstan is based on numerous legislative and regulatory documents, but medicines quality still remains a problem in the country. Over a period of 10 years (2004–2014), about 40,000 units of falsified medicines across 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 were published in a 2011 report that showed Kazakhstan with the highest overall proportion of substandard samples (23.3%). Though the WHO survey has limitations, including a low number of samples collected and tested and limited scope of medicines targeted, these results clearly indicate quality issues related to noncompliance with GMP, as well as issues with QC of medicines and regulatory enforcement.

PQM began receiving funding from USAID/Kazakhstan in FY13 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 MOH dated January 14, 2015, Kazakh manufacturers must have a GMP certificate for state registration of their medicines as of January 2018. Technical assistance provided by PQM is therefore of high importance.

From FY13 to FY15, PQM worked with two anti-TB medicines manufacturers 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 has not invested in the infrastructure of its facility, as it promised to do in the beginning of the project. However, Nobel Almaty is committed to continuing cooperation with PQM and improving its GMP standards. Although Nobel already has a national GMP certificate, certain areas require improvements to reach compliance with international GMP requirements.

The Ministry of Healthcare and Social Development entrusted the Kazakhstan FDA with the task of strengthening the capacity of NQCLs as Kazakhstan enters the Eurasian Economic Union, which requires mutual recognition of test results by its member countries. The Kazakhstan FDA chose three NQCLs in its national lab network to advance

toward WHO PQ and asked the USAID Mission for assistance on the WHO PQ through the PQM program. Its goal is to effectively control the quality of medicines in Kazakhstan, including the quality of anti-TB medicines.

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

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In January 2017, the PQM team visited the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM) to discuss the current status of implementation of CAPAs by the PQM-supported laboratories and agree on the next steps.

PQM is currently assisting three regional NCEM medicines quality control (MQC) laboratories in Karaganda, Kostanay, and Astana. Kostanay lab was selected as the leading lab, for which QMS documents will be developed and finalized with PQM support. This documentation will serve as the QMS pattern for other labs participating in the program.

Per PQM's recommendations, it also was agreed that NCEM will consider appointing a dedicated quality manager in each of the three MQC labs participating in the program. NCEM will also arrange onsite calibration of equipment in the labs in compliance with WHO and ISO 17025 requirements.

According to the agreement between PQM and NCEM, Oksana laboratory started providing revised QMS documents to PQM in February 2017. PQM reviewed the documents and provided feedback and recommendations to the laboratory. Also according PQM's recommendation, Oksana, Karaganda, and Astana labs started cross-audits of QMS by dedicated lab staff from each laboratory in March 2017. PQM provided a template for LIFs for WHO submission by the laboratories and will provide technical assistance in completing the documents.

As a next step, PQM would make follow-up assessment of the labs in May–June 2017. PQM will combine the assessment trip with a five-day hands-on training on the most essential testing methods (HPLC and dissolution) for at least two analysts from each of the three labs.

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**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**

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In January 2017, PQM visited and met with the Nobel Almaty Pharmaceutical Factory General Manager and staff.

Nobel's staff updated PQM on the status of the project. Nobel completed construction of the new site and is working on installation of engineering systems. Manufacturing equipment was installed, and validation of manufacturing equipment and computerized systems will be completed by April 2017. Nobel continues work on CAPAs resulting from the previous GMP assessment of PQM GMP specialists. Under the supervision of the PQM GMP consultant, Nobel closed over 30 findings, with 15 findings still open; the relevant corrective actions will be implemented at the new site.

In February 2017, a PQM GMP consultant visited the Nobel factory. He visited the new line for production of anti-TB medicines, which is equipped with new process equipment, laboratory equipment for in-process control, and clean premises and utilities. The operation is a significant improvement over the previous manufacturing site and increases the odds of improved QA standards. The site tour of the new line and further discussion of a layout brought to light some elements for improvement. The PQM consultant provided recommendations to the company.

The PQM consultant also conducted trainings for Nobel staff. Training on application of quality risk management to pharmaceutical operations included theoretical background and helped employees develop practical risk analysis skills. The training included hands-on exercises as part of risk analysis of cross-contamination.

PQM also conducted training on pharmaceutical water systems. Employees were provided with the templates of qualification protocols for purified water systems. Training on clean rooms in pharmaceutical production focused on

design and standards, prevention of cross-contamination, selection of optimal pressure drops between rooms, garments for clean rooms, qualification, and environmental monitoring.

Nobel staff were also trained on validation of computerized systems, which covered the following topics: application of computerized systems at a pharmaceutical facility; regulatory requirements; validation planning; risk analysis for implementation and validation of computerized systems; and QA in the projects on implementation of computerized systems, software categories, and validation. Equipment qualification was discussed, and recommendations for improvement were provided.

## Uzbekistan

### I. Quarter 2 Highlights

Implementation of PQM in Uzbekistan was delayed for several months, as the project was not approved by the Uzbekistan government. As a result of great support from the USAID Mission in Uzbekistan and coordinated work with stakeholders, PQM in Uzbekistan was eventually approved by the Prime Minister of Uzbekistan. This would allow PQM to start implementation of work plan activities in Q3.

### II. Country Context

Uzbekistan is situated in Central Asia. It covers an area of 448,978 km<sup>2</sup> with a population of 31,576,400. According to WHO, the estimated TB incidence in Uzbekistan is 82 per 100,000 individuals (Global TB Report, 2015). Uzbekistan is classified as a high multidrug-resistant tuberculosis (MDR-TB) burden country; 23% of new TB cases are MDR-TB, compared with 62% among previously treated cases.

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

Uzbekistan has an established national medicines regulatory authority, the Directorate of Medicines and Medical Equipment Quality Control (Uzbekistan FDA). Medicines regulation in Uzbekistan is based on numerous legislative and regulatory documents and 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 prequalification.

However, regional laboratories are neither ISO 17025 accredited nor WHO prequalified. Quality of medicines still remains a problem in Uzbekistan. In 2009, WHO conducted a survey on the quality of anti-TB medicines in six former Soviet Union countries, including Uzbekistan. The results (published in a 2011 report) showed that in Uzbekistan three out of seven samples of rifampicin capsules and three out of 11 samples of isoniazid tablets failed quality tests. Though the WHO survey has limitations, including the low number of samples collected and tested and limited scope of medicines targeted, these results clearly indicate 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. The government is supporting and encouraging the local manufacture of TB medicines. A new pharmaceutical company is being established that will focus on the production of anti-TB medicines while striving to comply with international GMP standards.

# Core Portfolio



# PQM Cross Bureau

## I. Quarter 2 Highlights

The PQM Cross Bureau program works to strengthen existing programs and address gaps in medicines quality across countries. This quarter, PQM achieved key objectives in the following areas:

- PQM drafted the Risk-Based Framework for Quality Assurance Systems Strengthening and the Risk-Based Post Marketing Surveillance (PMS) Implementation Guidelines.
- In collaboration with the Physikalisch-Technische Bundesanstalt (PTB), PQM provided training on CTD to participants from MRAs and manufacturers from East African Community (EAC) partner states.
- PQM leveraged available media to advocate the need for medicines QA systems.

The results from this quarter set the stage for PQM to begin implementing risk-based PMS activities and continue increasing awareness about the importance of medicines quality.

## II. Core/Health Element 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 Ending Preventable Child and Maternal Deaths (EPCMD), AIDS-free Generation (AFG), and Protecting Communities against Infectious Diseases (PCID).

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 in developing tools and approaches that could be piloted or deployed 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 priority areas for the OHS within the EPCMD priority countries are the focus for all programming priorities, including pharmaceutical systems strengthening and improving 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 System Strengthening. PQM support for Cross Bureau has been primarily focused on raising awareness for the importance of medicines quality, supporting regional networks, and helping to develop new approaches to strengthen medicine regulatory functions.

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

## III. Quarter 2 Progress by Objective

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### Objective 1 – Increase awareness of the importance of medicines quality

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PQM major contributions towards increasing awareness of the importance of medicines quality this quarter were focused on using various communication channels to deliver information to various stakeholders. The following activities within this objective were planned for the quarter:

- Attend selected international meetings.
- Use available media to advocate the need for medicines quality assurance systems.
- Identify and analyze media reports on incidents of poor-quality medicines.
- Update the internationally referenced MQDB.

In this quarter, PQM contributed to raising awareness for the importance of medicines QA, including two press releases highlighting Burma and Nigeria laboratory accreditations, one blog posting on World TB Day, and an article published in *Popular Science* magazine. PQM also identified new incidents of poor-quality medicines in the media, which were compiled in media reports on medicines quality. The MQDB was continuously maintained as a real-time, open-source database.

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

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During the quarter, PQM supported the EAC Medicine Registration Harmonization initiative to strengthen the MRAs' capacity to carry out regulatory functions. Planned activities include the following:

- Facilitate joint dossier review
- Mapping of PMS programs

Registering medicines through a joint dossier evaluation is a key challenge for the EAC harmonization initiative, limiting to the implementation of guidelines on harmonized medicines registration. To address this issue, PQM collaborated with PTB to conduct training on the CTD, validation life cycle, layout and process requirements, and HVAC systems. Through an integrated training concept, inspectors and manufacturers from partner states exchange their specific views to gain a better common understanding. The workshop complemented other GMP trainings that have been conducted in the region. As a next step, PQM will participate in the EAC joint dossier review scheduled for April 2017.

As a start to the mapping of PMS programs activity, PQM has begun drafting the relevant indicators. Over the next two quarters, PQM will finalize a set of indicators and collect data from focus countries.

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

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Allocating adequate resources to build and strengthen QA systems remains a challenge in LMICs, and establishing systems that are not sustained after donor support ends is a waste of scarce resources. Toward this end, PQM's models for self-sufficiency and sustainability aim to use a risk-based approach to medicines QA.

Planned activities for the quarter include the following:

- Finalize the Framework and the Guidelines.
- Map sustainability of QA/QC systems in EPCMD countries.

PQM drafted versions of major deliverables for this objective during Q2, including *Guidance for Implementing Risk-based Post-marketing Quality Surveillance in Low- and Middle-income Countries* and *A Framework for Risk-Based*

*Pharmaceutical Quality Assurance in Low- and Middle-Income Countries.* For these draft documents, PQM will subsequently seek feedback from WHO and select countries, then work to finalize and disseminate the documents. Implementation in select countries is planned as a successive activity.

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

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Finalize revision of HSAA - No additional work was required from PQM during the quarter for this collaborative tool, which has been finalized and posted online.

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

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Finalize e-Learning course content - delay in implementation; currently pending USAID approval of course outline proposal.

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#### **Objective 6 – Establish regulatory system country profiles**

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Select regulatory system indicators - delay in implementation; currently working on indicators based on assessment tools being developed.

Develop country profiles - draft outline of the profiles as a revision of previous versions has been developed and will be finalized next quarter.

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

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No activities planned for second quarter.

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

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Development of NEPAD's Framework for GMP Regional Roadmaps

At the start of this activity, consultation with New Partnership for Africa's Development (NEPAD) is ongoing. PQM received background information from NEPAD and is developing a concept paper.

## **PQM Core TB**

### **I. Quarter 2 Highlights**

1. During Q2, PQM continued to provide technical assistance to manufacturers of priority TB medicines as agreed upon by USAID and PQM. As a result of the continued technical assistance provided by PQM, Dong-A ST pharmaceutical company was able to submit its API Master File (MF) for clofazimine API to WHO PQ on February 15, 2017. Upon submission, it was accepted for review. Clofazimine is one of the highest priority products for USAID, as it is a key medicine for the shortened regimen for MDR-TB treatment, as recommended by WHO. Availability of quality-assured API on the global market would support the availability of manufacturing and increase availability of quality-assured clofazimine finished product for MDR-TB patients.

2. Dong-A ST's clofazimine finished product dossier is scheduled to be submitted to WHO in early April. Once the initial submission is complete, Dong-A's team will initiate work on the transition of API source from their existing source to their own API.
3. To help ensure an uninterrupted supply of anti-TB medicines in the U.S. market, a PQM team is diligently working on identifying a priority medicine for U.S. FDA submission. After weeks of research and discussions with key stakeholders in the United States, rifampicin was identified as the first priority product to be supported for U.S. FDA approval. Bringing new suppliers to the U.S. market will decrease a risk of shortage of medicines; this may also have a positive impact on medicines price reduction. In addition, U.S. FDA approval makes medicines eligible for supply through the Stop TB Partnership's Global Drug Facility. Therefore, this intervention potentially can increase the number of international quality-assured suppliers not only in the United States but also for the global public health market, particularly for countries benefiting from the GDF mechanism.
4. With the priority product identified for submission to U.S. FDA, PQM will draft and publish the Expression of Interest (EOI) for manufacturers of rifampicin. PQM will work with partners such as GDF to identify potential manufacturers and provide technical assistance to prepare and submit a dossier for U.S. FDA approval. Selection of a manufacturer is tentatively scheduled to take place in Q3.

## II. Core/Health Element Context

PQM's goal within the global TB treatment framework is to ensure the availability of affordable quality-assured anti-TB medicines for the public health market. PQM will use a systems strengthening approach to build local organizational and individual capacity, and develop strategic partnerships to ensure the availability of quality-assured anti-TB medicines.

PQM's work directly contributes to Objective 3.A. of the U.S. Government Global Strategy; in particular, it works toward "maintaining of a global supply of affordable, quality-assured TB medicines to ensure that all countries and their citizens are able to access life-saving drugs."

PQM also contributes to Objective 2.1.4 of the National Action Plan for Combating Multidrug-resistant Tuberculosis, which aims at "improving the global availability and affordability of quality-assured, second-line drugs."

The mobilization of global efforts for intensifying the fight against TB and achieving an end to the global epidemic is demonstrated by the adoption of the WHO's End TB Strategy by the World Health Assembly in 2014, its endorsement in several WHO Regional Committee meetings during 2015, and the inclusion of "ending the TB epidemic" as a target within the health-related Sustainable Development Goal (SDG) 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. U.S. Government Global Tuberculosis Strategy (2015–2019)* and *National Action Plan for Combating Multidrug-resistant Tuberculosis*. Both documents are consistent with the WHO End TB Strategy and outline the U.S. Government's support to ensuring the availability of affordable quality-assured 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. The uninterrupted availability of affordable, quality-assured anti-TB medicines is crucial to achieving the desired treatment outcomes for people with TB, as well as for preventing drug-resistant TB.

## III. Quarter 2 Progress by Objective

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

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Dong-A ST submitted its API MF for clofazimine to WHO PQ and was accepted for review in February 2017. Celltrion Pharma also submitted its linezolid FPP dossier to WHO PQ at the end of March. It has not yet been accepted for review. Rifampicin was selected as the TB product for U.S. FDA submission.

During Q2, PQM provided technical assistance to manufacturers in various stages for the following products:

- Clofazimine API and FPP: With PQM technical assistance, Dong-A ST finalized and submitted API MF for WHO prequalification. The contract manufacturing organization (CMO) working with Dong-A continued working on CAPA implementation, which was developed based on PQM's audit and WHO's and risk mitigations.
- Rifapentine API: The company continued working on implementation of CAPA from PQM's GMP assessment.
- Rifapentine FPP: PQM provided assistance to the company in product development.
- Gatifloxacin API and FPP: Both API and FPP companies continued working on CAPA implementation; CAPA was developed as result of PQM assessment.
- Kanamycin API: With PQM's assistance, the company conducted cross-contamination assessment.
- Kanamycin FPP: PQM provided assistance in the investigation of reported cases of adverse reaction. PQM also conducted a mock audit in February 2017 in preparation for WHO inspection.
- Linezolid FPP: PQM provided guidance to the company on submission of its dossier to WHO PQ. The dossier was submitted on March, 2017.
- PAS Na API: PQM conducted a mock audit of the facility to prepare for WHO inspection scheduled for April 17–20, 2017.
- Pyrazinamide API: Implementation of CAPA developed as a result of PQM's audit is in progress.
- Terizidone API: PQM continues to support the company's product development work.
- Rifampicin/isoniazid/ethambutol/pirazinamide (4 FDC): Pre-assessment questionnaires were submitted by the two manufacturers and reviewed by PQM. Baseline GMP assessment of both manufacturers are scheduled in April 2017.

To help ensure an uninterrupted supply of anti-TB medicines, PQM teams worked on the identification of the priority medicine that PQM would support for U.S. FDA submission. Through a literature review and series of discussions among PQM, USAID, and key stakeholders, the criteria for prioritization of the medicine for PQM's support were identified, and a scoring tool was developed. As a result of the exercise, PQM identified rifampicin as the first priority product to be supported for U.S. FDA approval. Bringing new suppliers to the U.S. market will decrease a risk of shortage of medicines; it may also have a positive impact on medicines price reduction. In addition, U.S. FDA approval makes medicines eligible for supply through Stop TB Partnership's Global Drug Facility. Therefore, the intervention potentially can increase the number of international quality-assured suppliers not only in the United States but also on the global public health market, particularly for the countries benefiting from the GDF mechanism.

As a result of the continued technical assistance provided by PQM, Dong-A ST pharmaceutical company was able to submit its API MF for clofazimine API for WHO PQ on February 15, 2017. Upon submission, it was accepted for review.

The PQM GMP team will continue to provide technical assistance to the manufacturers. PQM staff will draft and finalize the EOI for U.S. FDA submission to be published for the manufacturers. The selection of the manufacturer will be made in June 2017.

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

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On World TB Day, PQM was active on social media to emphasize the importance of the quality of TB medicines for achieving the desired health outcomes for patients.

PQM started preparations for the manufacturers' workshop and MRAs. The objective of the workshop is to raise awareness about pharmaceutical quality and to provide information to MRAs and manufacturers about opportunities for using PQM technical assistance to strengthen quality systems. The announcement and agenda of the workshop are finalized. PQM started working on workshop logistics and engaging the guest speakers.

One press release dedicated to World TB Day was published by PQM staff.

PQM will finalize a contract for the workshop venue and confirm guest speakers' logistics. The PQM GMP team will continue to work with manufacturers to provide technical assistance.

## **PQM Core NTD**

### **I. Quarter 2 Highlights**

PQM helped the manufacturers of praziquantel make progress toward completing the BE requirement for WHO PQ. The approach and process for the selection of the manufacturers was confirmed. The EOI was finalized and will be posted in Q3.

PQM's assistance to manufacturers to improve their quality standards will continue. PQM's support for the BE study will incentivize the manufacturers to complete WHO PQ and will speed the global availability of praziquantel.

### **II. Core/Health Element Context**

Using a systems-based approach, PQM offers technical assistance in several areas to achieve the above stated strategic objectives. PQM's working philosophy includes technical components that begin with thorough situational analysis; focus on a stepwise, systems-based approach; elevate risk management that is pragmatic, proportionate, and prioritized; provide hands-on and follow-up support; are governed by current regulatory QA/QC best practices; and seek collaboration and partnership. Moreover, PQM's approach fosters sustainability by linking regional, national health, and pharmaceutical strategies; attaining partner buy-in and commitment; leveraging regional harmonization initiatives; addressing financing and human resources; and advocating for accountability and transparency.

Many of these approaches are replicated globally but tailored to fit the needs of individual countries or regions. These approaches include building the capacity of MRAs to review and approve quality essential medicines and strengthen their ability to protect their own populations from poor-quality medicines. Specifically, PQM works with national and regional regulatory authorities to build sustained capacity for medicines evaluation, manufacturing inspection, and surveillance. PQM supports NQCLs through hands-on training and technical assistance to improve laboratory standards, with one goal being to help laboratories attain international recognition, such as ISO accreditation and/or WHO prequalification.

PQM also helps NQCLs implement or improve PMS programs. One aspect of PMS is field-based MQM, which involves laboratory staff collecting medicine samples at sentinel sites. These samples are screened in the field using Minilab™ and/or other field-based screening tools, and the samples are sent for confirmatory testing in the laboratory.

PQM's systems-based approach extends to medicines manufacturers. PQM experts in GMP travel to manufacturing sites to help companies improve their GMP compliance and develop dossiers to submit to the MRAs, WHO PQ program, and/or stringent regulatory authorities, thereby ensuring security in the supply and availability of essential priority medicines for public health.

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

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

As PQM continues support for manufacturers to achieve prequalification of NTD medicines, some constraints for manufacturers have become evident, including a scarcity of suppliers for API 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 expert review panel (ERP) process. This process allows manufacturers to partake in a rapid quality risk assessment of their product dossier and the level of GMP compliance at their 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 the GMP requirements, as well as a lack of funding for conducting BE studies in a CRO that is compliant with good clinical practices. One significant advantage for manufacturers of NTD products 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 BE studies at a future date.

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

### **III. Quarter 2 Progress by Objective**

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#### **Objective 1 – Increase availability to quality assured NTD medicines**

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In Quarter 2, PQM provided technical assistance for the following NTD medicines:

##### **Praziquantel API**

PQM is currently supporting four manufacturers of praziquantel API. PQM provided technical assistance to one manufacturer to prepare and submit a CAPA plan to WHO in March 2017. PQM provided technical assistance to a second manufacturer to prepare for WHO's re-inspection. PQM provided technical assistance to a third manufacturer in implementation of a CAPA plan developed as result of PQM's audit. PQM evaluated pre-assessment questionnaire, DMF, WHO inquiries, and photos of the plant for a fourth manufacturer. A site visit is tentatively planned for Q3.

##### **Praziquantel FPP**

PQM is currently supporting three manufacturers of praziquantel FPP. PQM provided technical assistance to one manufacturer in product development as API using the new API source. PQM helped two other manufacturers in planning and production of validation batches.

##### **Albendazole API**

PQM is supporting two manufacturers of albendazole API. PQM conducted GMP assessment of one manufacturer in Q1, and the assessment report was provided in Q2. Now the company is in the process of implementing CAPA. The second manufacturer is in the process of preparing validation batches for WHO PQ.

##### **Albendazole FPP**

PQM is providing technical assistance to two manufacturers. PQM conducted a brief walk-through in one facility and has identified potential cross-contamination issues that the company will address. PQM continued technical assistance to a second manufacturer on product development; an onsite visit is planned in Q3. PQM identified another company that is in the product development stage, and PQM's technical assistance is being considered.

#### **Mebendazole FPP**

PQM engaged a new manufacturer of mebendazole FPP for participation in the WHO PQ program and provided recommendations on product development queries.

PQM started preparation for the situation analysis on the availability of quality-assured priority NTD medicines in five high NTD burden countries (Nigeria, Ethiopia, Tanzania, India and Indonesia). PQM identified and entered into a contract with a consultant to conduct the situation analysis in Q3. One outcome of the study will be identification of local manufacturers that PQM could potentially support.

The PQM GMP team is continuing to provide technical assistance at various stages to ensure that manufacturers are making progress toward WHO PQ.

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### **Objective 2 – Technical support for bioequivalence study**

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PQM finalized the approach for providing assistance to praziquantel manufacturers in conducting a BE study for WHO PQ, including a financial contribution toward the cost of the study. USAID agreed with the approach, and an EOI (which will be published in Q3) was developed. PQM will identify and evaluate manufacturers for PQM assistance. This activity is coordinated with the Bill and Melinda Gates Foundation, which plans a similar activity.

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

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The planning for joint Core TB/NTD workshop for manufacturers and MRAs was initiated. The country selected is Thailand, and the dates are July 25–27, 2017.

PQM started preparation for the workshop for manufacturers and MRAs. The objective of the workshop is to raise awareness about pharmaceutical quality and to provide information to MRAs and manufacturers of anti-TB and NTD medicines about opportunities to use PQM technical assistance to strengthen quality systems. The announcement of the workshop and the agenda are finalized. PQM began working on the workshop logistics and engaging guest speakers.

## **PQM Core MNCH**

### **I. Quarter 2 Highlights**

- Twenty-six total participants from manufacturers and MRA members from four countries attended the EAC training in Kenya. The training focused on how to compile a product dossier in CTD format; validation life cycle; qualification of equipment; and layout requirements for control of HVAC, water, steam, and gas systems. The training was interactive with case studies, other group activities, and questions from the participants. Participants' evaluation of the training was very positive. The objective of PQM's support is to encourage dossier submission for EAC joint review. PQM also advocates to the EAC to prioritize MNCH products in their joint review calendar.
- PQM continued to support manufacturers of different priority MNCH products. This included review of the pre-assessment questionnaire and a GMP assessment visit to a magnesium sulfate manufacturer. The assessment report will be issued to the manufacturer in Q3. PQM will guide the manufacturer on the CAPA implementation and development of its FPP dossier in Q3.

PQM will continue technical assistance to manufacturers of priority MNCH products in Q3.

Participants will be able to use knowledge gained from the training to carry out their duties and ensure good-quality, safe, and effective medicines are manufactured and available in EAC member states.

## II. Core/Health Element Context

Through funding from USAID, PQM began the delivery of technical assistance for MNCH in 2009. Below are examples of key PQM accomplishments in support of USAID MNCH strategies and initiatives:

- WHO PQ of the first zinc dispersible tablet product from Nutriset.
- Development and publication of five monographs (zinc sulfate tablets, zinc sulfate oral solution, zinc gluconate tablets, vitamin A oral liquid preparation, and chlorhexidine gluconate topical gel) containing test methods and specifications to analyze child and newborn health medicines for quality during PMS.
- Regulatory approval of Universal's chlorhexidine gel product in Kenya, the first chlorhexidine product manufactured in East Africa.
- Development of Minilab™ QC screening procedures for four possible serious bacterial infection PSBI medicines (benzathine benzylpenicillin injection, benzylpenicillin sodium or potassium injection, gentamicin injection, and procaine benzylpenicillin injection), including the new short regimen (a Minilab™ procedure for amoxicillin dispersible tablets already exists).

In 2015, the SDGs were adopted by world leaders to build on MDG success. SDG Goal 3, “Ensure healthy lives and promote well-being for all at all ages,” encompasses targets similar to USAID’s EPCMD initiative.

The EPCMD initiative focuses resources on 24 priority countries and toward life-saving interventions that have the greatest impact on mortality. These 24 countries, primarily in sub-Saharan Africa and South Asia, account for 70% 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 ensures an uninterrupted supply of quality-assured medicines, but also strengthens medicines regulatory capacities to protect against poor-quality medicines, which is the essence of PQM’s technical expertise.

## III. Quarter 2 Progress by Objective

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

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- Chlorhexidine solution: PQM continued remote assistance to one manufacturer. The packaging machine qualification protocol was received and review by PQM. The comments on the protocol were provided to the manufacturer.
- Chlorhexidine gel: with PQM support, a dossier was developed and submitted for review by FHI 360 and the EAC in Q1. The dossier is still under review. PQM will provide assistance to the manufacturer if there are any queries from the reviewers.

- Magnesium sulfate FPP: PQM is providing technical assistance to three manufacturers. One manufacturer finished product development and completed a registration batch with PQM's technical assistance. A second manufacturer is in the process of product development. In Q2, PQM conducted GMP assessment of the third manufacturer. The assessment report will be developed and shared with a manufacturer in Q3. The CAPA plan will be developed based on the assessment findings.
- Oxytocin injection: the manufacturer supported by PQM is in the product development stage; GMP assessment is scheduled for Q3.
- Oxytocin API: PQM provided technical assistance to one manufacturer. The company is preparing for PQM's mock audit to be conducted in Q3.
- Amoxicillin FPP: PQM supported one manufacturer. Currently the company is implementing the CAPA plan, which is based on PQM's audit and recommendations.

One GMP assessment was conducted by PQM for a magnesium sulfate FPP manufacturer.

PQM GMP staff will continue to provide technical assistance to manufacturers.

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### **Objective 2 – Provide technical leadership on MNCH medicine quality assurance**

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Twenty-six total participants attended a PQM training in Kenya for manufacturers and MRA members from four countries. The training focused on how to compile a product dossier in CTD format; validation life cycle; qualification of equipment; and layout requirements for control of HVAC, water, steam, and gas systems. The training was interactive with case studies, other group activities, and lots of questions from the participants. Participants' evaluation of the training was very positive.

## Management Overview

PQM continued to focus on working with the USAID Mission and Core Health Element team to secure approval for FY17 work plans during Q2. By the end of March 2017, 20 out of 26 work plans (77%) had been fully approved, with an additional three work plans tentatively or partially approved. In early April 2017, one additional work plan received full approval, bringing PQM's total to 21 work plans fully approved and two work plans partially approved.

During Q2, PQM also instituted a new set of project management processes and tailored tools to support successful program implementation. PQM trained staff, both at Rockville headquarters and at select field office locations, on systems and project management practices to increase the adoption of key concepts, lessons learned, and tools to manage project information.

PQM Director Jude Nwokike also attended a key event during Q2, the January 2017 accreditation ceremony of the National Agency for Drug Administration and Control (NAFDAC) Zonal Laboratory of Agulu for ISO/IEC 17025:2005 accreditation. The accreditation ceremony was attended by several high-level officials, including the Minister of Health, Professor Isaac Adewole, NAFDAC's Acting Director-General, Yetunde Oni, and Deputy Governor of Anambra State, Dr. Nkem Okeke. Mr. Nwokike presented during the accreditation ceremony and noted that Nigeria is the first African country supported by PQM with two ISO accredited pharmaceutical laboratories—a major accomplishment for the country.



Yetunde Oni, Isaac Adewole, Nkem Okeke, and Jude Nwokike attending the NAFDAC Zonal Laboratory of Agulu accreditation ceremony.