Promoting the Quality of Medicines

Promoting the Quality of Medicines (PQM) Program

FY 2017 Fourth Quarter Report
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U.S. Pharmacopeial Convention

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About the Promoting the Quality of Medicines (PQM) Program

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

As of September 2017, USAID supports PQM's work in 20 countries, 2 Regional Missions, 1 Cross Bureau program, and 4 core health programs.

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Table of Contents

Acronyms

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

Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance in partnering countries to strengthen quality assurance (QA) systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance helps to build the capacity of medicines regulatory authorities (MRAs) and QA systems. PQM supports the manufacture of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH). PQM also provides support to increase the utilization of medical product quality information for decision-making. The U.S. Agency for International Development (USAID) supports PQM's work in 20 countries and in two regional programs in Asia and Latin America. This report summarizes results achieved during the fourth quarter of FY 2017, from July 1 to September 30, 2017.

PQM's first Intermediate Result area is to strengthen medical product 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. During this quarter, PQM continued its contribution to the revision of the law 94/012/CTRN on pharmaceutical legislation in Guinea. PQM played a key role in the development of the Pharmaceutical Manufacturer GMP Inspection Directive approved and issued by the Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA), which sets a legal binding framework on good manufacturing practices inspection and also provides clear direction on how to process and access applications, handle complaints, and set the responsibilities of inspectors. In Indonesia, the Therapeutic Products national quality control laboratory of Indonesia's National Agency for Drug and Food Control submitted the laboratory information file (LIF) and related documents to WHO to begin the process for World Health Organization (WHO) prequalification (PQ). In Nigeria, PQM's technical support to the National Agency for Food and Drug Administration and Control's (NAFDAC) pharmacovigilance and post-marketing surveillance directorate and the ISO accreditation of three NAFDAC laboratories have resulted in income generation for sustainability and in strengthened capacity to conduct PMS. The New Partnership for Africa's Development listed NAFDAC's Central Drug Control Laboratory in Yaba, Lagos, as an African Regional Center of Regulatory Excellence, which provides an opportunity for the laboratory to play a major regional role in monitoring and testing medicines quality across countries in Africa. In Bangladesh, PQM provided technical assistance to the Directorate General of Drug Administration to complete WHO's nine functions for self-assessment and develop an institutional development plan. In Burma, U.S. Ambassador Scot Marciel visited the ISO 17025 accredited pharmaceutical chemistry laboratory in Nay Pyi Taw, noting the equipment donated by PQM with support from USAID/President's Malaria Initiative (PMI), and acknowledged the benefits that PQM's technical assistance brought to the laboratory.

The second Intermediate 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, and MNCH—is necessary to address national health priorities and plans. PQM works with manufacturers to improve compliance with WHO standards, helping 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. Earlier in FY 2017, as a result of PQM's support in Pakistan, four chlorhexidine 7.1% gel products were approved for registration by the Drug Registration Board, and in Q4 PQM followed up to obtain final approval on the price by the Prime Minister; once the local manufacturers' products are available, not only will there be an increase in quality-assured chlorhexidine 7.1% gel in Pakistan, but the manufacturers will also look into the possibility of exporting their product to other countries in the Asia region. Also during Q4, two PQM-supported manufacturers obtained WHO PQ for two priority products: praziquantel API and capreomycin FPP. Additional sources of a quality-assured product may lead to a potential drop in price.

The increased utilization of medical product quality information for decision-making is PQM's third Intermediate Result area. The collection, analysis, and use of data on medical products quality to support evidence-based decision-making are 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. In September 2017, PQM supported the Liberia Medicines and Health Products Regulatory Authority (LMHRA) to conduct an exercise to remove selected antimalarial monotherapies from circulation in Nimba County, resulting in the removal of 27,600 packs of amodiaquine monotherapy (of 3 tablets each) from the market and 143 cartons of medicine from inspected facilities. In total, the confiscated products were worth an estimated $68,000 USD (over 8 million Liberian dollars), and LMHRA issued five citations to cite key violators to an administrative hearing. In Ghana, PMS results indicated that 7 out of 50 zinc sulfate tablets (14%) sampled from the Greater Accra region failed the disintegration test; as a result, the Ghana Food and Drug Administration instituted regulatory actions, and the manufacturer recalled all failed batches from the market and agreed to start monthly checking of control samples of all batches. In Nigeria, PQM facilitated a workshop on good storage and distribution practices for marketing authorization holders of oxytocin injection; key regulatory decisions made during the workshop included that prospective market authorization holders without suitable storage facilities will not be given marketing authorization of oxytocin in Nigeria. Additional regulatory actions taken this quarter include the confiscation of 1,183 ampoules of poor-quality oxytocin from the market in 2 states in Nigeria.

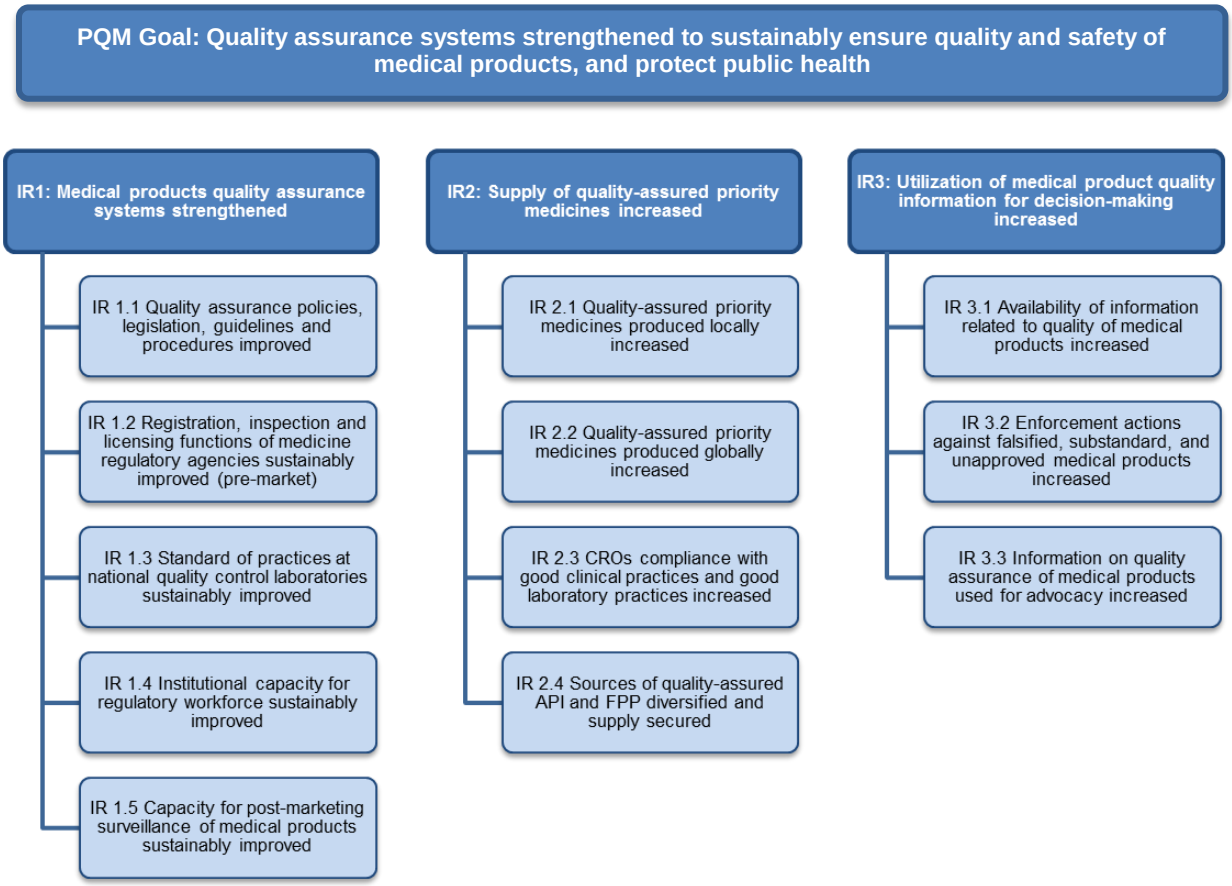
Program Background

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

During FY 2017, PQM implemented projects in 20 USAID country Missions, 2 Regional Missions, 1 Cross Bureau program, and 4 core health programs.

Results Framework

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



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

Result Highlights

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

Description of Sub-IRs

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

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

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

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

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

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

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

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

Sub-IR 1.4 Institutional capacity for 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, particularly bioequivalence aspects of good clinical practices (GCP), good manufacturing practices (GMP), and good laboratory practices (GLP), including quality control (QC) testing procedures and laboratory equipment maintenance.

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

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

Sub-IR 1.5 Capacity for post-marketing surveillance of medical products sustainably improved
Ensuring the quality of medical products throughout the supply chain presents challenges that extend beyond the registration and procurement processes. Substandard medicines may occur due to poor manufacturing practices or as a result of poor storage conditions or practices. In addition, weak regulatory systems leading to unregulated distribution and sale of medicines and porous country borders facilitate the introduction of substandard, falsified, and unapproved medicines. To help address these challenges, PQM collaborates with MRAs to establish and strengthen PMS programs that regularly examine the quality of medicines throughout the supply chain.

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

Overview of FY 2017 Fourth Quarter IR1 Achievements

Key Results and Highlights

Select Q4 Data Points for IR1

Number of individuals trained in QA-/QC-related topics	483
Number of QC laboratories supported	50
Number of QC laboratories that participated in proficiency testing and passed	7
Number of policies/law/regulations updated/developed and submitted for adoption	1

During this quarter, PQM continued its contribution to the revision of the law 94/012/CTRN on pharmaceutical legislation in Guinea. PQM supported the work of the commission appointed by the Minister of Health to finalize the legislation. The final text was adopted by this process and named "Preliminary Draft Law on Medicines, Other Health Products and Pharmaceutical Exercise." It was submitted to the Minister of Health in the first week of September 2017. The draft will be studied by the Cabinet of the Minister of Health in order to become the "Law Project on Medicines, Other Health Products and Pharmaceutical Practice." This Law Project will be submitted to the government to be adopted by the Council of Ministers and submitted to the National Assembly.

The Ethiopian Food, Medicine and Health Care Administration and Control Authority (EFMHACA) approved and issued a Pharmaceutical Manufacturer GMP Inspection Directive in accordance with article 55 of proclamation No. 661/2009 that set a legal binding framework on GMP inspection. This directive, which began implementation in September 2017, also provides clear direction on how to process and access applications, handle complaints, and set responsibilities of inspectors. The directive also lays the foundation for essential elements of GMP inspection to improve the transparency, accountability, traceability, and competence of inspectors in enforcing requirements for EFMHACA to conduct local and foreign GMP inspections. PQM played a key role in the development of this directive. The improvement in the coverage and quality of foreign and local manufacturers' inspection contributes to the improved access of quality-assured medicines by ensuring that quality is built into the product during the manufacturing process. In addition, presence of the needed capacity with the required integrity help to expedite provision of marketing authorization to medicines for those meeting GMP requirements by providing timely response, while deterring those that do not comply with GMP.

The most significant achievement during Q4 in Indonesia was the submission of the laboratory information file (LIF) and related documents to WHO to begin the process for WHO PQ of PTBB, the Therapeutic Products NQCL of Indonesia's National Agency for Drug and Food Control (BPOM). This milestone represents multiple years of intensive training and technical assistance to BPOM, and will signify a historic national achievement for Indonesia if successful. A WHO-prequalified national medicines quality control laboratory will help ensure that essential medicines provided by the government will be subjected to high-quality QC testing on an ongoing basis. This will also support the national post-marketing surveillance program implemented by BPOM for public and private sector sampling and testing, as well as position BPOM as a regional leader in the Association of Southeast Asian Nations (ASEAN) for medicines quality assurance. PQM hopes that the national laboratory will also serve as an important resource for the local pharmaceutical industry, increasing confidence in the national MRA and in overall compliance for production and quality control.

In Nigeria, PQM's technical support to the National Agency for Food and Drug Administration and Control's (NAFDAC) pharmacovigilance and post-marketing surveillance (PV/PMS) Directorate and the ISO accreditation of three NAFDAC laboratories have resulted in income generation for sustainability and in strengthened laboratory staff capacity and skills to routinely conduct PMS. In July, the National Tuberculosis and Leprosy Control Program (NTBLCP) requested NAFDAC to lead a survey and conduct quality control tests for 150 samples of first- and second-line anti-TB medicines to be collected across the country. PQM reviewed the draft protocol jointly put together by NAFDAC, NTBLCP, and the Institute of Human Virology of Nigeria (IHVN) for the survey of anti-TB medicines in Nigeria public health facilities. NTBLCP and IHVN will provide the funds for NAFDAC to conduct testing of the samples, generating revenue for the laboratories. This development demonstrates sustainability in NAFDAC's PMS and laboratory services. PQM reassured NTBLCP and IHVN about NAFDAC's competence to lead the survey and conduct reliable QC testing.

Also this quarter, NAFDAC and Catholic Relief Services (CRS), a Global Fund principal recipient, signed a memorandum of understanding (MOU) for testing all Global Fund-procured antimalarial medicine samples. The MOU outlines that CRS will pay for samples to be tested by NAFDAC and that NAFDAC will perform routine monitoring of Global Fund-procured samples in public health and storage facilities. In Q4, the New Partnership for Africa's Development (NEPAD) listed NAFDAC's Central Drug Control Laboratory in Yaba, Lagos, as an African Regional Center of Regulatory Excellence. NEPAD is an economic development program of the African Union, and selection of the laboratory demonstrates its capacity as a center of excellence for the entire continent of Africa. This designation provides an opportunity for the laboratory to play a major regional role in the support of monitoring and testing medicines quality across countries in Africa.

In Bangladesh, PQM provided technical assistance to the Directorate General of Drug Administration (DGDA) to complete WHO's nine functions for self-assessment, which was completed in July 2017. Of the nine assessment functions, PQM field staff supported in four, including Laboratory Access and Testing, NRA Lot Release, Clinical Trials Oversight, and Regulatory Inspection System. In addition, PQM provided support to develop an institutional development plan using WHO-accessed tools, standard operating procedures (SOPs), and guidance documents. PQM has collaborated extensively with WHO on the Coalition of Interested Partners pilot in Bangladesh and recently on the use of the Global Benchmarking Tool for NRA assessments in Pakistan and in the Economic Community of West African States.

Lastly, in Burma, U.S. Ambassador Scot Marciel visited the ISO 17025 accredited pharmaceutical chemistry laboratory in Nay Pyi Taw. Dr. Khin Chit from the Department of Food and Drug Administration (DFDA) and Dr. Lu Lu Kyaw Tin Oo from PQM guided the Ambassador and his team through the laboratory. The Ambassador noted the high-performance liquid chromatography (HPLC) system and dissolution tester donated by PQM with support from USAID/President's Malaria Initiative (PMI) and acknowledged the benefits that PQM's technical assistance brought to the laboratory.

IR2: Supply of Quality-Assured Priority Medicines Increased

Description of Sub-IRs

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

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

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

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

Sub-IR 2.3 CROs' compliance with Good Clinical practices and Good Laboratory Practices increased

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

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

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

Overview of FY 2017 Fourth Quarter IR2 Achievements

Key Results and Highlights

Select Q4 Data Points for IR2

Number of manufacturers supported toward GMP standards	51
Number of products achieving WHO PQ	2 (capreomycin FPP, praziquantel API)
Number of CROs supported	4

Number of Manufacturers Provided with Technical Assistance in FY 2017 Q4

Countries/ Core Programs	Number of Manufacturers	Product Types
Core MNCH	8	chlorhexidine FPP, magnesium sulfate FPP, oxytocin API, oxytocin FPP, and amoxicillin FPP
Core TB	13	clofazimine API, clofazimine FPP, cycloserine API, rifapentine API, rifapentine FPP, gatifloxacin API, gatifloxacin FPP, kanamycin API, kanamycin FPP, linezolid FPP, PAS Na API, pyrazinamide API, and rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC)
Core NTD	14	praziquantel API, praziquantel FPP, albendazole API, albendazole FPP, and mebendazole FPP
Ethiopia	1	ethambutol FPP
Nigeria	7	amoxicillin DT FPP, oxytocin FPP, magnesium sulfate FPP, zinc sulfate FPP, chlorhexidine gel FPP, and artemether lumefantrine FPP
Indonesia	2	levofloxacin FPP, oxytocin FPP, and amoxicillin DT FPP
Pakistan	4	chlorhexidine gel FPP
Kazakhstan	1	levofloxacin FPP and moxifloxacin FPP
Uzbekistan	1	levofloxacin FPP and moxifloxacin FPP

Earlier in FY 2017, as a result of PQM's support in Pakistan, four chlorhexidine 7.1% gel products were approved for registration by the Drug Registration Board and prices were fixed by the Federal Drug Pricing Committee. During Q4, PQM followed up with the Pakistan federal government and succeeded in getting final approval on the price by the

Prime Minister. Consequently, registration letters were issued to all four manufacturers, thus clearing the last pending requirement for local production. All four manufacturers are now preparing the production of commercial batches. The first batches of chlorhexidine 7.1% gel are likely to be available during the first quarter of FY 2018. Once the four local manufacturers' products are available in the marketplace, not only will there be an increase in the availability of quality-assured chlorhexidine 7.1% gel in Pakistan, but the manufacturers will also look into the possibility of exporting their product to other countries in the Asia region.

Also during Q4, two PQM-supported manufacturers obtained WHO PQ for two priority products: praziquantel API and capreomycin FPP. Hisun Pharma is the first manufacturer to become prequalified for praziquantel API. Praziquantel is an important medicine for treating schistosomiasis, and having a quality-assured API source is vital for the production of quality finished products. NCPC International's WHO PQ of capreomycin FPP, an anti-TB medicine, provides an additional source of a quality-assured product for global procurement agencies. With its own API source, NCPC's prequalification of capreomycin FPP may lead to a potential drop in price.

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

Description of Sub-IRs

The collection, analysis, and use of data on medical products evaluation, inspection, and post-approval surveillance supports evidence-based decision-making critical for promoting access to quality-assured products and for reducing and eliminating substandard and falsified products. PQM supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory actions and are disseminated to all stakeholders. By working with local, national, and international partners, PQM helps bring awareness to the use of data to improve transparency and accountability in the pharmaceutical sector, inform decision-making, shape public policies on pharmaceuticals, and support the attainment of public health objectives.

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

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

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

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

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

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

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

PQM raises awareness about the dangers of substandard and falsified medicines, providing information to the public and government stakeholders by supporting local, regional, and global initiatives on medicines quality. Activities often

include hosting and attending partner meetings, developing regional databases and alert systems, advocating for the allocation of resources to improve pharmaceutical quality systems, and encouraging collaboration among stakeholders. PQM develops e-learning courses on medicines quality assurance, participates in educational courses organized by international partners, collaborates with local universities to develop QA-related content for pharmaceutical curricula, and supports studies and operational research on quality assurance and regulatory systems strengthening.

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

Overview of FY 2017 Fourth Quarter IR3 Achievements

Key Results and Highlights

Select Q4 Data Points for IR3

Number of samples collected and tested	1,691
Number of regulatory actions taken	28

In September 2017, PQM supported the Liberia Medicines and Health Products Regulatory Authority (LMHRA) to conduct an exercise to remove selected antimalarial monotherapies from circulation in Nimba County. While Liberia is 1 of the 49 countries that has taken steps to ban the use of oral artemisinin-based monotherapy, medicines quality surveillance reports have consistently demonstrated the widespread use of amodiaquine monotherapy for the treatment and management of malaria in Liberia. WHO recommends combination therapy to treat malaria and discourages artemisinin-based monotherapies. The exercise resulted in the removal of 27,600 packs of amodiaquine monotherapy (of 3 tablets each) from the market. Additionally, 143 cartons of medicine (over 100,000 pieces of assorted unregistered and falsified quinine tablet, artemether injection, and other products) were removed from inspected facilities. In total, the confiscated products were worth an estimated $68,000 USD (over 8 million Liberian dollars), and LMHRA issued five citations to cite key violators to an administrative hearing. Meanwhile, a stakeholders' and 34 awareness campaigns on the danger of using antimalarial monotherapy to treat malaria were held in cities, towns, and villages.

In Ghana, PMS results indicated that 7 out of 50 zinc sulfate tablets (14%) sampled from the Greater Accra region failed the disintegration test. One of the batches that failed the disintegration test also failed the assay test. As a result, GFDA instituted regulatory actions, and the manufacturer recalled all failed batches from the market. Additionally, the manufacturer has agreed to start monthly checking of control samples of all batches for hardness testing to ensure uniformity and will also conduct stability studies on a reformulated batch of the product that contains an extra quantity of a disintegrant.

In Nigeria, PQM facilitated a workshop on good storage and distribution practices for marketing authorization holders of oxytocin injection. Key regulatory decisions were made during the workshop include that prospective market authorization holders without suitable storage facilities will not be given marketing authorization of oxytocin in Nigeria. Additional regulatory actions taken this quarter include the confiscation of 1,183 ampoules of poor-quality oxytocin from the market in 2 states of the Federation.

Africa

Benin

I. Quarter 4 Highlights

PQM trained NQCL staff on the use of handheld Raman spectrometers to detect falsified medicines. NQCL management and PQM discussed the laboratory's draft strategic plan and FY 2018 activities.

II. Country Context

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

NQCL has hired a consultant to develop a 5-year strategic plan for the laboratory. PQM reviewed the draft strategic plan and discussed some sections with NQCL management. Comments and recommendations will be provided to NQCL in early Q1 FY 2018.

PQM also discussed with the laboratory management activities for FY 2018. NQCL agreed to prioritize fixing electrical problems that have put sensitive laboratory equipment out of service, including the new HPLC system that was donated jointly by PMI, Agilent, and USP. NQCL will contribute to solving this issue by covering the cost of fixing defective electrical installation for the whole laboratory. This will affect its operations while work is being performed, but it is necessary, as the laboratory has not been fully operational.

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

Training on handheld Raman spectrometer in Benin

Upon request from the PMI team in Benin, PQM procured and delivered a handheld Raman spectrometer to NQCL. Four staff members (one female and three males) received training on its use. During the training, the staff developed methods for screening antimalarial medicines such as the combinations artemether–lumefantrine and artesunate–amodiaquine. The laboratory will use the device for quick detection of falsified artemether–lumefantrine and artesunate–amodiaquine, as well as other select medicines for which suitability of handheld Raman use can be demonstrated. NQCL will use the device in combination with Minilab™. The two screening methods are complementary. For some pharmaceutical products, there is no Minilab™ method, and for others handheld Raman spectrometer is not suitable. By having both Minilab™ and the handheld Raman spectrometer, NQCL is now better equipped to support the regulatory authority in conducting post-marketing surveillance of a larger number of pharmaceutical products.

As matter of fact, on the last day of training, PQM staff asked the laboratory manager to bring samples of any medicines from the laboratory. The trainees were able to develop methods for screening acetaminophen and amoxicillin, among other medicines. The laboratory received eight samples of Pfizer's Cytotec (misoprostol) from the Directorate of Pharmacy, Medicine and Diagnostics, which had received complaints about the lack of efficacy of

Angola: PQM is finalizing the country close-out report for submission to the Angola USAID Mission.

some batches of this product. However, NQCL had not been able to test the samples due to electrical problems that put its HPLC system out of service, and had planned to send the samples to an external laboratory. With the handheld Raman spectrometer, the staff were able to identify one falsified Cytotec. Three samples will require further testing. PQM staff suggested to NQCL to send only three samples to an external laboratory. This example shows the importance and usefulness of using a risk-based approach to medicines testing. PQM instructed NQCL to verify the quality of pharmaceutical products using different methods before using them as reference for screening samples collected during post-marketing surveillance activities.

Burkina Faso

I. Quarter 4 Highlights

In Burkina Faso, PQM facilitated quality monitoring of antimalarial medicines as part of PMS activities. The Directorate General of Pharmacy, Medicines and Laboratories (DGPML) collaborated with the National Laboratory of Public Health (LNSP) to collect 172 samples of antimalarials. Screening and testing has been carried out, and confirmation of the results is underway. PQM will facilitate drafting of the PMS final report and dissemination of the PMS results.

To strengthen NQCL's QMS, PQM assisted LNSP's Directorate of Medicine Control (DMC) in reviewing existing SOPs and identifying which of them need to be developed or revised.

II. Country Context

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Strengthen the capacity of the NQCL

To prepare the DMC (the medicine quality control laboratory) for ISO 17025, PQM helped it to determine the list of SOPs it must have in place. The list includes 59 SOPs: 33 that are new and need to be developed and 24 that need to be revised. PQM has started assisting DMC in drafting the new SOPs and revising selected ones.

Objective 2 – Strengthen post-marketing surveillance of antimalarial medicines

PQM facilitated post-marketing surveillance of antimalarial medicines in eight regions. In collaboration with DGPML, PQM developed an antimalarial MQM protocol. The sampling plan was developed by taking into consideration the number and volume of antimalarials imported last year, accessibility to sampling sites (road conditions), and security in the areas considered for sampling. DGPML and LNSP teams collected 172 samples. After conducting visual inspection, products that were stored above storage conditions (higher than 30ºC), looked suspicious, or were from manufacturers with known quality issues were selected for further testing. The teams selected 140 samples for

screening test using thin-layer chromatography (TLC); of these, 113 were tested and 27 could not be tested. Two samples were found noncompliant with quality specification. These results are undergoing verification.

Ethiopia

I. Quarter 4 Highlights

PQM provided support in the ongoing improvement of EFMHACA's medicine registration information system (MRIS) by partnering with AIDSFree. Enhancing the system requires well-versed technical knowledge on medicine registration in order to ultimately ensure that the system generates structured information and becomes more useful to the reviewers and their managers to evaluate application dossiers. PQM played a leading role in conducting a stakeholders' workshop to enrich the recall directive and completed development of draft zero for submission to EFMHACA's management. EFMHACA also approved and issued a Pharmaceutical Manufacturer GMP Inspection Directive in accordance with Article 55 of Proclamation No. 661/2009 that set a legal binding framework on GMP inspection. This directive, which began implementation in September 2017, also provides clear direction on how to process and access applications, handle complaints, and set responsibilities of inspectors. In addition, EFMHACA has officially adopted an inspection checklist developed with PQM support to serve as a standard tool to inspect those importers and wholesalers for which EFMHACA is mandated to monitor good storage/distribution/recall practices. The checklists' relevance in terms of standardizing inspection practices and sensitizing the medicine facilities to build internal QMS is significant.

PQM conducted an assessment on the availability and utilization of guidelines for good storage practices, good distribution practices, and pharmaceutical product recall of 94 stakeholders, including regional regulatory bodies, manufacturers, importers, and wholesalers (August 14–27, 2017). The final report is being prepared and will be shared with relevant stakeholders. Highlights from the preliminary findings of the assessment were also presented by PQM at the annual regulatory review meeting, which was conducted September 4–8 in at Assosa, Benishangul gumz regional state. The review meeting pulled all federal and regional regulatory bodies to share their experiences, discuss their challenges, and plan for alignment of activities. In addition to the presentation, PQM also supported organization of the meeting. During the meeting, participants identified strategic initiatives to be implemented in the coming year.

PQM provided support toward maintaining ISO accreditation and expanding scope to three physicochemical test methods by assisting EFMHACA to develop three QMS SOPs and providing training to staff. Calibration of 16 EFMHACA laboratory instruments was performed by the National Metrology Institute (NMI) and consultants, and training on QMS also provided to branch laboratories.

PQM worked with the Addis Ababa University School of Pharmacy to prepare a module on QMS. This is a core course in the regulatory affairs postgraduate program and will be used as training material by in-country professors.

PQM provided technical assistance to local a manufacturer, Cadila Pharmaceutical, following its WHO inspection to address and rectify deficiencies identified during the inspection, as well as to prepare corrective and preventive actions (CAPAs) to respond to the findings. PQM also supported training of staff from the regional bioequivalence center (RBEC) on advanced bioequivalence and clinical trials to address the gaps in technical competency as per the WHO PQ mock audit findings. Procurement and supply of relevant laboratory instruments were also supported to help the center comply with requirements of the WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL).

With support from PQM, EFMHACA carried out a second round collection of PMS samples to meet the targeted sample size as per the FY 2017 PMS protocol. In addition, procurement of laboratory supplies needed to test the samples was completed and delivered to EFMHACA, and testing has begun. PQM also continued its support on EFMHACA pharmacovigilance activities in the preparation and categorization of Adverse Drug Event (ADE) reports, as well as in participation in pharmacovigilance forum meetings to review ADE reports related to poor-quality medicines. On the basis of this review, a regulatory measure was taken to recall one test reagent, which was found to be defective. PQM also conducted weekly supportive supervision at healthcare facilities that are carrying out cohort event monitoring on antiretroviral medicines.

PQM participated in the Intergovernmental Authority on Development's (IGAD) third-round meeting of member-country MRAs, which took place in Ethiopia on August 1–3, 2017. The third day of the meeting, in which PQM and other partners participated, was focused on sensitization of donors. MRAs from member states discussed technical issues during the 2 days and came up with a proposal to achieve a harmonized regulatory system in accordance with agreed-upon international standards within 5 years.

II. Country Context

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

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

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

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

III. Quarter 4 Progress by Objective

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

During Q3, the Clinical Trial Authorization Guideline was posted on EFMHACA's official website for public comment. Technical assistance was also provided in the improvement of the MRIS, the overall medicine registration system toward international standards, and the review process of dossier applications pending marketing authorization approvals.

In Q4, PQM continued to support the ongoing improvement of the MRIS by partnering with AIDSFree. Since enhancement of the system demanded changing different forms and tools, a to-do list was prepared by the technical working group, and the action plan has since been implemented. Nine major activities were identified, including reviewing checklists, identifying mandatory and optional document attachments, preparing a group variation list, setting report requirements for marketing authorization, and updating the list of SRA medicines. Improvements in the system require well-versed technical knowledge on medicine registration processes in order to ultimately ensure the system generates structured information/reports and becomes useful to EFMHACA experts and managers. Toward this end, PQM has been providing continued technical support through its involvement in the technical working group and the change management group.

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

During Q3, PQM provided trainings on medicine distribution and storage requirements to EFMHACA and Ethiopian airlines cargo. PQM provided mentorship of EFMHACA staff to strengthen their inspection practices and build capacity and skills on QMS for ISO 9001:2015 and ISO17020:2012. That same quarter, an inspection manual for regional regulatory bodies and a proposal to evaluate the availability and utilization of guidelines was also completed. Additionally, PQM supported EFMHACA in the development of a pharmaceutical products recall directive.

In Q4, as a continuing activity with respect to developing the recall directive, PQM played a leading role in conducting a stakeholders' workshop to enrich the directive (July 30–August 4). Professionals representing EFMHACA, PQM, the USAID Procurement and Supply Management project, and hospitals participated in the review of the directive. Draft zero is complete and ready for submission to EFMHACA management. In addition, EFMHACA approved and issued a Pharmaceutical Manufacturer GMP Inspection Directive in accordance with Article 55 of Proclamation No. 661/2009 that set a legal binding framework on GMP inspection. This directive, which began implementation in September 2017, provides clear direction on how to process and access applications, handle complaints, and set the responsibilities of inspectors. The directive also lays the foundation for essential elements of GMP inspection to improve transparency, accountability, traceability, and competence of inspectors in the process of enforcing requirements for EFMHACA to conduct local and foreign GMP inspections. PQM played a key role in the development of this directive. The improvement in the coverage and quality of foreign and local manufacturers' inspection contributes to improved access to quality-assured medicines by ensuring that quality is built into the product during the manufacturing process. In addition, having capacity helps to expedite the provision of marketing authorizations for those meeting GMP requirements by providing timely response, while deterring those that do not comply with GMP.

On August 11, EFMHACA officially adopted an inspection checklist developed with PQM support to serve as a standard tool to inspect importers and wholesalers for which EFMHACA is mandated to monitor good storage/distribution/recall practices. PQM also provided a half-day training to nine EFMHACA inspectors. The guideline for Good Storage, Distribution, and Pharmaceuticals Recall was used as a reference to develop the checklist, which touches on a range of topics, including premises, hygiene, temperature, environmental control, equipment, documentations, supplier and customer qualification, QMS, and internal audit—all of which are critical to maintain the quality, safety, efficacy, and traceability of medicines. The checklist's relevance in terms of standardizing inspection practices and sensitizing the medicine facilities to build QMS is significant. It will also help to improve supply chain security and integrity, avoid infiltration of falsified medicines, implement good storage and distribution practices, and (in the long run) eventually address medicines quality issues that can cause serious risks to public health.

This quarter, PQM conducted an assessment on the availability and utilization of guidelines for good storage practices, good distribution practices, and pharmaceutical product recall of 94 stakeholders, including regional regulatory bodies, manufacturers, importers, and wholesalers (August 14–27). Highlights from the preliminary results showed that 61 (65%) of the institutions were aware of the presence of the guidelines; 50 (53%) responded orally that they had received or accessed the guidelines, 36 of which (72%) were found to have the guidelines physically either in hard or soft copy. Other findings include that 44 (47%) of the institutions are using the guidelines for routine activities. The assessment showed that lack of awareness and weak distribution of the guidelines were the top two reasons for not having the guidelines at their facility. The final report is being prepared and will be shared with relevant stakeholders to be used for streamlining of activities in order for guidelines to be availed and used properly.

On September 4–8, PQM supported a review meeting hosted in Assosa, Benishangul gumz regional state, which was attended by 77 participants. The review meeting included representatives from all federal and local branches of EFMHACA, regional and city administration regulatory authorities, the Ethiopian Public Health Institute (EPHI), Ethiopia's Plan Commission, Ethiopia's House of Peoples' Representatives, and different implementing partners. The meeting is a key annual event in which regulatory authorities share their experiences, discuss their challenges, and plan for alignment of their activities. During the meeting, strategic initiatives identified for the coming year included focusing on establishment of internal audit system within health facilities, strengthening implementation of rational drug use, establishing an audit-based inspection system, and collaborating to combat trade in illegal food and medicines. In addition to supporting facilitation of the meeting, PQM made a presentation on the preliminary assessment results regarding the availability and utilization of guidelines.

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

During the previous quarter, PQM conducted supportive supervision at all four EFMHACA branch laboratories, provided hands-on training to Bahirdar Branch Laboratory staff, and trained NMI staff on calibration. Support was also provided to identify and procure primary reference standards for weight calibration for NMI to build its capacity so that it expands the scope of calibration.

In Q4, PQM provided support toward maintaining ISO accreditation and scope expansion. In FY 2017, the plan was to add three additional physicochemical test methods in addition to the existing accredited test methods. In line with this goal, three QMS SOPs were prepared related to titration, Fourier transform infrared, and polarimetry. Training was also given to 7 staff (6 male and 1 female) with technical assistance on development of training materials from PQM while fully funded and cascaded by EFMHACA. Daily logbooks and verification logbooks were prepared. In addition, to meet major QMS requirements for maintaining ISO17025 accreditation, the calibration of 16 EFMHACA laboratory instruments was completed by consultants from CCG with PQM support. The remaining calibration activities are to be undertaken by NMI using EFMHACA funds, which demonstrates the realization of the sustainability strategy that PQM has designed. The cumulative result of the above-mentioned support is progress toward achieving scope expansion of accreditation and maintenance of the already accredited test parameters, which ultimately increases the credibility of results generated by the laboratory. Assessment of the laboratory will be conducted by the end of October.

As part of building QMS at each branch EFMHACA laboratory, lecture-based and hands-on training on basic principles of ISO 17025 QMS requirements was given to the four branches' laboratory staff (July 24–September 10), including 16 staff (12 male and 4 female). The training will be cascaded by EFMHACA staff to regions once their capacity is built by PQM—a key transition to sustain capacity-building and oversight of branch laboratories by EFMHACA. The training is crucial for the branch laboratories to develop and implement QMS documents.

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

In the past quarter, the WHO site inspection on Cadila Pharmaceuticals with respect to ethambutol table took place. In Q4, PQM provided technical assistance to Cadila Pharmaceuticals to address and rectify deficiencies identified during the WHO inspection, as well as in the preparation of CAPA to respond to the findings.

In addition, as a follow-up from the second-round joint assessment (UNIDO, WHO, PQM, EFMHACA, and MOH) of local manufacturers, and as part of the National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia (2015–2025), PQM was assigned to prepare a document that summarizes and classifies findings from the joint assessment. PQM has been working accordingly to make this document available to the committee and EFMHACA. PQM also provided ongoing support in the review, finalization, and implementation of local manufacturers' CAPAs. This will help to establishment current GMP-compliant manufacturers, which ultimately contributes to ensuring the supply of quality-assured medicines from local industries to the public. The expansion of the pharmaceutical industry is in line with both local and international sustainability development goals. The next step is to conduct follow-up inspection jointly with EFMHACA. CAPAs prepared by all local manufacturers will be sent to EFMHACA as an official follow-up document for GMP compliance, as stipulated in the GMP roadmap document.

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

In the past quarter, PQM supported EFMHACA to train and deploy sample collectors to the field and complete the collection of antimalarial and MNCH medicine samples for PMS. Procurement of chemicals and reference standards also began. PQM provided support to develop the protocol, identify sampling areas, and determine sampling size to conduct PMS on oxytocin in collaboration with Monash University.

In Q4, procurement of laboratory supplies to conduct testing of the collected antimalarial and MNCH medicines was completed. The laboratory consumables were delivered to EFMHACA, and testing of collected samples has been started at the Medicine Quality Assessment laboratory. Identification, quantification, procurement, and delivery of these supplies is one of the limiting factors to start testing on time. Timely results would help EFMHACA take regulatory measures in case substandard, falsified, or unapproved medicines are found in the market and ultimately help to protect the public from dangers posed by these medicines by preventing further proliferation.

In addition, as a continuing activity, a second round collection of samples was carried out In Addis Ababa with the support from PQM as part of FY 2017 PMS to meet the sample size number targeted in the protocol. During the first round, there was a shortage of medicines in the market, which resulted in a collection of fewer samples. During this round, a total of 40 MNCH products and 60 antimalarial medicines were collected, bringing the total to 200 MNCH products and 400 antimalarial medicines. The next step in FY 2017 is to complete testing the samples, writing the report, and sharing results.

Objective 6– Strengthen EFMHACA governance and management system

PQM participated in the IGAD member countries' third-round meeting of MRAs, which took place in Ethiopia on August 1–3. The third day of the meeting, in which PQM and other partners participated, focused on sensitization of donors. MRAs from member states discussed technical issues during the 2 days and came up with a proposal for achieving a harmonized regulatory system in accordance with agreed-upon international standards within 5 years. Market authorization, pharmacovigilance, inspection, and PMS were identified as immediate priority focus areas. The proposal will be submitted to the Council of Ministers of member states for adoption. Attendees of the meeting included representatives from IGAD member states (Ethiopia, Somalia, Kenya, Sudan, South Sudan, and Uganda), international organizations (WHO and World Bank), and partners (PQM and UNFPA).

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

In Q4, PQM provided technical assistance to the Addis Ababa University School of Pharmacy to prepare a module on QMS, a core courses in the postgraduate master's degree program for regulatory affairs. The course module has completed development and is under editorial review. Once review of the module is completed, the school will use its own local staff to provide training instead of relying on professors from overseas, which will ensure sustainability of the program in the absence of external support to the program.

Objective 8 – Support the Regional Bioequivalence Center (RBEC) to be compliant with good laboratory practices (GLP)

PQM provided assistance in training staff on advanced bioequivalence studies and clinical trials. A 5-day theoretical and hands-on training was organized for 3 RBEC staff in Jordan to build their technical capacity (September 10–15). The training was essential to address gaps in technical aptitude, as per the WHO PQ mock audit findings. In addition, as part of building RBEC's capacity, PQM supported procurement and supply of relevant laboratory instruments to help RBEC comply with WHO GPPQCL requirements. Building the capacity of staff in such specialized areas will help develop in-country capacity to advance RBEC toward become a recognized bioequivalence study center for manufacturers in the region. This will contribute toward improved access to bioequivalence study services, potentially reduce cost of generic drug development, and ultimately improve access to quality-assured generic medicines for the population of the East Africa region.

Objective 9 – Support the pharmacovigilance activities of EFMHACA

On the invitation of USAID/Ethiopia, PQM is supporting pharmacovigilance activities, one objective of this being to use the existing PV infrastructure to also advance product quality reporting. In Q4, PQM supported the preparation and categorization of ADEs that were reported to EFMHACA during FY 2017. PQM participated and provided technical assistance in two pharmacovigilance forum meetings. This forum, which is attended by the facility inspection and quality control directorate, reviews ADE reports that are related to product defects or poor-quality medicines. During the forum meetings, discussions took place for approximately 10 medical products, including family planning products, infusions, reagents, and antibiotics. A regulatory measure was taken to recall the salmonella antigen test reagent. PQM also provided supervisory support to health care facilities that are carrying out cohort event monitoring on antiretroviral medicines and collecting ADE data. The supportive supervision was helpful to discuss facility-specific challenges and provide feedback proactively. Due to this active follow-up and support, 1,162 ADE data items were collected through active surveillance. PQM also reviewed the SOPs developed by the facility inspection directorate to be used in the management of product quality defect reports that are obtained through the pharmacovigilance system.

IV. Lessons Learned

The support provided to NMI is resulting in an exemplary outcome, as it provided a lesson on how to build and utilize in-country resources through enhancing collaborative efforts among local institutions to sustain key EFMHACA requirements on equipment calibration. The technical assistance provided by PQM to NMI has been a showcase in demonstrating the practicality of utilizing local capacity to address EFMHACA's needs on laboratory instrument calibration. This is a considerable milestone in terms of progressive transitioning from dependence on overseas expertise to reliance on in-country resources for needs related to laboratory equipment calibration. In addition, these new capabilities expanded the Institute's scope of services to include accreditation for the calibration of pressure and temperature instrumentation. To date, this expanded capacity has decreased EFMHACA's use of international contract service providers by two-thirds and reduced annual calibration costs by 58 percent. NMI's ability to offer these services to EFMHACA, local manufacturers, and other associated industries assures that laboratory instrumentation is properly calibrated so that potentially life-threatening quality concerns in medicines can be identified.

Ghana

I. Quarter 4 Highlights

In August 2017Q4, in accordance with USAID's goal to improve GMP compliance of local manufacturers of ACT antimalarial medicines toward WHO prequalification, PQM collaborated with the Ghana Food and Drug Administration (GFDA) to issue an expression of interest (EOI) to identify local manufacturers of ACT tablets interested in receiving PQM's technical assistance. PQM received interest submissions from four local manufacturers. An initial assessment of an evaluation questionnaire submitted as part of the interest is ongoing. PQM will work with GFDA to screen eligible manufacturers in order to focus on those that have the necessary infrastructure in place. Technical assistance will be based on CAPA generated after a full assessment of the manufacturing site.

Following the Q3 release of the PMS report for zinc sulfate tablets, which highlighted the failure of some batches, GFDA initiated a regulatory action mandating the manufacturer to recall all failed batches from the market. Additional

actions are also being required by GFDA to ensure the quality and safety of zinc sulfate tablets available to its population.

Planning for the next round of PMS of antimalarial samples is progressing steadily. Necessary reagents and chemicals have been procured and supplied to GFDA. Minilab™ kits procured for this activity have been delayed at the port of entry, but GFDA is taking steps to clear the Minilab™ test kits from Ghana customs in preparation for the commencement of the project. The number of sentinel sites is now being increased from 7 to 10.

II. Country Context

In Ghana, the PQM program was funded by PMI in FY 2008 to strengthen the QA of antimalarials in the country. PMI Ghana has funded PQM to provide technical assistance and build capacity to improve efforts to ensure medicines quality in the country. The program in Ghana has focused on GFDA support by ensuring the QC of medicines prior to registration and on PMS of antimalarials in the marketplace. The antimalarial MQM program in Ghana has led to the identification of several falsified and substandard medicines, which has prompted GFDA to recall several batches of antimalarials from the market and to refer the illegal activities to law enforcement agencies. Based on the outcome of antimalarial MQM over the years, GFDA 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.

PQM has also received funds from the Maternal and Child Health program at USAID/Ghana since 2011 to strengthen the quality control of MNCH commodities (such as uterotonics medicines) in Ghana. The outcome of the FY 2015 MQM report on the quality of uterotonics (oxytocin and ergometrine) indicated that a high percentage of uterotonics in the Ghanaian market do not meet the required quality standards, which could have serious implications for maternal mortality in the country. PQM continues to support MQM activities to monitor the quality of MNCH commodities in the Ghanaian market.

III. Quarter 4 Progress by Objective

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

In Q4, GFDA drafted an overarching PMS guideline and submitted it to PQM for review. Chemicals and reagents needed for the next round of medicines quality surveillance were purchased and supplied to GFDA for dissemination to the various sentinel sites. Minilab™ test kits and consumables are currently being cleared with Ghana's customs; once received, risk-based sampling of antimalarial and analgesic medicines based on the developed protocol will commence. GFDA has also increased the number of sentinel sites from 7 to 10 to ensure better PMS coverage, a testament to GFDA taking increasing ownership of PMS activities.

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

In collaboration with PQM, GFDA undertook a second round of PMS for zinc sulfate tablets. The project began with sampling products at various sites across the Greater Accra Region on January 24–26, 2017. Results from the surveillance indicated that 7 out of the 50 zinc sulfate tablets (14%) sampled failed the disintegration test. One of the batches that failed the disintegration test also failed the assay test.

Following the PMS, GFDA management formulated a number of recommendations, including the following:

- The manufacturer should recall the nonconforming batches from the market.
- GFDA should ensure the manufacturer initiates an investigation to determine the root cause of the nonconformance and presents a CAPA to GFDA.
- GFDA should meet with stakeholders to disseminate the results and create awareness of the need for further surveillance programs.
- GFDA should conduct further rounds of PMS for zinc sulfate tablets over a period to establish additional data about the quality of the product on the Ghanaian market.

Following the issuance of the surveillance report, GFDA has instituted regulatory actions, and the manufacturer recalled all failed batches from the market. Additionally, since further investigation of the failure suggested tablet hardness, the manufacturer has agreed to begin monthly checking of the control samples of all batches to undertake

hardness testing at all compression stages, which should ensure uniformity. The manufacturer will also conduct stability studies on a reformulated batch that will contain an extra quantity of crospovidone (a disintegrant).

The surveillance report has been shared with the USAID/Ghana Mission.

Objective 3 – 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

A formal ISO 17025 accreditation certificate for the GFDA laboratory was issued with scope covering four laboratories—pharmaceutical physical chemistry, pharmaceutical microbiology, medical devices, and food microbiology. Maintaining this accreditation reflects that the GFDA laboratory continues to accurately and reliably asses the quality of medicines and medical devices in accordance with internationally acceptable standards.

In Q4, PQM carried out an inventory of SOPs and QMS documents developed in collaboration with GFDA laboratory. Based on GFDA records, 213 documents comprising 92 SOPs, 24 QMS documents, 4 guideline documents, 45 work instructions, and 48 forms were developed and are effective (in use) since 2014 to date.

PQM has also provided equipment and consumables, such as HPLC syringe filters and analytical balances, to ensure the laboratory accreditation is not jeopardized.

Objective 4 – Increase the availability of quality assured locally manufactured priority (antimalarial) medicines

To increase the availability of quality-assured priority medicines, local manufactures must comply with GMP. PQM proposed to assist local manufacturers of USAID priority medicines (antimalarials) to improve the GMP compliance of their facilities in Ghana. In Q4, an EOI to identify local manufacturers of ACT antimalarial medicines that meet set technical criteria was issued. The EOI advertisement was published on August 14, 2017, and also emailed to all ACT manufacturers in Ghana. Four ACT manufacturing companies have expressed interest so far and are currently being evaluated for consideration to receive technical assistance from PQM. A full assessment visit planned for September has been rescheduled for October 2017.

Guinea

I. Quarter 4 Highlights

During this quarter, PQM continued to support the revision of the national pharmaceutical law process. The final draft of the revised law entitled "Preliminary Draft Law on Medicines, Other Health Products and Pharmaceutical Exercise" was submitted to the Minister of Health for approval in September 2017.

Based on the recommendations drawn from the assessment of the National Directorate of Pharmacy and Laboratories' (DNPL) registration department, PQM provided five modules aligned with Common Technical Document (CTD) format to serve as guides for the registration process.

For the National Laboratory for the Quality Control of Medicines (LNCQM), PQM procured and installed a Karl Fischer titrator (used to determine moisture and water presence in medicines) and an analytical precision balance (which provides highly precise and accurate weighing). These two pieces of equipment are necessary for medicines quality control. PQM provided training to 10 laboratory staff on the use and maintenance of the newly procured equipment. PQM consultants also repaired five pieces of laboratory equipment: an HPLC, two ultraviolet spectrometers, a balance, and a rotary evaporator machine.

PQM consultants reviewed GLP with the laboratory staff and provided five SOP documents for the Karl Fischer titrator, analytical balance, and HPLC to serve as reference for day-to-day use. A guide for the quantification of the analytical balance was also provided to the laboratory staff. These SOPs will be an integral part of the LNCQM quality manual.

II. Country Context

Together with other donors and USAID partners, PQM supports efforts to strengthen the pharmaceutical system. Like other African countries, Guinea is often disproportionately affected by the burden of poor-quality medicines. PQM can

play a key role in strengthening the pharmaceutical system and the capacity of the national drug regulatory authority to assure the quality of medicines in the supply chain through registration, inspection, and QC activities. Malaria is the primary cause of consultations, hospitalizations, and deaths in Guinea—it especially affects children under 5 years of age. In 2011, Guinea was included in PMI; USAID and partners in Guinea are not only procuring malaria commodities but are also helping to strengthen health and pharmaceutical systems.

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

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

III. Quarter 4 Progress by Objective

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

Revision of Law 94/012/CTRN on pharmaceutical legislation
In Q4, PQM continued its contribution to the revision of Law 94/012/CTRN on pharmaceutical legislation by conducting several workshops and meetings, including:

- Participation at the meeting with the national pharmaceutical committee, international experts (Systems for Improved Access to Pharmaceuticals and Services (SIAPS) consultant), and others to discuss proposals for the organization and practice of pharmaceutics in Guinea.
- Participation in the work of the commission appointed by the Minister of Health to finalize the entire law project. The final text was adopted by this process and named "Preliminary Draft Law on Medicines, Other Health Products and Pharmaceutical Exercise." It was submitted to the Minister of Health in the first week of September 2017.

The USAID Mission, Minister of Health, Guinea DNPL, and General Inspector of Health acknowledged and highly appreciated the major contribution to attain this achievement of finalizing the law draft. Next steps include the following:

- The draft will be studied by the Cabinet of the Minister of Health in order to become the "Law Project on Medicines, Other Health Products and Pharmaceutical Practice."
- This law project will be submitted to the government to be adopted by the Council of Ministers and submitted to the National Assembly.
- The texts of application of the new law (six texts) will be prepared.
- The Minister of Health and USAID Mission asked PQM to continue working with DNPL and the commission during the adoption of this law project by the Council of Ministers before its submission to the National Assembly.

After approval of the revised pharmaceutical law, called pre-project, there is a need to develop texts of application of this law. The texts define the requirements needed to apply the revised law. The requirements include a set of decrees—Acts that clearly define how to apply the legislation. For example, the law indicates market authorization is required to sell any medicines in Guinea. The application text would provide the set of requirements needed from the application to register the medicines at DNPL. After this step is taken and all registration requirements are fulfilled, the applicant would be granted marketing authorization to sell the registered medicine in the Guinean market. PQM will be involved in drafting the application texts with the commission and other members of the MOH.

Objective 2 – Continue strengthening DNPL capacity in product registration

Assistance to DNPL registration department
During Q2, PQM conducted an assessment of the DNPL registration department and provided recommendations for improving the registration processes. As a follow-up to this activity, in Q4 PQM provided a document called "Guidelines for Medicines Registration in Guinea." It is an adaptation of requirements to international standards, taking account of the limited human resources of the country. The second document related to how to use an automatized system called SIAMED (previously installed by DNPL via WHO) and what the functionalities of the system are was also provided.

To improve the registration process in Guinea, PQM provided DNPL with five modules aligned with the CTD format, including those on administrative data and proposals, product information, and others.

As next steps, PQM will continue providing assistance to DNPL for the registration system through the development of SOPs and work instructions. PQM will also support the strengthening of medicine registration activity and improve governance in this area.

Objective 3 – Enable DNPL to assume MQM responsibilities

PQM will finalize the PMS draft protocol based on WHO and international guidelines and recommendations from the PMS workshop that took place in Coyah in July 2017. This draft will also take into account risk-based PMS. The PMS protocol will then be submitted to DNPL and key stakeholders for validation and approval prior to the implementation of the first PMS exercise in Guinea.

Objective 4 – Strengthen QC capacity of LNCQM

PQM continues to support and strengthen LNCQM's capacity through the training of the laboratory staff, procurement and installation of new laboratory equipment, and repair and preventive maintenance. PQM procured a Karl Fisher and analytical balance, which were installed on September 11, 2017.

During this quarter, PQM consultants provided theoretical and hands-on training to 10 laboratory staff (9 males, 1 female) on utilization, preventive maintenance, and troubleshooting of the newly procured equipment. Preventive maintenance or repair were also performed on two UVs, an HPLC, a balance, a rotary evaporator, a vacuum pump, a melting point apparatus, a titrator, and a water distiller. The laboratory's status since the last visit was assessed and updated. PQM consultants reviewed GLP and provided SOP documents for the Karl Fischer titrator, analytical balance, and HPLC to serve as reference for day-to-day use. A guide for the quantification of the analytical balance was also provided to the staff. These trainings will help the laboratory to start conducting compendial testing using international standard methods that will move it toward international accreditation.

Liberia

I. Quarter 4 Highlights

In September 2017, PQM supported LMHRA and the National Malaria Control Program (NMCP) to conduct an exercise to remove selected antimalarial monotherapies from circulation in Nimba County. While Liberia is 1 of the 49 countries that have taken steps to ban the use of oral artemisinin-based monotherapy, medicines quality surveillance reports have consistently demonstrated the widespread use of amodiaquine monotherapy for the treatment and management of malaria in Liberia. WHO recommends combination therapy to treat malaria and discourages artemisinin-based monotherapies.

Strengthening LMHRA's regulatory and quality assurance capacity for antimalarial medicines in Liberia has helped curb the circulation of antimalarial monotherapy. This exercise manifested the confiscation of over $68,000 USD worth of antimalarial monotherapy and other unregistered antimalarial medicines. The confiscated products were incinerated in the presence of key stakeholders and WHO and EPA representatives. Ten different types of unregistered antimalarial medicines were identified, and LMHRA issued citations for five major violators to an

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

administrative hearing.

II. Country Context

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

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

In Liberia, PQM is focused on:

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

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

III. Quarter 4 Progress by Objective

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

During this quarter, PQM planned to conduct dossier evaluation training. However, due to the fire incident at the laboratory in May 2017, PQM has postponed this training until November 2017.

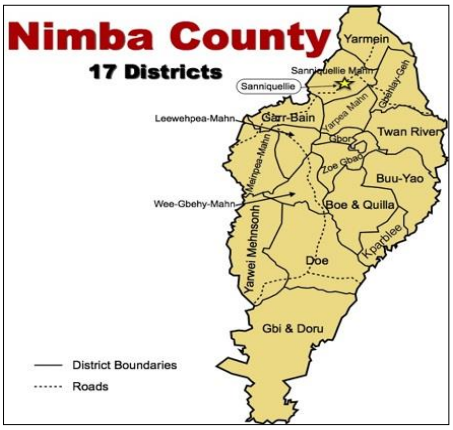
Objective 2 – Continue strengthening the quality control of LMHRA QC lab toward ISO 17025 accreditation

The recent fire incident affected the implementation of PQM's initiatives in the country, and Liberia's medicines quality control capacity was severely affected. As a result, PQM assisted LMHRA in developing a concept note to work with the Global Fund to build a transitional laboratory. PQM also supported LMHRA in finding an alternative solution for testing the quality of antimalarials submitted for registration and collected under the PMS program. These samples will be tested at the USP laboratory in the interim.

Objective 3 – Build the capacity of LMHRA on the post-marketing surveillance program for the monitoring of the quality of antimalarial medicines

Inspection and removal of antimalarial monotherapy from medicines shops, pharmacies, and health facilities in the 17 districts of Nimba County

The LMHRA/NMCP combined PMS and monotherapy exercise was conducted in the 17 districts of Nimba County for 9 days (August 22–29). A total of 343 pharmacies, medicine stores, open markets, and health facilities were inspected. The exercise resulted in the removal of 27,600 packs of amodiaquine monotherapy (of 3 tablets each) from the market. Additionally, 143 cartons of medicines (over 100,000 pieces of assorted unregistered and falsified quinine tablet, artemether injection, and other products) were removed from the inspected facilities. In total, the confiscated products were worth an estimated $68,000 USD (over 8 million Liberian dollars).



The incineration of these products was conducted by the EPA of Liberia, LMHRA, and NMCP, in the presence of a WHO representative, MOH, county authority, the press, and the general public.

The majority of recalled monotherapies were more pronounced in Garr Bain (38%), Zoe–Gbao (20%), and Sanniquellie-Mah (1%5). These districts are close to the porous border with Guinea.

Public Awareness and Dissemination Meetings
During this exercise, LMHRA and NCMP organized 34 public awareness sessions that were held in towns, villages, and cities in Nimba County. The main observations from these meetings were:

- Sellers and consumers have limited information about antimalarial monotherapy use and ACT as recommended treatment for malaria.
- Sellers and consumers were unfamiliar with how to identify unregistered or falsified antimalarial medicines.
- Unregistered and falsified antimalarial medicines can be cheaper, which may encourage the general public at the district level to purchase from illicit markets.
- Quality ACTs are not readily available in Nimba County for wholesale and distribution.

A dissemination meeting was held in Ganta City on September 7 to present findings from the monotherapy recall exercise. The meeting was attended by 58 participants from the Nimba County Health Team, NMCP, LMHRA, and DEA. Also present were the Liberia National Police, civil society groups (e.g., Marketing Association, Concern Women), and the Nimba County Medicines Store Association. Main outcomes from this meeting indicated that there is a need to:

- Conduct training on visual and physical inspection.
- Coordinate activities with LMHRA at the central and regional level and inform LMHRA on registered products.
- Work closely with the association of pharmacists and civil society.

A detailed report on this exercise, along with next steps, is being prepared and will be shared with key stakeholders.

Dissemination meeting to present findings from monotherapy recall exercise

Objective 4 – Promote regulatory actions and raise awareness about poor quality medicine in country and at regional levels

In addition to the five regulatory actions taken during the monotherapy exercise, PQM is working with LMHRA on the organization of a regional meeting with MRA directors from the sub-region, including Sierra Leone, Ivory Coast, Burkina Faso, and Senegal, to share the outcomes of this exercise and to build a network toward joining efforts to combat the circulation of monotherapies and unapproved and falsified medicines. This meeting is planned for November or December 2017 in Liberia.

Mali

I. Quarter 4 Highlights

The highlight of this quarter was a dissemination workshop that PQM facilitated on PMS activities conducted between April and August 2017. The workshop was also used to share the outcome of the joint mission by the National Laboratory of Health (LNS), Directorate of Pharmacy and Medicine (DPM), National Directorate of Health (DNS), Central Medical Store (PPM), and National Malaria Control Program (PNLP) to take actions on falsified quinine sulfate. Participants in the workshop were from DPM, DNS, LNS, PPM, Regional Directorate of Gao, Kayes, Koulikoro, Mopti, Segou, Sikasso, Pharmacists National Council, WHO, and other institutions. During PMS activities, 586 samples were collected. PQM conducted an assessment of key institutions involved in the pharmaceutical quality assurance system and assisted LNS in revising SOPs.

II. Country Context

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Strengthen the capacity of the National Quality Control Laboratory in Mali

To strengthen LNS' analytical capacity and QMS, PQM assisted the laboratory and QA managers in developing a form to assess the capability of each analyst. The analysts were interviewed and the forms filled out. The information collected will be used to develop an LNS training plan. LNS is currently revising all of its SOPs. During a recent visit to LNS, the LNS QA manager sought the PQM Senior Program Manager for assistance to develop CAPAs to address deficiencies identified by auditors of LNS' microbiology laboratory. This was done at an all-staff meeting, which gave an opportunity to look into the challenges that other LNS services were facing and propose solutions that will apply to overarching activities. The Senior Program Manager provided suggestions for the CAPAs. PQM reviewed LNS procedures, including SOPs for microbiology laboratories, and suggested to the QA manager to avoid duplication of overarching SOPs. PQM helped the QA manager revise two of these procedures, including Document Control and Procedure of Procedures.

Objective 2 – Strengthen Post-marketing surveillance of antimalarial medicines in Mali

PQM facilitated a workshop to disseminate the results of the PMS activities conducted between April and August 2017. The workshop was also used to share the outcome of the joint mission by LNS, DPM, DNS, PPM, and PNLP to investigate the incident of falsified quinine sulfate found at three regions and take regulatory actions. PMS activities were carried out in the District of Bamako and the regions of Koulikoro, Mopti, Segou, and Sikasso. Participants in the workshop were from DPM, DNS, LNS, PPM, Regional Directorate of Gao, Kayes, Koulikoro, Mopti, Segou, and Sikasso, Pharmacists National Council, WHO, and other institutions.

During PMS activities, 586 samples were collected. Following visual inspection, a risk-based approach was applied to 256 samples selected for further testing. Six samples (three Coartem and three quinine sulfate) were found to be noncompliant, lacking API. Falsified Coartem was found in the informal market, while falsified quinine sulfate was found in the public sector.

Samples selected for testing in Mali

The joint mission to investigate the source of falsified quinine took place on August 7–13 in the regions of Koulikoro, Segou, and Sikasso. This was the first joint mission organized after the development of the strategic action plan for improved communication, coordination, and collaboration among DPM, LNS, and Health Inspectorate (HI) to address the lack of or slow regulatory action on PMS of pharmaceuticals and other health products. PQM contributed to development of the strategic action plan, which was spearheaded by the WHO country office. Investigators met with local authorities before visiting the sample collection sites. The main results of the investigations include the following:

- No falsified quinine sulfate was found at the health centers visited.
- Health centers do not procure medicines from regional PPM warehouses; some products were procured from unauthorized wholesalers.
- Other suspicious medicines were found (erythromycin, cotrimoxazole, vitamin B, ferrous sulfate, and unauthorized combination of chlorpheniramine–ibuprofen). In the past, falsified erythromycin had been found, and DPM had issued order for its removal. In 2010, falsified quinine sulfate was found during MQM of antimalarials, indicating that supply chain control needed strengthening.
- Local authorities in Koulikoro ordered these products quarantined; in Sikasso, the local authority committed not to sign any purchase order for procurement of pharmaceutical products from outside of PPM without a certificate of nonavailability from the latter.
- LNS provided training on visual inspection of pharmaceutical products to health center professionals.

Workshop participants provided the following recommendations:

- Disseminate PMS results at the regional level.
- Expand PMS activities using screening techniques to other medicines.
- Include other institutions in PMS activities.
- DNS should include sampling and screening of medicines as one of its activities (this will facilitate the implementation of PMS activities at the regional level).
- Publicize PMS activities.

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

Laboratoire de Biologie Moléculaire Appliquée (LBMA) has completed the first two milestones in each of the two subawards (Efficacy of ACTs and Resistance of SP and Amodiaquine Used in Seasonal Malaria Chemo-prophylaxis).

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

Following the assessment of DPM in May, PQM conducted an assessment of key players in the medicines quality assurance system, including LNS, PPM, National Centre of Reference for Pharmacovigilance, HI, National Council of Pharmacists Association, and National Council of Physicians Association. The gaps identified and recommendations to address them will be shared and discussed with all stakeholders at a workshop to be organized in November 2017. Among the recommendations that need immediate attention is the establishment of a mechanism to implement the strategic action plan for coordination among DPM, LNS, and HI. It is suggested to create a liaison committee with one or two representatives from each institution that will meet weekly and provide meeting minutes within 24 hours following the meeting. The management should meet monthly and submit a report to the Secretariat General.

IV. Key Challenges

Although the personnel situation has improved with the hiring of new staff, LNS is still facing challenges of personnel turnover. Two management personnel were forced to leave LNS but were quickly replaced.

Mozambique

I. Quarter 4 Highlights

This quarter, PQM built the capacity and skills of eight laboratory staff (four male, four female) on instrument performance verification and equipment maintenance. Mastering these skills will help the laboratory staff troubleshoot and fix basic equipment problems and conduct performance verification of HPLC and timers without the need of a paid outside vendor. This is in line with PQM's efforts to support the laboratory to become self-sustaining in certain areas.

PQM conducted an oxytocin study in Maputo city and Maputo province to assess the quality of oxytocin injection in these locations. Information from this study will inform whether a wider study is needed and whether there is a need to take any regulatory actions to safeguard the supply and use of this product.

PQM developed a costed architectural plan for the national quality control laboratory (LNCQM) expansion to provide information it anticipated the Global Fund would request during the grant-making meeting in September; this aims to justify the request for grant support for LNCQM expansion.

PQM also provided support to the Pharmaceutical Department (PD) for the revision of the price schedule for services and the development of a national medicine policy.

II. Country Context

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

PQM conducted a rapid assessment of the PD's QA/QC capabilities in December 2010, which revealed that LNCQM's infrastructure, equipment, and staff were inadequate to provide QC services. The assessment also identified a lack of PMS of medicines quality. In 2011, PQM and PD partnered to establish an MQM program that included training on screening 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 laboratory. To date, LNCQM has improved its technical capacity in analytical testing, proficiency, and use of key equipment. Through this PQM training, LNCQM is better able to collaborate with other Portuguese-speaking countries.

III. Quarter 4 Progress by Objective

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

This quarter, PQM's technical specialist visited LNCQM to provide hands-on training on preventive maintenance and performance verification of the HPLC and timer equipment in the laboratory. This activity built the capacity and skills of eight laboratory personnel (four male, four female) on how to maintain and verify the equipment without an outside vendor. During this training, support was provided to the laboratory on instrument categorization and risk-based prioritization, as well as on how to develop an instrument master list, performance verification plan, and SOPs for usage and software administration. The technical assistance provided will help the laboratory align its practices with internationally recognized GLP. Support was also provided to install newly acquired equipment in the laboratory.

Another PQM specialist travelled to Maputo this quarter to provide technical support for repairing and maintaining malfunctioning laboratory equipment. During this trip, using a hands-on training approach, an assessment of the status of laboratory equipment was conducted, malfunctioning equipment fixed, and an equipment maintenance plan

developed. Training included building skills on how to perform routine maintenance and replacement of malfunctioning parts for fume hoods, HPLCs, UV/Vis, and potentiometric titrator T50 equipment. The purpose of this training was to build the knowledge and skills of laboratory staff to carry out basic troubleshooting and repairs of malfunctioning equipment before procuring the services of an outside vendor for repairs.

To support LNCQM in preparing for the planned Global Fund grant making meeting on the laboratory expansion grant request, PQM engaged an architect to develop a costed architectural plan for the laboratory expansion project. The plan was finalized and submitted to LNCQM before the planned meeting.

To facilitate equipment maintenance, training on performance verification, and the oxytocin sample testing, PQM procured reagents, spare parts, and reference standards for the laboratory.

Through PQM's support, Mozambique has been a member of the Network of Official Medicines Control Laboratories (NOMCoL) since around 2010. NOMCoL offers unique inter-laboratory testing (ILT) activities for participating laboratories to improve performance and harmonize methodologies for medicine analysis to detect substandard and falsified medicines. This quarter, PQM facilitated discussions between NOMCoL and LNCQM for participation in this year's ILT. Results from ILT are expected by the next quarter.

PQM conducted a rapid assessment of the food and water laboratory's capabilities and strengths to develop recommendations on how this facility can potentially complement LNCQM with tests that LNCQM does not have the capacity to perform (sterility and bacterial endotoxin test for oxytocin injection). The final report will be available next quarter.

Objective 2 – Support and strengthen post-marketing surveillance

This quarter, PQM conducted an oxytocin study and collected oxytocin injection samples from Maputo city and Maputo province in response to the country's request to assess the quality of oxytocin injection in the local supply chain. The 50 samples collected for the study were mostly from different levels of public sector facilities, with minimal samples from the private sector due to unavailability of the product at the facilities sampled. Results from this study will provide a snapshot of oxytocin injection quality at the sample collection sites and will inform decisions about the need for further investigation and regulatory actions.

PQM built the capacity and skills of LNCQM staff through hands-on compendial testing of the medicine samples collected. Confirmatory tests will be conducted by an external laboratory. The final report is expected next quarter.

Objective 3 – Provide technical assistance to the Pharmaceutical Department

PQM provided technical assistance to the PD to conduct a comparative assessment of fee schedules for MRAs in the region. This information was requested by PD to inform and justify revision of its fee schedule for PD services in preparation for the signing of the new pharmaceutical law by the president.

PQM also provided background information on global standards and recommendations on development and implementation of a national medicine policy including information on establishment of a working group committee that will be charged with development of the national medicine policy.

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

No updates this quarter.

Nigeria

I. Quarter 4 Highlights

This quarter, analytical results for assay and disintegration time of Daily Need's amoxicillin 250 mg dispersible tablet (DT) that was reformulated with PQM's support confirmed compliance with USP 40–NF 35 specification. This key step is a notable milestone as Nigeria gradually moves toward having its first quality-assured locally produced amoxicillin DT to treat respiratory tract infections, including pneumonia, which is one of the leading causes of death among children under 5 in Nigeria.

PQM also worked with NAFDAC to complete the review of the Drug Evaluation and Research Directorate inspectors' guide that was started in Q3. The inspectors' guide, which acts as a working manual for GMP inspectors, is a critical part of NAFDAC's regulatory framework and will facilitate the implementation of regulations and improve compliance and enforcement actions for the production of quality medicines in Nigeria.

Another milestone this quarter is that the technical support provided to NAFDAC's PV/PMS Directorate and the ISO accreditation of three NAFDAC laboratories has resulted in income generation for sustainability and strengthened the capacity and skills of laboratory staff to carry out PMS as a routine activity. In July, the National Tuberculosis and Leprosy Control Program requested NAFDAC to lead the survey and conduct quality control tests for 150 samples of first- and second-line anti-TB medicines to be collected across the country. PQM reviewed the draft protocol jointly put together by NAFDAC, NTBLCP, and the Institute of Human Virology of Nigeria (one of two Global Fund principle recipients for TB) for the survey of anti-TB medicines in Nigeria public health facilities. PQM recognized deficiencies in the draft protocol and provided technical guidance to improve the following: developing the sampling plan; differentiating national TB guidelines from a QA protocol; identifying sample tools; and providing scientific rationale for sample size, a template for sample information, and guidance for budgeting. PQM facilitated discussions among NTBLCP, IHVN, and NAFDAC and provided input to amend the MOU for NAFDAC to access Global Fund resources for medicines quality testing. In this MOU, NAFDAC will generate revenue to further sustain laboratory services and PMS activities through payment received from Global Fund for TB, HIV and malaria medicine sample testing.

PQM reassured NTBLCP and IHVN of NAFDAC's competence to lead the survey and conduct reliable QC testing. NTBLCP and IHVN will provide the funds for NAFDAC to test the samples, generating revenue for the laboratories. This development demonstrates sustainability in both the PMS and laboratory services of NAFDAC.

Another milestone this quarter included NAFDAC's Yaba laboratory being listed as a Regional Center of Regulatory Excellence by the New Partnership for Africa's Development. NEPAD is an economic development program of the African Union, and selection of the laboratory demonstrates NAFDAC's major regional role in the support of monitoring and testing medicines quality across countries in West Africa.

PQM also built the capacity and skills of staff from different agencies during this quarter. PQM trained 35 National Institute of Pharmaceutical Research and Development (NIPRD) staff (15 females, 20 males) on QMS in preparation for ISO/IEC 17025 accreditation, as well as 16 NAFDAC PV/PMS Directorate staff (5 females, 11 males) on the use and application of the TruScan™ device to support MQM. The NIPRD technical training was successful, and the staff were eager to learn. Participants scored an average of 43 percent on pre-tests. After the training, a post-test score showed an improvement of 77 percent. PQM is increasingly leveraging funds with NIPRD and NAFDAC for these trainings. NAFDAC funded the procurement of 10 TruScan™ devices; NIPRD and NAFDAC provided funds for the training expenses, and PQM provided technical assistance.

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

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

PQM's overall goal in Nigeria is strengthening NAFDAC's regulatory capacity and increasing the supply of locally manufactured quality-assured priority medicines. To accomplish this goal, PQM will continue to provide technical assistance to NAFDAC, the Federal Ministry of Health, the Pharmacists Council of Nigeria, 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 4 Progress by Objective

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 sulfate injection, and ready to use therapeutic foods [RUTF]) in compliance with international quality standards

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, including antimalarials and critical medicines for mothers and children. Technical assistance is provided to local manufactures throughout the process to become approved by an SRA or local national regulatory authority, from early initiatives to the final submission of the application or dossier.

In Q2, PQM supported Daily Needs Industries, a local manufacturer, to reformulate amoxicillin DT to ensure compliance with quality standards. This new formulation is cost effective for local production and yielded quality products. The new formulation process reduces manufacturing time and consumption of energy, with an estimated $80,000 USD in savings compared to the previous formulation. This quarter, an investigative procedure for qualitatively and quantitatively assessing the reformulated product was conducted in Rockville, MD, in the United States. The results for assay (to determine the content or quality of the product) and disintegration time (time required for a dosage form to break up into granules of specified size or smaller under carefully specified conditions) showed 100-percent compliance with the USP 40–NF 35 specification. Nigeria is gradually moving toward having its first quality-assured locally produced amoxicillin DT to treat respiratory tract infections, including pneumonia—one of the leading causes of death among children under 5 in Nigeria. Next steps for Daily Need include process validation for commercial batches, continuation of accelerated stability studies (expected to be completed next quarter), and conclusion of dossier compilation that meets SRA standards or demonstrates compliance with donor agencies' procurement requirements, as this will expand the procurement reach of this product beyond Nigeria.

Also this quarter, Emzor Pharmaceuticals indicated interest in the production of ready-to-use therapeutic foods. The PQM GMP group provided technical support in the requisite facility design; as next steps, PQM will provide technical guidance on equipment selection.

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

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 two possible results 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 laboratories. WHO PQ aims to increase the supply of quality-assured priority medicines by applying unified standards of acceptable quality, safety, risk, and efficacy to guide procurement decisions by United Nations agencies and other entities involved in procuring bulk medicines.

Entrenched sustainability of USAID's support to NAFDAC through the PQM program
This quarter, NAFDAC and Catholic Relief Services (CRS), a Global Fund principal recipient, signed an MOU for testing all Global Fund-procured antimalarial medicine samples. The MOU outlines that CRS will pay for samples to be tested by NAFDAC and that NAFDAC will perform routine monitoring of Global Fund-procured samples in public health and storage facilities. PQM assisted in brokering the negotiation and protocol review process between CRS and NAFDAC and ensuring that the fee was appropriate. With this increased source of revenue, NAFDAC will be in a much better position to expand and maintain the accreditation status of its laboratories.

NTBLCP requests NAFDAC conducts PMS of anti-TB medicines in public health facilities
This quarter, meetings between NTBLCP, IHVN, and NAFDAC commenced for PMS for anti-TB medicines in Nigeria. PQM reviewed the draft protocol jointly put together by the three organizations for the survey of anti-TB medicines in public health facilities. The review process included developing the sampling plan; differentiating guidelines from protocol; identifying sample tools; and providing scientific rationale for sample size, a template for sample information, and guidance for budgeting. PQM also provided input into the MOU between NTBLCP and NAFDAC. This development will increase income revenue for NAFDAC to support self-sustained routine PMS activities.

Presentation of ISO/IEC17025:2005 accreditation certificate to NAFDAC Kaduna regional laboratory
Last quarter, ANAB made an official notification of ISO/IEC17025:2005 accreditation in seven scopes (HPLC, ultra-violet visible spectroscopy, pH measurement, dissolution, loss on drying, Karl Fischer water content determination, and uniformity of dosage form) to NAFDAC's Kaduna regional laboratory. This quarter, the USAID Deputy Mission

Director and USP CEO presented the ISO/IEC17025:2005 accreditation certificate to the Honorable Minister of State for Health and the Acting Director General of NAFDAC. In attendance to grace the ceremony was the United States Ambassador to Nigeria, represented by Ms. Erin Holleran; USAID Deputy Mission Director; USAID Health, Population, and Nutrition team; representatives from the Pharmaceutical Society of Nigeria; President of the Consumer Protection Council; Registrar-Institute of Public Analysts of Nigeria (IPAN); Director General of NIPRD; representatives from CRS; and several other dignitaries. This is the third laboratory in Nigeria to attain ISO/IEC 17025 accreditation with PQM's support. Next steps include the preparation for expansion of scope in microbiology for the three laboratories scheduled to commerce next quarter. Microbiology tests are required for certain USAID priority MNCH commodities.

NIPRD intensifies preparation for accreditation
PQM developed a roadmap for accreditation with the management of NIPRD last quarter. As part of implementing the roadmap, NIPRD is expecting a $10 million USD grant from the Japanese government to support equipment procurement. PQM has begun hands-on training to key personnel in the laboratory and completed all procurement for laboratory consumables. Next steps include preparation for a mock audit of the laboratory, which is scheduled for next quarter.

Objective 3 – Strengthen NAFDAC's Registration Unit (R&R) capacity to manage registration information

PQM collaborated with NAFDAC's Registration and Regulation Directorate to ascertain the needs for development of a medicines registration information management system that improves efficiency in product registration processes. This quarter, PQM made a formal presentation of a completed assessment report to the management of NAFDAC. Some of the short-term recommendations are already being implemented. This includes the inspector's guideline recently reviewed by PQM and an approved MOU between NAFDAC and Merck Life Science for bulk supply of chemicals and reagents. Additionally, the Central Bank of Nigeria will be releasing a sum over $2 million USD for the purchase of equipment and reagents to the NAFDAC. The PQM team also worked with the NAFDAC Registration and Regulation Directorate to complete the revision of three SOPs: (1) forwarding samples of drug products to the laboratory for analysis; (2) processing import permit for medical devices; and (3) assigning NAFDAC registration numbers to medical devices products following Food and Drug Regulatory Committee approval. Next steps include the approval and operationalization of the reviewed SOPs.

Objective 4 – Strengthen NAFDAC Drug Evaluation and Research Directorate capacity for inspections and dossier evaluation

The Drug Evaluation and Research Directorate is committed to the development and continued improvement of its QMS to ensure a robust and effective inspectorate that will guarantee safe, effective, and quality medicines. The Directorate has been using an inspection guideline that was last reviewed in 2009. In Q3, PQM started providing technical support to the Directorate to review the inspectors' guideline to ensure it is harmonized with regional and international standards. This quarter, the revision process was completed with a section-by-section review. Areas of amendment included development of templates for CAPA, confidentiality declaration, conflicts of interest, inspection meeting agenda, SOP on group GMP inspection using the pharmaceutical inspection scheme/convention approach, and a model for risk-based GMP inspection. The operationalization of the guideline commenced with foreign facility inspection in India facilitated by NAFDAC. Next steps include the ratification of the revised guide by NAFDAC, step-down training on the use of the guide to other Directorate staff by PQM-trained NAFDAC staff, and one round of inspection at two different local manufacturers.

Objective 5 – Strengthen NAFDAC's PMS Directorate capabilities

PQM Nigeria focuses on building NAFDAC's capacity to perform PMS as a regulatory function, which is aimed at assessing product quality in the market. This includes monitoring the quality of marketed products throughout all levels of the supply chain. As part of a multipronged approach in addressing the challenge of oxytocin storage conditions in Nigeria, PQM facilitated a workshop on good storage and distribution practices for marketing authorization holders of oxytocin injection. In attendance were the NAFDAC Acting Director General, directors of the various directorates, the PQM team, the Chairman and Executive Secretary of the Pharmaceutical Manufacturers Group of Manufacturers Association of Nigeria, the President of the Pharmaceutical Society of Nigeria, and representatives of the Pharmacists Council of Nigeria.

Key outcomes of the meeting included:

- Prospective market authorization holders without suitable storage facilities will not be given marketing authorization of oxytocin in Nigeria.

- NAFDAC will increase collaboration with the Nigeria customs service to ensure sensitive (cold chain) pharmaceutical products are fast-tracked; this includes speedy clearance from the ports and different storage process for both sensitive and non-sensitive products.
- Cold chain products (selling products directly to the public) will be directly marketed to avoid the interval time involved in the logistics and legalities related to the importation process of these products.
- Temperature tracking and trending should be done for temperature sensitive products to ensure they are maintained at the recommended temperature for optimal efficacy
- Market authorization holders will, explore low-cost cooling systems.
- Broader participation of all stakeholders will include the Nigeria customs service, freight companies, and both informal and formal health care providers in subsequent workshops.

A next step after the workshop was the continuation of poor-quality medicine batch collection from all affected health facilities and markets to ensure that ineffective products cannot be accessed and used. In a testament to NAFDAC's successful regulatory action implementation, in Quarter 4, a total of 1,183 ampoules of poor-quality oxytocin were confiscated from the market in 2 states of the Federation.

The FY 2017 second round of PMS of antimalarial medicines in Nigeria was carried out successfully by NAFDAC with technical assistance from PQM in the six geopolitical zones this quarter. Four regional laboratories carried out Minilab™ tests of 820 sampled antimalarial products, and confirmatory tests were carried on the samples by the ISO certified laboratories. Data analysis of the results is expected next quarter.

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

PQM serves as a global technical leader in medicines quality assurance and collaborates with a number of partners to advocate for medicines quality. Technical leadership support from PQM entails contributing to an expanding body of knowledge on pharmaceutical quality-related health systems research, as well as developing and disseminating innovative, efficient, and risk-based 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.

This quarter, PQM held a meeting with the USAID-funded Maternal and Child Survival Program (MCSP). This fact-finding meeting had the intent of possible collaboration with a PQM-supported local manufacturer, Nemel Pharmaceuticals. MCSP was satisfied with the cost of amoxicillin DT locally produced by Nemel. The company installed production capacity of 35 million doses within 48 weeks and has a supply chain system that covers the 6 geopolitical zones of the country, including the patent proprietary medicine vendors (also known as downscale medicine sellers). The brand is also packed in blister packs, which protect against humidity, thus retaining the quality of the medicine until it reaches the end user. PQM plans to continue support to Nemel Pharmaceuticals toward the production of quality-assured amoxicillin DT.

PQM build built and strengthened QMS capacity and skills for 42 IPAN staff (25 males, 17 females) in the area of quality audit. Topics covered include understanding of internal audit; beginning and scheduling of an ISO audit; internal audit cycles; ISO/IEC audit requirements; management review of requirements; development of a basic audit program; selection, training, and qualification of auditors; and writing of proper deficiency statements. PQM trained 16 NAFDAC PV/PMS Directorate staff (5 females, 11 males) on the use and application of TruScan™ device to support PMS. PQM provided technical support in the development of an SOP for the device, which was adopted by the directorate. Pre- and post-knowledge checks were administered to verify the levels of understanding; virtually everyone scored above 76 percent in the post-test, which was a great improvement from the initial average score of 48 percent. In addition, 35 NIPRD staff (15 females, 20 males) were trained on test methods in preparation of ISO/IEC 17025 accreditation. Topics covered include good weighing practices, loss on drying, uniformity of dosage unit, and ultra-violet spectroscopy.

Senegal

I. Quarter 4 Highlights

To support the National Quality Control Program (LNCM) in conducting medicines quality surveillance, in Q4 PQM assisted the laboratory in finalizing and compiling all documents needed to be the recipient of the Fixed Amount Award (FAA). This FAA will allow LNCM to build its capacity in effectively managing USAID funds. After approval of the FAA by USAID/Washington and Mission, PQM will support LNCM in executing FAA activities FAA by adopting a risk-based PMS system. This PMS system will make sampling and testing more efficient and sustainable in Senegal. The main outcomes of the FAA include PMS report on the quality of essential medicines, including antimalarials, in the established nine sentinel sites.

II. Country Context

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

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

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

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

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

West Bank and Gaza

I. Quarter 4 Highlights

This quarter was devoted to developing the FY 2018 work plan. The draft plan was submitted to the Mission for approval on September 12, 2017.

Asia

Bangladesh

I. Quarter 4 Highlights

PQM's activities during Q4 FY 2017 were focused on the implementation and support of Objectives 2, 3, and 4 in the approved work plan. This quarter's highlights include the following:

- PQM provided technical assistance to DGDA to complete WHO's nine functions for self-assessment, which was completed in July 2017. PQM field staff supported four of these assessments, SIAPS supported two, and WHO supported three. The PQM-supported functions included Laboratory Access and Testing, NRA Lot Release, Clinical Trials Oversight, and Regulatory Inspection System (RIS). PQM also provided support to develop an institutional development plan using WHO-accessed tools, SOPs, and guidance documents.
- PQM conducted a 1-day training on PMS for 13 DGDA inspectors on July 26, 2017. This training emphasized monitoring of medicines quality at the district level.
- PQM engaged a consultant in pharmaceutical policy and legislation to review DGDA's regulatory acts and policy and to provide recommendations on how to strengthen the policies and regulations in relation to medicines quality. This activity was done in collaboration with SIAPS and WHO to provide valuable input on the nine functions of MRAs in developing countries.
- PQM conducted a 4-day training on the effective/proper use of pharmacopeias (USP, British Pharmacopoeia, and International Pharmacopoeia), good laboratory management practices, and development of a risk-based protocol for product testing for registration and surveillance. The training was held September 17–20 at the National Control Laboratory (NCL) in Dhaka. Participants were laboratory managers and quality controls analysts from both NCL and Drug Testing Laboratory (cDTL) in Chittagong. This training will help managers and analysts to implement a risk-based testing approach to optimize compendia testing of medicines in order to reduce redundancies and optimize the cost of testing services.
- PQM provided NCL with personal protective equipment, reagents, and standards to boost safety and overall capacity to test medicines quality. In addition, computers, printers, and a projector were provided to enhance good documentation practices.
- PQM supported NCL's Assistant QA Manager, Dr. Nasima, to participate in a course on the Quality of Medical Products and Public Health at Boston University on July 10–14. She is a critical member of NCL, responsible for validating and releasing analytical results to clients. Dr. Nasima is also the QA manager, a role that allows her to oversee the overall quality of analytical work within DGDA.
- PQM Director Jude Nwokike and Director GPH Asia Souly Phanouvong attended the WHO Coalition of Interested Partners meeting on July 24–25 in Dhaka. PQM Bangladesh staff actively supported the preparation and facilitation of the meeting. PQM staff provided an update on program activities in the country and detailed justification for the newly proposed DGDA organogram and the human resource needs.
- The Deputy Director of DGDA, along with 16 participants from 6 companies (NIPRO JMI Pharma, Radiant pharma, Eskayef Pharma, Delta Pharma, Beacon Pharma, and GLOBE Pharma), participated in a workshop for National Medicines Regulatory Authorities and Manufacturers of Medicines for Treatment of Tuberculosis and Neglected Tropical Diseases, held July 25–27 in Bangkok, Thailand. The meeting presented manufacturers with information about PQM works and is collaborating with manufacturers to improve the availability of quality-assured essential medicines.
- PQM's Chief of Party and Technical Manager attended the antimicrobial resistance workshop at DGDA on August 9–10; this workshop was organized by WHO under guidance from DGDA and the Directorate General of Health Services (DGHS). The emphasis of this workshop was to develop a national strategy to reduce the consumption of antibiotics in Bangladesh. Bangladesh has a National Strategy and National Action Plan for Antimicrobial Resistance Containment, which includes product market quality surveillance.
- PQM attended the FY 2018 work plan peer-review meeting with USAID at the Management Sciences for Health office to justify technical and programmatic activities outlined in the work plan as they relate to the USAID/Bangladesh health sector program. The peer review meeting enables USAID/Bangladesh to highlight the different activities of its implementing partners and to foster inter-agency collaboration among partners.
- PQM HQ technical staff worked with newly hired technical consultants on USP processes and procedures and provided an orientation on PQM's technical framework and its implementation in Bangladesh.

II. Country Context

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Conduct a well-designed gap analysis on regulatory system related to the quality assurance and quality control systems, develop FY 2017 work plan, and take part in the peer review work plan meeting

Activities in relation to this objective were completed in FY 2016 Q4.

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

In terms of laboratory capacity building, PQM has been providing technical guidance/input to NCL in the following areas to strengthen its QMS and move the laboratory toward ISO 17025:2005 accreditation:

- PQM worked alongside NCL management and technical staff to follow up on its CAPA progress against the findings from the internal audit and the PQM audit. In Q4, 15 CAPAs were closed; the remaining CAPA are planned to be completed by December 31, 2017.
- PQM worked closely with NCL to develop and review critical SOPs to improve the traceability of work processes, quality control, and instrument life cycle. In this quarter, PQM provided guidance and input to develop and/or update SOPs in the following areas:
    - Communication with all stakeholders
    - Procedure of publications of passed (Released) and failed (Not Released) lots in the website
    - Material purchase, receipt, and storage
    - Analytical method transfer
    - Acceptance criteria
    - Dissolution SOP for 8 vessels
    - Column management
    - SOP for Polarimeter
    - SOP for dissolution for 14 vessels
    - Method validation
- PQM provided guidance and input to the following document preparation:
    - Flow chart of vaccine release
    - List of imported vaccines
    - List of local vaccines
    - Training calendar for DGDA
    - Column installation form
    - Laboratory inspection form
    - Intermediate check of equipment
- All NCL out-of-specification, deviation, and change control reports during 2016–2017 have been reviewed in the area of investigation, root cause analysis, risk assessment and action plan, and closing evidence collections. Logbooks were reviewed accordingly.
- PQM provided support to NCL to develop its annual requirement list of reference standards, reagents, and chemicals focusing on FY 2018 in order to identify its need for smooth operation. The approved vendor documents and list for reagent, chemicals, and calibration service providers were also reviewed.

- On September 13, PQM Bangladesh staff conducted a hands-on training on column installation/performance check for HPLC. After this training, participants installed and validated the column.
- A PQM expert conducted a 4-day training on the effective and proper use of pharmacopeias (USP, British Pharmacopoeia and International Pharmacopoeia), good laboratory management practices, and development of a risk-based protocol for product testing for registration and surveillance. The training was held September 17–20 at NCL in Dhaka. Laboratory managers and laboratory analysts from both NCL and cDTL participated in this training. Participants learned how to develop a risk-based testing protocol based on risk factors identified toward compendia testing. This training was attended by 22 participants (19 from NCL and 3 from cDTL).
- On September 17, PQM HQ staff reviewed the proposed NCL organogram to assess expertise and skills for the new NCL staff positions. PQM reviewed the job descriptions of NCL staff and made recommendations to improve the NCL laboratory organogram to better support DGDA's mandate and NCL's functions.
- To ensure the safety of staff in the laboratory, a fire control system was implemented at NCL. Items installed include18 fire extinguishers and 50 smoke detectors with addressable control loop panel for fire detection, as well as other items as identified by the assessment.
- One of the bottlenecks that NCL is facing is the lack of critical laboratory equipment, including an HPLC system with auto-sampler, dissolution tester, Karl Fischer, friability tester, disintegration tester, analytical microbalance, UV-Vis spectrophotometer, vacuum oven, reference weights, and mechanical calibration kit. To overcome the deficiencies, PQM worked with DGDA and NCL management to develop a priority list of equipment/instruments for the laboratory. PQM is exploring possible sources of funds for the purchase, installation, and operationalization of the equipment. By acquiring the equipment/instruments, NCL will improve its testing capability and ensure products meet quality assurance standards.

Summary of Laboratory Progress from July 1 to September 30, 2017

Items	Number of Items
SOP Review and Development	Approved and implemented SOP: 3 SOPs drafted, and under review by NCL: 7
CAPA status up to 18 September 2017	
CAPA by PQM (2016) from gap analysis findings (39)	28 CAPA completed Rest of 11 CAPA under follow up (long term plan)
CAPA by PQM (2017) (24)	Completed: 1 Drafted & waiting for approval: 13 Under follow up: 10
CAPA by NCL Internal Audit - June 2017 (26)	Completed: 14 Under follow up: 12
Different type of documents preparation (7)	1. Flow chart of vaccine release 2. List of imported vaccines 3. List of local vaccines 4. Training calendar for DGDA 5. Column installation form 6. Laboratory inspection form 7. Intermediate check of equipment

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

On July 27, Eskayef personnel came to PQM Dhaka office to meet with PQM Director Jude Nwokike. The PQM Director discussed with Eskayef the process to move forward to utilize technical assistance from PQM for priority medicines (MNCH, family planning, and TB) to achieve WHO PQ.

To emphasize the critical nature of the availability of quality-assured anti-TB and NTD medicines, on July 25–27, PQM hosted a 3-day workshop in Bangkok, Thailand, titled "Ensuring the Quality of Medicines on the Public Health Market." The objective of the workshop was to raise awareness about pharmaceutical quality and provide information to MRAs and manufacturers of anti-TB and NTD medicines about opportunities for using PQM technical assistance to strengthen quality systems. The workshop discussed PQM technical assistance, the WHO PQ process, current GMP, dossier requirements, and risk assessment for cleaning validation, among other topics. The DGDA Deputy Director, along with 16 participants from 6 companies in Bangladesh, participated in the workshop.

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

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

As mentioned above, PQM worked with WHO to prepare DGDA's Self-Assessment toward WHO PQ (Maturity Level 3); the PQM Bangladesh team was assigned to lead the four functional areas among the nine WHO-recommended functions.

The PQM Director and the Director GPH Asia participated in the WHO Coalition of Interested Partners meeting on July 24–25. The PQM Bangladesh team members also actively participated in the meeting. An update on PQM's activities since March 2016 was provided at the meeting, along with a detailed justification of the DGDA proposed organogram presented by the Director GPH Asia. The PQM Director explained the key considerations in developing the DGDA organogram that allows adequate operations and functions.

PQM conducted a 1-day training on PMS data analysis for 13 DGDA inspectors toward the establishment of PMS on priority medicines in selected geographical locations/districts. A survey on risk-based PMS among the district inspectors/DGDA officials will be completed in October 2017 to identify the most critical factors present in different geographical areas, focusing on TB, MNCH, and family planning products. The risk-based data will help to select appropriate sites to implement GPHF Minilabs™ as an early detection system of falsified or substandard medicines. Ultimately, Minilabs™ and the risk-based system will help to reduce number of samples tested and analyzed in the laboratory.

PQM engaged a pharmaceutical policy and legislation consultant to review DGDA's existing regulatory acts and policies, as well as to support SIAPS in the revision of legislation, policy, and regulation as appropriate to ratify the DGDA revised functions and organizational structure. On July 30, the consultant visited DGDA and met with the Director General, DGDA directors, SIAPS, and WHO. She discussed with them and collected relevant information and documents for her analysis and recommendations.

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

PQM staff have met and initiated discussions to implement one activity in Q4 under Objective 5. To accomplish this, PQM Bangladesh prepared a draft proposal to organize a workshop to be held in November 2017 with the personnel of national priority health programs—including the National Tuberculosis Program (NTP) and Central Medicine Store Depot—to explain the purpose of a national QA/QC policy and obtain their input. The proposed workshop will address a QA policy and QC mechanism to ensure that medicines obtained through the priority health programs meet with national standards for product distribution among the general public.

IV. Key Challenges

Operational Challenges:

- Safety and security remain a concern in Bangladesh. Since August 2017, half a million Rohingya refugees arrived in the southeast region of Bangladesh, near the border with Myanmar. The current Rohingya refugee crisis may lead to protests and demonstrations in Dhaka, including the Gulshan and Baridhara areas of the city. The Global Security Director is closely monitoring the security situation.

V. Lessons Learned

- Program performance is limited by the scarcity of critical staff with relevant skills and experience at DGDA and NCL/cDTL. The availability of highly motivated, skilled personnel is the key to success.
- Coordination and alignment of activities between USAID implementing partner organizations is essential in establishing common goals and activities to improve public health in Bangladesh through the health sector program of the USAID Bangladesh Mission.

Burma

I. Quarter 4 Highlights

PQM wrapped up the FY 2017 work plan activities by successfully completing the following activities:

- Technical training on GLP (data integrity and laboratory safety), HPLC, loss on drying, and dissolution for DFDA newly recruited staff. A total of 24 new staff (24 female) received technical lectures and hands-on training during a 9-day training visit by PQM. The activities were dominated by group hands-on laboratory training, question and answer sessions, and (most importantly) review and confirmation of calculations based on data interpretation and analytical understanding of the techniques.
- A thorough discussion with the USAID Mission regarding the work plan and concept notes
- PQM's visits of the new DFDA laboratory construction sites.

II. Country Context

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

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

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

II. Quarter 4 Progresses by Objective

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

PQM delivered a technical training on GLP (data integrity and laboratory safety), HPLC, loss on drying, and dissolution to the newly recruited DFDA staff. A total of 26 new staff (1 male and 25 female) received technical lectures and hands-on training during a 9-day training. The activities were dominated by group hands-on laboratory training, question and answer sessions, and (most importantly) review and confirmation of calculations based on data interpretation and analytical understanding of the techniques.

Dr. Yanga K. Dijiba coaching a participant during the hands-on training on dissolution

The PQM team visited the two physical pharmaceutical chemistry laboratory construction projects in Nay Pyi Taw and Mandalay. PQM found that the new facility in Mandalay needs additional changes to meet ISO 17025 requirements for accreditation and is far from meeting WHO PQ requirements. For safety purposes, PQM recommends having two elevators in the facility: one for chemical and equipment transportation and another for human transportation. PQM provided an additional recommendation to interconnect rooms in the facility to allow human flow and provide security evaluations. PQM's recommendations for the Nay Pyi Taw Laboratory layout were adopted, the new space is now adequate, and planning for the laboratory's relocation has begun.

In Q4, PQM also met with Ms. Karen Cavanaugh, the Office of Public Health Director, and Dr. Feliciano Monti, PMI advisor, in Yangon at the U.S. Embassy. The meeting included discussion of proposed work plan activities for FY 2018 and the budget reprogramming for FY 2017. PQM was informed by the Mission that the Malaria Operations Plan from 2017 was increased, giving PQM additional budget for the FY 2018 work plan. The meeting also included a discussion of a concept note with proposed activities outside the work plan that the USAID Mission requested should be separated from the work plan. The group discussed DFDA acquisition of handheld Raman devices and the need for ISO accreditation of the Mandalay laboratory.

PQM also attended the USAID/Burma's Implementation Partners' Meeting in Yangon.

U.S. Ambassador Mr. Scot Marciel's visit to DFDA
U.S. Ambassador Scot Marciel acknowledged all the good work and achievement of DFDA under the Director General, Dr. Than Htut. In turn, Dr. Than Htut expressed appreciation for the U.S. Government and USAID's support to DFDA through the PQM program.

Dr. Than Htut briefed Ambassador Marciel on the expansion of DFDA from a small division into a department. DFDA has expanded field offices in all states and regions in the previous year, and currently it is expanding to the district level.

The Ambassador has been visiting Burma since 2005, at which time the quality of medicines—especially antimalarials and anti-TB medicines—was problematic. He expressed interest in DFDA's perspective on the quality of these medicines currently. The DFDA team responded that, due to the expansion of DFDA, the department can now conduct PMS activities more frequently with an emphasis on antimalarials. The number of poor-quality antimalarials found in the market is decreasing over time, but the quality of anti-TB medicines still remains an issue.

Ambassador Marciel asked Dr. Htut about the main challenges that DFDA may face in coming years. The Director General outlined three main challenges:

- Capacity building of DFDA staff as the department expands.
- Expansion of infrastructure—the government budget is not adequate for rapid expansion and establishment of new facilities throughout the country.
- Awareness raising of the general public on the safety of food, drugs, cosmetics, and medical devices.

Dr. Htut reflected on the 4 "Ls" strategy deployed by DFDA: Laws/Legislation, Laboratory, Links, and Loyalty. Dr. Htut also expressed his gratitude to the Ambassador for USAID's support through PQM's technical assistance, which enabled DFDA's pharmaceutical chemistry laboratory to achieve ISO 17025 accreditation.

Ambassador Marciel concluded by saying that the U.S. Embassy's top priority is to support the provision of technical assistance to areas in need and learning from previous lessons in order to continually improve in the future.

Ambassador Marciel also visited the ISO 17025 accredited pharmaceutical chemistry laboratory in Nay Pyi Taw. Dr. Khin Chit from DFDA and Dr. Lu Lu Kyaw Tin Oo from PQM guided the Ambassador and his team through the laboratory. The Ambassador noted the HPLC system and dissolution tester donated by PQM with support from USAID/PMI and acknowledged the benefits that PQM's technical assistance brought to the laboratory. The Ambassador then visited the new construction project of DFDA Nay Pyi Taw laboratory, where PQM provided technical assistance on design, configuration, and layout of the laboratory. The first of the two new laboratories will be inaugurated at the end of October, and DFDA is inviting OPH Director Karen Cavanaugh to attend the inauguration ceremony. The Ambassador and his team concluded the visit after thanking the DFDA team and PQM for organizing the occasion.

Dr. Khin Chit, Deputy Director General from DFDA explains on Assay testing to Ambassador Scot Marciel and his team

Cambodia: The project close-out report is being finalized prior to submission. The project close-out report and transition plan will be disseminated to the country's key stakeholders/partners in the next quarter.

Director General Dr. Htut led Ambassador Marciel and team through the new laboratory construction in Nay Pyi Taw

Indonesia

I. Quarter 4 Highlights

The most significant achievement during Q4 was the submission of the LIF (and related documents) to WHO to begin the process for PQ of the PTBB NQCL of BPOM. This milestone represents multiple years of intensive training and technical assistance to BPOM and will signify a historic national achievement for Indonesia if successful. PQM will continue to support the laboratory toward a successful conclusion. A WHO-prequalified national medicines quality control laboratory will help ensure that HIV/AIDS, tuberculosis, malaria, and other essential medicines provided by the government will be subjected to high-quality QC testing on an ongoing basis. This will also support the national post-marketing surveillance program implemented by BPOM for public and private sector sampling and testing, as well as position BPOM as a regional leader in ASEAN for medicines quality assurance. PQM hopes that the national laboratory will also serve as an important resource for the local pharmaceutical industry, increasing confidence in the national MRA and in overall compliance for production and quality control.

This quarter, PQM commenced the pilot of the Jakarta DKI Minilab™ project, which resulted from a decree by the Head of BPOM mandating BPOM Jakarta DKI to test run the equipping of mobile vans with Minilabs™ to enable mobile field screening at government and private sector storage facilities and other sites. USAID also requested that PQM include cost-effectiveness in the overall analysis of the pilot, which will compare full compendial testing with the screening used in this pilot.

During Q4, PQM engaged in numerous trainings and ongoing technical assistance with BPOM, MOH, manufacturers, and partners such as the Indonesian Pharmacist's Association and the University of Indonesia. PQM also hired three new staff during Q4: a project coordinator, senior project coordinator, and M&E specialist.

II. Country Context

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

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

PQM's overall vision and strategic engagement with Indonesia is to support all aspects of medicines QA from the point of manufacture or import, through the supply chain, down to the service delivery point. To this end, PQM has designed a comprehensive approach for engaging directly with manufacturers, regulators, government disease programs, supply chain specialists and warehouses, CROs, and official medicines QC laboratories across the

country. This holistic approach ensures that all aspects of medicines quality 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 4 Progress by Objective

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

After 3 years of intensive PQM training and technical assistance, the Medicines Laboratory within the PTBB Division of the National Quality Control Laboratory of Drug and Food (PPOMN) at the regulatory authority Badan POM has finalized and submitted its LIF and associated documents (e.g., EOI) for WHO PQ of the laboratory. This marks a significant milestone in PQM's technical assistance program in Indonesia, as the PTBB laboratory is the first Indonesian laboratory to submit to WHO for prequalification. With an additional laboratory in the pipeline for WHO PQ, the Indonesian Badan POM is positioning itself as a regional resource for neighboring countries and within ASEAN for medicines quality assurance.

PQM conducted a training of trainers to support the development of a pool of central-level PPOMN experts who will routinely provide training support to the provincial institutions on technical areas. PQM spent the first week training experts on the subject matter (e.g., impurities analytical method for antiretroviral (ARV) medicines), followed by classroom and practical training on pedagogy. During the second week, the newly trained trainers conducted a week-long analytical training at the PTBB for 16 BBPOM QC laboratories. A second, similar training will be done in October for another 16 laboratories, for a total of 64 trainees from 32 provincial BBPOM laboratories to gain experience on impurities analysis. This is an important topic in support of BPOM's overall capacity building, since the institution does not currently have adequate resources to conduct impurities analysis in the event it is required in a given monograph. In the long term, impurities testing will help BPOM to fully implement compendial testing, and will also enable the laboratory system to identify potential issues with storage and distribution in the post-market environment leading to product degradation.

In September, the Jakarta DKI Minilab™ pilot project began with an initial training session held at the provincial BBPOM laboratory. A decree from the Head of BPOM mandated that the BBPOM Jakarta DKI pilot a test run of equipping mobile vans with Minilabs™ to enable mobile field screening at government and private sector storage facilities and other sites. The mobile laboratories will also be used for collaborative exercises with the provincial and district health offices, as well as for public education and outreach. Results from the Jakarta DKI pilot project will be summarized in recommendations made to the Head of BPOM, who will then decide to replicate the project elsewhere. USAID has also requested that a cost-effectiveness component be included in the overall analysis, comparing full compendial testing with the screening used in this pilot.

BPOM will then initiate the drafting of appropriate policy to officially incorporate basic field screening into the official national post-marketing surveillance priority guidelines and system. This has the potential for substantial impact on the overall capacity of the PMS system by increasing sample throughput, reducing costs and waste, and creating a more efficient mechanism for conducting quality control on both private sector and government medicines. This is especially important as universal health coverage scales up over the next 2 years, with a concomitant increase in the overall amount of essential medicines consumed by the government in need of quality assurance.

PQM presented at the national 32-province Laboratory Technical Discussion Forum convened in Jakarta on September 18–20. With over 200 BPOM staff present, PQM discussed the potential use and advantages to incorporating basic screening technologies into the national PMS system, which currently utilizes compendial testing for all collected samples (depending on analytical laboratory capacity, equipment, methods, and other factors). PQM participates in this annual technical forum as a trusted partner providing technical expertise, advocacy, and recommendations for continuous improvement of laboratory practices. This is the fourth year of PQM's participation in such an event.

With support from PQM Indonesia, BBPOM Denpasar established a WHO Prequalification Implementation Plan, with an expected timeline of the end of 2018 for submission of its LIF to WHO. The Head of BBPOM Denpasar signed an official work order enabling the provincial laboratory to implement this plan and work toward WHO PQ as part of its official duties. To jumpstart implementation of this plan, in Q4 analytical training on gas chromatography was held at BBPOM Denpasar and included analysts from BBPOM Manokwari from West Papua. This week-long training focused on ensuring sufficient technical skills as part of implementing the WHO PQ plan for Denpasar, in which gas chromatography will be an area of accreditation under the laboratory's eventual prequalification.

Also during Q4, a training on internal audits and data integrity was held at the BBPOM Denpasar laboratory, with participants also from BBPOM Jayapura laboratory in Papua. The training included follow-up from the previous QMS assessment and was designed as part of the WHO PQ Implementation Plan.

Upcoming activities in Q1 FY 2018:

- PQM will conduct an extensive Minilab™ training and continue collecting samples for Minilab™ Pilot Project in BBPOM Jakarta DKI.
- PQM will conduct analytical techniques trainings for BBPOM Jayapura and BBPOM Jakarta during Q1 FY 2018.
- PQM will support the training of trainers National Analytical Training on Impurities for 16 provincial QC laboratories–round 2.
- PQM will facilitate and oversee the testing of TB medicines collected in the MOH–BPOM joint sampling activity in 11 provincial BPOM QC laboratories.
- The provincial QC laboratory of Jakarta DKI will demonstrate the Minilab™ operation in launching of the National Action Plan for Eradication of Drug Abuse (invited VIPs include the President of Indonesia, and Ministers of Health, Policy, and MRA), scheduled for October 4.

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

During Q4, PQM began reviewing Kalbe Farma's levofloxacin 500 mg tablet product dossier prior to submission to WHO for Prequalification (aimed at submission by Q1 FY 2018), with over 90 percent of its CAPA completed and in compliance with WHO's guidelines.

At the end of Q4, a training workshop on conducting bioequivalence studies according to international standards was convened for three CROs (Equilab International, Pharma Metric Laboratories, and San Clin Eq). The participants also included representatives from BPOM (regulatory), the University of Indonesia, and members of the Bioequivalence Communications Forum. Following the training, an extensive GLP/GCP audit of CRO Pharma Metric Laboratories was conducted to qualify the CRO for the eventual conduct of bioequivalence studies associated with products destined for WHO PQ and other mechanisms requiring international standards of clinical and analytical practices for bioequivalence studies.

Upcoming activities Q1 FY 2018 include:

- Prior to the WHO audit, PQM will conduct an extensive mock audit of Kalbe Farma following submission of PD for WHO PQ.

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

PQM's strategy in partnering with MOH and BPOM is in the context of implementing the PMK 75/2016 regulation, which requires increased quality assurance activities on government program medicines. PQM's partnerships with the National AIDS and National TB programs have generated a number of novel mechanisms for increasing quality control activities and data sharing between MOH and BPOM. During Q4, PQM Indonesia helped negotiate and secure funding for third-party government contracts between MOH and the MRA (BPOM) for testing ARV medicines from 16 provincial MOH sites in Indonesia, to be tested at the BPOM NQCL, PTBB. The Ministry of Health, utilizing both locally manufactured and imported ARVs via a single-source provider (Kalbe Farma), funded by government budget, is contracting the PTBB laboratory as a third-party contractor to get information on the quality of ARV products for programmatic purposes (procurement, selection, and regulatory actions in the case of out-of-specification results). PTBB is currently receiving intensive support from PQM on a WHO PQ project, which it anticipates to be completed this year. The ARVs to be tested represent both locally manufactured and imported products, and this is the first time that a comprehensive sampling and testing of ARVs will be conducted in Indonesia. Based on the results, MOH can take action in the case of Special Access Scheme (SAS) imported products, which are not currently under the jurisdiction of BPOM.

The first such activity of its kind in Indonesia, the joint sampling and testing serve as a pilot to implement the MOH Regulation 75/2016 which was initiated by PQM to ensure adequate quality assurance for TB, HIV, and other government medicines in Indonesia. Eleven provincial BPOM institutions (North Sumatra, DKI Jakarta, West Java, East Java, Bali, East Nusa Tenggara, North Maluku, North Sulawesi, South Kalimantan, Papua, West Papua) conducted joint sampling exercises between MOH and BPOM under a Global Fund–USAID–PQM collaborative exercise to implement PMK 75/2016. Meetings were held with MOH, TB, PQM, and Global Fund on establishing timelines, budgets, field sampling plans, and working with BPOM on drafting field sampling technical guidelines. Field sampling activities focused on sampling government disease program medicines, primarily for TB with some ARV products, collected from government facilities and tested at the provincial BBPOM laboratories. Sample testing, data dissemination, and follow-up action plans are anticipated for Q1 FY 2018, including a final evaluation. This activity is part of a $2 million procurement contract between USP and the Global Fund to leverage TB disease control funds to support capacity building for QC testing at the provincial laboratories to international standards. Procurement is still in process, with delivery expected in October 2017. Testing results will be disseminated during subsequent MOH–BPOM workshops, as well as planning for the next phase of sampling and testing. Samples tested during this activity are covered under BPOM's national post-marketing surveillance priority sampling system. BPOM and MOH will work during FY 2018 to revise the sampling strategy, including sampling technical guidelines, to implement PMK 75/2016 to increase the number of government disease control program medicines that are routinely tested during post-marketing surveillance. This is a major milestone in the movement toward a more robust and comprehensive system for monitoring public sector medicines in Indonesia and a significant accomplishment for the PQM Indonesia team.

PQM Indonesia, in partnership with the Indonesia Pharmacists' Association (IAI), supported an initiative on the implementation of Indonesian's MOH regulation 72/2016 on Good Pharmacy Practices (GPP) for Hospital Pharmacies in response to a major fake vaccine scandal in Indonesia in 2016. Following discussions with USAID and the U.S. Centers for Disease Control and Prevention, PQM Indonesia embarked on a partnership to support IAI through a pilot project to draft and implement SOPs for GPP for hospitals to create more stringent procurement and monitoring practices, reducing the risks for infiltration of the supply chain for both falsified and substandard medical products. PQM Indonesia supported IAI to sign MOUs, which outline the details of implementing the GPP PMK, and identifying SOPs to be developed as part of this implementation, with 40 hospitals in Bekasi district in Java, a hotspot for the fake vaccine distribution from 2016. The recent event following assessments and MOU signing was extensively covered in national media.[1] [2] [3]

PQM Indonesia support to IAI also included sponsorship of the annual scientific symposium, gathering thousands of public and private sector/industry pharmacists from Indonesia. PQM sponsored two symposia during September's IAI Scientific Forum in Tangerang, Indonesia, with topics presented by WHO, the National TB Program (national director), and PQM on the pharmacist's role in TB control in Indonesia, the pharmacist's role in combating substandard and falsified medicines, and supply chain management in the public sector. The impact from PQM's symposia is already being seen, with requests for technical assistance on establishing SOPs for compounding, supplier verification, and other quality assurance activities for compounding and GMP for local hospitals.

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

PQM Indonesia is currently in process for renewal of the expatriate work permit and stay visa, which expired September 30, 2017. The office must secure recommendations from MOH and BPOM following the USAID assignment letter, followed by a 12-step approvals process.

During Q4, PQM hired former BPOM Deputy Dra. Retno Tyas Utami as a Senior Technical Advisor consultant. She has extensive global expertise in GMP and works with BPOM and as an advisor to WHO, and she will help to implement activities under Objective 2.

PQM Indonesia hired a project coordinator, senior project coordinator, and M&E specialist.

The USP Indonesia office was relocated to its new address at Menara Prima in Mega Kuningan, following extensive site selection and fit-out and is now a dedicated facility for all programs and operations.

[1] http://threevenue.com/ragam/Implementasi-good-pharmacy-practice-pastikan-kualitas-obat-bagi-pasien/
[2] http://www.beritasatu.com/kesra/445984-iai-dorong-peningkatan-kompetensi-apoteker.html
[3] http://suaraindonews.com/kota-bekasi-pilot-project-optimalisasi-permenkes-no-72-tahun-2016/

Pakistan

I. Quarter 4 Highlights

PQM has been providing technical support to four potential manufacturers of CHX 7.1% gel to improve their current GMP. As a result of this support, four new CHX 7.1% gel products were approved for registration by the Drug Registration Board. Another important step was pursuing the recommendation of price fixation; the price fixing was completed during Q3. During Q4, PQM followed up on this with the federal government and succeeded in obtaining final approval on the price the Prime Minister. Consequently, registration letters were issued to all the manufacturers, thus clearing the last pending requirement for local production. All four manufacturers are now preparing the production of commercial batches. The first batches of CHX gel are likely to be available during Q1 FY 2018. Once the products of the four local manufacturers (M/s Atco Laboratories, M/s Aspin Pharmaceuticals, M/s Akhai Pharmaceutical & Zafa Laboratories) are available in the marketplace, not only will there be an increase in utilization in Pakistan but also the manufacturers will look into the possibilities of exporting CHX gel to other countries in the Asia region in need of this product. PQM Pakistan is satisfied with the success in addressing this challenge, as the availability of locally produced CHX gel will contribute to reducing neonatal mortality caused by umbilical cord infections.

II. Country Context

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

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

III. Quarter 4 Progress by Objective

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

Follow up on Zafa and Akhai's assessment for CAPA implementation and provide further assistance to address deficiencies as needed, specific to manufacturing processes and procedures requirements for manufacturing of CHX and other MNCH Products (zinc DT, oxytocin, ORS)
New areas identified for PQM support include the following:

- In Pakistan, an assessment of the causes of maternal mortality in public and private hospitals points toward postpartum hemorrhage as the main reason for death following childbirth.[4] The use of oxytocin alone, as the first medicine of choice, plays a central role in the treatment of postpartum hemorrhage.[5] PQM has identified that the country is in need of local production of oxytocin injection, as the only manufacturer in the country has stopped production of this important lifesaving medicine.
- Pneumonia is the leading cause of under-5 child mortality globally, with an estimated 1.2 million deaths annually. As many as 60 percent of these occur in just 10 countries: Bangladesh, D.R. Congo, Ethiopia, India, Kenya, Niger, Nigeria, Pakistan, Tanzania and Uganda.[6] In 2011, WHO updated its recommendations

[4] Haemorrhage and Maternal Morbidity and Mortality in Pakistan Sadiah Ahsan Pal OMI Hospital, Karachi.
[5] WHO recommendations for the prevention and treatment of postpartum hemorrhage.
[6] Every Woman Every Child, *Amoxicillin - Product Profile*, United Nations Foundation, Washington, 2012 at http://www.everywomaneverychild.org/component/content/article/1-about/305-amoxicillin-product-profile-

for the home treatment of pneumonia in the context of Integrated Management of Childhood Illnesses, replacing co-trimoxazole with amoxicillin 250 mg as the new first-line treatment for childhood pneumonia.[7] The availability of amoxicillin in DT form simplifies the administration and dosage of treatment, and PQM has identified that amoxicillin 250 mg DT is not available in Pakistan.

- Diarrheal diseases are a leading cause of childhood morbidity and mortality in developing countries and an important cause of malnutrition. In 2003, an estimated 1.87 million children below 5 years died from diarrhea, and 8 of 10 of these deaths occur in the first 2 years of life. On average, children below 3 years of age in developing countries experience three episodes of diarrhea each year.[8] The use of zinc in the management of childhood diarrhea is recommended by WHO/UNICEF because zinc has been found to reduce the duration and severity of diarrhea and prevent subsequent episodes. Pakistan is among the 15 countries that account for about 75 percent of the deaths due to children diarrhea.

Based on the above analyses and assessing the requirement of the country's health system, PQM has identified the manufacturers that have the potential and willingness to manufacturer MNCH products such as oxytocin, amoxicillin DT, and zinc DT, and co-packing of oral rehydration salts with zinc DT. The identified potential manufacturers will be supported during FY 2018; if required, technology transfer from a reliable source will be considered to enhance the manufacturing of these products, especially oxytocin.

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

Support DRAP's QMS staff in laboratory equipment calibration, validation, and qualification

Development of specifications is a crucial component of ensuring the quality of pharmaceutical products. Innovators are responsible for the development of analytical methods to test products, which are relied upon by regulators. However, until the specifications appear in publicly available pharmacopeias, it remains a challenge to develop the specifications and analytical methods for the generic products as copies of the product developed by the innovator. The only scientifically sound solution is for the generic product manufacturer to develop its own methods of analyses based on the general chapters given in pharmacopeias. However, this poses a challenge to regulators, whose basic responsibility is ensuring the safety, efficacy, and quality of pharmaceutical products. The Drug Registration Board decided to meet the challenge by ensuring that the generic manufacturer must meet and follow either innovator specifications and methods or pharmacopeial specifications. However, when generic products are being developed, neither the innovator methods nor pharmacopeial monographs are available. Thus, generic manufacturers have to develop their own specifications and methods of analysis, and the Drug Regulatory Authority has to approve the specification and analytical methods developed by the manufacturer.

In this context, the regulators need to be trained on analytical method validation so the analytical method submitted by the generic manufacturer can be evaluated. Training material was developed with the objective of building the capacity of regulators on analytical method validation evaluation, both through documentary assessment and in the laboratory. A 3-day training was conducted at CDL Karachi, which was attended by drug analysts and registration dossier evaluators from DRAP and provincial health authorities; in total, 23 persons (15 male, 8 female) attended. Mr. Azmat Hayat and ad hoc consultant Dr. Iftikhar Jafri imparted the training. The highly interactive training resulted in an improved understanding of analytical method validation assessment in the laboratory and through documentary evaluation to enhance testing capabilities.

Support the establishment of a monitoring system for post-marketing surveillance program

PQM continues to work to strengthen the country's health system and arranged a consultative meeting in Islamabad between DRAP and provincial health authorities. The objective was to discuss the development of a framework for collaboration between DRAP and provincial health authorities on PMS and data sharing to ensure the quality of medicines in the market and combat the presence of falsified and substandard medicines the country. The meeting was also attended by the young DRAP officers, who had an opportunity to understand the process of developing regulations and benefit from the experience of senior government officials at the meeting. The total number of attendees was 33 (29 male, 4 female), of which 12 (8 male, 4 female) were newly inducted assistant directors.

[7] WHO, *Factsheet: Pneumonia*, WHO, Geneva, April 2012 at http://www.who.int/mediacentre/factsheets/fs331/en/.
[8] A manual for physicians and other senior health workers Second Revision of WHO/CDD/SER/80.2

The activity began with a presentation by Mr. Ghani on international best practices and the experience of Health Canada. All provinces made presentations on the PMS activities they are conducting in order to give a clear understanding to all participants about their similarities and differences so that a common system for national application can be developed. Subsequently, participants were divided into three groups to develop proposals for establishing a national PMS framework that has a built-in mechanism for sharing information and regulatory actions taken by each province. This will ensure timely action against falsified and substandard products in the market throughout the country.

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

Based on advocacy from PQM, DRAP's Directorate of Pharmaceutical Evaluation and Registration decided to apply the CTD to replace the existing Template of Form '5' for local manufacturing of medicines, Form '5A' for imported products, Form '5D' for new molecules for local manufacture, and Form '5E' for patented medicines for registration application of medicines. The legal formalities for adopting the new template were fulfilled by DRAP with the publication of the adoption in the Government Gazette Notification.

The biggest challenge in this process has been that regulators and the industry in general are not ready for adoption of CTD template. In order to facilitate DRAP's efforts, PQM decided to train the regulators and the industry to adopt the new template by utilizing available resources without a financial implication for the program, as the activity was managed within the available budget for FY 2017. USAID approved this additional activity. During Q3, trainings were held on CTD dossier preparation and evaluation. PQM understands that DRAP needs to prepare regulators on related aspects of product development. PQM Pakistan hired the services of a former director from Health Canada, Mr. Sultan Ghani, for preparation of the course material and to impart the trainings to the regulators. In Q4, two trainings at Lahore and Karachi were arranged for DRAP and provincial health authorities on current GMP. Both trainings were attended by DRAP officials and provincial health authorities. In Lahore, there were 35 participants (21 male, 14 female); in Karachi, there were 21 officials (13 male, 8 female) from DRAP and the Punjab Ministry of Health. In these very interactive sessions with case studies, participants were able to learn about new trends in GMP and the challenges they will face as regulators in improving the manufacturing standards of the industry as a whole.

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

During Q4, no activities were conducted due to logistical reasons.

IV. Key Challenges

Programmatic Challenges: The non-availability of a multiple entry visa remained a big programmatic challenge, hindering the ability of PQM's technical team to provide technical assistance. The situation is likely to improve after office registration is granted by the government, as the policy allows for a 1-year multiple entry visa for international nongovernmental organization officials traveling for program-related work. In the meantime, the technical gap has been addressed through the inclusion of ad hoc consultants based in Pakistan.

At the federal level, the Appellate Laboratory, which is pivotal in the quality control system of Pakistan, is also facing challenges. PQM is making efforts to equip and operationalize the laboratory. Once equipment and required staff are in place, PQM will then build the laboratory's capacity and strengthen its QMS.

V. Lessons Learned

PQM works closely with DRAP to strengthen its regulatory capacity, but engagement with provincial health authorities has revealed their need for additional technical assistance; this is particularly true in the smaller provinces, where greater promotion of standardization of processes and actions are necessary in order to protect public health.

Philippines

I. Quarter 4 Highlights

In support of the objective of strengthening the Philippines Food and Drug Administration's (FDA) post-marketing quality surveillance program, PQM and FDA conducted a workshop in the Philippines on the risk-based PMS

guidelines developed by PQM. The workshop, conducted on September 11–14, was attended by 40 participants, including personnel from FDA headquarters and all the country's regional offices. One workshop objective was to assess current protocols utilized in Philippines' FDA PMS program to identify gaps and challenges in implementation. At the end of the workshop, FDA was able to complete the first draft of the PMS guidelines, which incorporates elements of PQM's risk-based PMS approach.

During Q4, the PMS for monitoring the quality of TB medicines was more focused on the public sector (the national TB directly observed treatment, short-course (DOTS) center) after PQM completed a majority of the sampling and testing activity in the private sector (pharmacies at eight sentinel sites across the country).

From June to August 2017, PQM visited and inspected 117 TB DOTS facilities in Region 4A (Calabarzon). A total of 217 samples were collected and tested using GPHF Minilab™ kits. From these, 55 were submitted to the FDA laboratory for confirmatory testing, and all of them passed.

While performing these activities, the following observations were made:

- Medicine supplies at most DOTS facilities are received from the provincial health office located at Quezon City, but several are received through local government purchase from private distributors or pharmacies.
- Expired medicines were found to be stored alongside unexpired medicines in some facilities.
- Medicines with quality issues, such as pediatric formulations with leakage or caking and adult fixed-dose combinations with cracked and moist tablets, were spotted and reported by staff during the interview.
- Among 233 DOTS centers/facilities in region 4A (Calabarzon), PQM randomly selected 117 DOTS centers (50%) to visit, and found out that only 22 of 117 selected facilities (18.8%) were monitoring and keeping records of medicine storage temperatures. During the visit, PQM personnel were able to record in some facilities storage temperatures higher than the 30°C required for TB medicines.
- Some facilities have inadequate storage space, with unclean and poor storage conditions.
- One facility was found to have evidence of rodent infestation.

II. Country/Health Element Context

According to WHO, the Philippines has an estimated 417 per 100,000 prevalence rate of TB, with an estimated 11,100 multidrug-resistant tuberculosis (MDR-TB) cases in 2015. The Department of Health (DOH) NTP recognizes the numerous challenges in improving TB medicines supply and management in the country. Based on the 2015 Joint Program Review, these challenges include the complete absence of a logistics management information system for first-line medicines, poor storage conditions and practices, inadequate medicines QA systems, and low-quality pediatric medicines. This is exacerbated by limited consideration for QA in the procurement, dispensing, and storage practices for medicines at health facilities. The Philippines FDA and DOH continue to work and seek support to address the challenges to assuring the quality of medicines and their supply at the regional level.

In collaboration with the Philippines FDA and DOH NTP, PQM strengthens medicines QA/QC in the supply chain through monitoring the quality of anti-TB medicines as part of the country's PMS. PQM also provides FDA with technical and professional assistance to enhance its regulatory capacity to register and evaluate pharmaceutical products; this assistance includes the introduction and build-up of internationally accepted quality standards, processes, and procedures, as well as of FDA satellite laboratories toward achieving ISO/IEC 17025 accreditation.

To mobilize policymakers, regulators, and health professionals, PQM also helps NTP to disseminate up-to-date information about medicines quality and to raise awareness among the general public about medicines quality issues.

III. Quarter 4 Progress by Objective

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

Activity 1.1: Training for FDA inspectorate group

- Activity completed.
- Expected key output completed (training manual, staff assessment report, training report, and evaluation).

- Training Workshop on Good Storage and Distribution Practices for Philippines Regulatory Authority conducted on June 26–30.
- Participants who successfully completed the training workshop: 24 (7 male, 17 female)

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

Activity 2.1: PQM in collaboration with FDA to develop updated PMS strategy

- Activity completed.
- Workshop on PQM's risk-based PMS guidelines conducted in Philippines on September 11–14.
- Expected key output completed (first draft FDA PMS Guidelines completed)
- Participants who successfully completed the workshop: 40 (11 male, 29 female)

Activity 2.2: Training of Trainers (ToT) on the updated PMS strategy

- This activity was dropped from the PQM work plan due to budget limitations. The Philippines FDA is developing and will conduct this training to staff/inspectors based on what they learned from the PMS workshop on the strategy, guideline, and methodologies.

Activity 2.3: Implement PMS in selected regions

- PQM established PMS programs for first-line TB medicines (ethambutol HCl, isoniazid, pyrazinamide, and rifampicin) and their fixed-dose combinations at eight sentinel sites in the Philippines. The sentinel sites are required to collect at least 5 samples per month or 15 samples per quarter. These samples were initially tested using the GPHF Minilab™ kit. All failed/doubtful samples and 10 percent of passing samples are subsequently submitted to the FDA laboratory for confirmatory testing. The sample collection and quality testing of TB medicines provides data on medicines quality for products available in the market. The FDA relies, in part, on the information obtained from PQM to identify and take regulatory action against poor-quality TB medicines, which complements the objectives of the National TB Control Program.

Medicine Quality Surveillance for TB Drugs FY 2017

Collected and Tested Samples at PQM Site using the Minilab™ Kit					Collected in DOTS facilities in Region 4A and Tested using the Minilab™ Kit
Sentinel Site	**Q1 (Oct – Dec 2016)**	**Q2 (Jan – Mar 2017)**	**Q3 (Apr – Jun 2017)**	**Q4 (Jul – Sep 2017)**	**Jun – Aug 2017**
Bicol	49	0	20	0	N/A
Calabarzon	13	61	48	0	217
Cebu	27	10	0	0	N/A
Davao	23	6	3	0	N/A
Iloilo	13	27	0	15	N/A
La Union	0	17	53	0	N/A
Pampanga	0	0	79	0	N/A
Zamboanga	8	0	35	0	N/A
Total (collected):	**133**	**121**	**238**	**15**	**217**
Pass (tested)	133	112	236	15	213
Fail/Doubtful (tested)	0	9	2	0	4
Confirmatory Analysis/ Quality Testing					
No. of samples submitted	9	13	27	2	55
Pass	9	13	27	2	55
Fail	0	0	0	0	0

The 8 PQM sentinel sites collected and tested a total of 507 samples for FY 2017, satisfying the requirement of 5 samples per site per month or 480 samples per year. The 51 samples submitted to the FDA laboratory passed

confirmatory testing; thus, no poor-quality medicines were found. Most of the sentinel sites completed their activities during Q3 FY 2017.

During FY 2017, PQM reported four medicines with probable registration violation. Subsequent FDA investigation reported that two of the four had no violation:

- Non-branded Rifampicin manufactured by Lloyd laboratories, Inc., for Westfield Pharmaceuticals, Inc., with drug registration number DR-XY18290. The manufacturer exhausted its labeling materials, and the product was considered valid for use until December 2017.
- Zynaphar tablet manufactured by J.M. Tolmann Laboratories, Inc., for the Generics Pharmacy, Inc., with drug registration number DRP-1403-02. The product was manufactured prior to approval of the new brand name.

PQM is still waiting for the investigation report of the remaining two products: Rimactazid tablet manufactured by Interphil Laboratories, Inc., for Sandoz Philippines Corporation with drug registration number DR-XY25238 and non-branded Isoniazid manufactured by Drugmaker's Laboratories, Inc., for Biotech with the drug registration number DR-XY9721.

The FDA Product Research and Standards Development Division shared the final report on Fixcom 3, batch/lot no. 14FXC3 06. The failed sample was detected in December 2015 in Region 6. The product failed the dissolution test conducted by the FDA laboratory. However, no more retention samples of that lot were available from the manufacturer and trader (Lloyd Laboratories, Inc., and Natrapharm, Inc.); instead of the failed one, other lots were collected. Appropriate tests were performed for these lots and for the remaining samples of lot no. 14FXC3 06. Only lot no. 14FXC3 06 failed confirmatory testing. However, according to FDA Philippines SOP, the retention sample of a particular product needs to be tested in order to reach a final conclusion on its quality, so no recall for the said lot ensued.

From June to August 2017, PQM visited and inspected 117 DOTS facilities in Region 4A or Calabarzon. A total of 217 samples were collected and tested using the GPHF Minilab™ kit. From these, 55 samples were submitted to the FDA laboratory for confirmatory testing. All of these samples passed the confirmatory test. During the facility inspection, the following observations were made:

- Most of the medicines in DOTS facilities originated from the provincial health office located at Quezon City. However, some facilities also receive medicines from private distributors or pharmacies through local government purchase.
- Expired medicines are found alongside unexpired medicines in some facilities. This is not a good practice, as it may result in dispensing expired medicines, further harming the patient.
- Staff reported that they previously experienced medicines quality issues, such as pediatric formulations with leakage or caking and adult fixed-dose combinations with cracked and moist tablets.
- Less than half of the facilities have available a storage temperature monitoring device, and only 22 of 117 facilities (18.8%) are recording or monitoring their storage temperatures.
- PQM personnel were able to record in some facilities storage temperatures higher than the 30°C required for TB medicines.
- Some facilities have inadequate storage space, with unclean and poor storage conditions.
- One facility was found to have evidence of rodent infestation. Bite marks were found on the labels of some pediatric TB medicines.

Activity 2.4: Develop PSA video communication campaign and advocacy messages for TB

- This activity was dropped from the PQM work plan due to budget limitations and measurable indicators for the impact of this activity.

Activity 2.5: Develop medicine QC guidelines for use at RHU level of supply chains and DOTS

- The final draft was completed of the medicine QC guidelines and visual inspection and check list (currently under review by PQM).

IV. Key Challenges

The main challenges faced in the performance of PQM program activities in the Philippines are:

- Collection of adequate medicine samples from DOTS centers according to FDA Philippines requirements was quite challenging because TB medicines are replenished based on the total number of units required for complete treatment of each patient. There is a need for FDA to coordinate with the TB program and central medical stores to determine a feasible approach for replenishing TB medicines samples collected for testing from DOTS centers.
- The inadequate number of FDA staff at sentinel sites delays the immediate testing of TB medicines collected.
- The transfer or relocation of a sentinel site (case of Cebu sentinel site) affects the flow of activities and may even cause misplacement/loss of the information and data.
- The geographical features or locations of several DOTS facilities in Region 4A create a transportation challenge, affecting activities timeline or even hindering the visits in several instances,
- Several DOTS staff are newly hired or recently transferred and unable to provide needed information.

V. Lessons Learned

The lessons learned for this quarter:

- Proper communication among relevant stakeholders improves processes, as exemplified by the letter from the Office of the Department of Health Disease Prevention and Control Bureau that helped coordination among NTP and TB coordinators and staff in the field for inspection and sample collection.

RDMA: The project close-out report is being finalized prior to submission. The project close-out report and transition plan will be disseminated to the country's key stakeholders/partners in the next quarter.

Eastern Europe & Central Asia

Kazakhstan

I. Quarter 4 Highlights

During Q4, PQM made progress in implementation of FY 2017 work plan activities:

- Per PQM's recommendation, the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM), established a Quality Team, which revised its QMS documents and developed uniform quality management documentation for the three laboratories with PQM's technical assistance.
- Under PQM's guidance, the NCEM Quality Team prepared LIFs of Karaganda, Kostanay, and Astana laboratories. PQM also supported the translation of the LIFs and relevant documents from Russian into English.
- Karaganda NQCL submitted an application for WHO PQ.
- PQM provided further remote technical assistance to Nobel Almaty Pharmaceutical Factory.

PQM is providing technical assistance to NCEM to prepare its three medicines quality control laboratories for WHO PQ by strengthening its QMS to meet WHO PQ and ISO 17025 requirements. Eventually, this would contribute toward ensuring the quality of medicines on the Kazakhstan market.

Remote assistance to Nobel Almaty Pharmaceutical Factory will facilitate commissioning operations at the new site and ensure GMP compliance at the new site. Eventually, this will contribute to production of quality-assured products on the market.

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^2. The country has a population of 17.29 million.

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

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

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

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

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

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

GMP standards. Although Nobel already has a national GMP certificate, certain areas require improvement to reach compliance with international GMP requirements.

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

III. Quarter 4 Progress by Objective

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

Per PQM's recommendation based on the assessment of three medicines quality control laboratories in Kostanay, Astana, and Karaganda for their compliance with ISO 17025 and WHO GPPQCL standards in June 2017, NCEM established a Quality Team formed by representatives from the three laboratories participating in PQM program and led by QA representative of Almaty headquarters laboratory. The Quality Team revised the QMS documents of the three laboratories according to PQM's recommendations. The revised documents were reviewed by PQM, and comments were provided. The revised QMS documents will be also shared with other NCEM laboratories, which will help the NCEM laboratories move toward uniform QMS in all of their laboratories.

The NCEM Quality Team developed LIFs for Karaganda, Kostanay, and Astana laboratories with PQM's extensive support. PQM provided translation of the finalized LIFs and relevant QMS documents from Russian into English.

In August 2017, Karaganda NQCL submitted application for WHO PQ. The timeline for submission of applications for WHO PQ by Kostanay and Astana laboratories is being discussed by NCEM. PQM will continue support to the laboratories in responding to the queries from the WHO PQ team.

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

In Q4, PQM continued remote assistance to Nobel Almaty Pharmaceutical Factory.

During this period, Nobel Almaty Pharmaceutical Factory went through several inspections. The company was audited by the National Kazakh GMP Inspectorate and two sites of the factory (previously assessed by PQM) confirmed their compliance with national GMP requirements. Currently Nobel manufactures two anti-TB medicines, levofloxacin and moxifloxacin, in one of these facilities.

Nobel Almaty Pharmaceutical Factory was also inspected by Abbott Laboratories, as Nobel does contract manufacturing. The training in validation of computerized systems provided by PQM in February 2017 helped Nobel respond to the findings identified by Abbott. Per the audit results, Nobel prepared a CAPA plan, which was approved by Abbott; Abbott confirmed that Nobel would continue contract manufacturing of the product at their facility.

In Q4, PQM continued revision of documents on qualification of equipment and drafted some sections of the Validation Master Plan for the new site. PQM will continue remote assistance to Nobel by reviewing documents on qualification of water and air systems. PQM and Nobel will also discuss a possible visit of PQM's consultant to Nobel for onsite assistance with qualification of equipment and engineering systems. The new site at Nobel will commence first operations by the end of 2017. Nobel plans to apply for local GMP certification in January 2018, and PQM will continue providing technical assistance in preparation for that.

Uzbekistan

I. Quarter 4 Highlights

Implementation of the PQM program in Uzbekistan started in Q3 FY 2017. In Q4, PQM worked with Nobel Pharmsanoat, manufacturer of anti-TB medicines, by providing remote assistance in a number of GMP- and dossier-related topics.

PQM also conducted a study tour for Uzbek participants at USP Headquarters. During the study tour, PQM had an opportunity to discuss further PQM activities and plans for the future with Uzbek representatives.

II. Country Context

Uzbekistan is situated in Central Asia. It covers an area of 448,978 km^2 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 MDR-TB burden country; MDR-TB reaches 23 percent among new cases and 62 percent among previously treated cases.

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

Uzbekistan has an established national MRA: the Directorate of Medicines and Medical Equipment Quality Control (Uzbekistan FDA). Medicines regulation in Uzbekistan is based on numerous legislative and regulatory documents. There is a network of QC laboratories in the country. The central laboratory (State Center of Expert Examination and Standardization of Drugs) is ISO/IEC 17025 certified and seeking WHO PQ. However regional laboratories are neither ISO 17025 accredited nor WHO prequalified.

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

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

III. Quarter 4 Progress by Objective

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

Technical assistance to manufacturers of anti-TB medicines to strengthen their quality-assurance systems
As commissioning and start-up operations at the new site will start no earlier than January 2018, in Q4 PQM provided remote assistance to the company, including review of documents for compilation of dossier for WHO PQ and review of reports on transfer of equipment from the current facility to the new facilities (both penicillin and non-penicillin sites). A gap assessment of the new facility will be planned upon completion of commissioning and start-up operations at the new non-penicillin site.

Objective 2 – Strengthen the medicines quality assurance system by building the human capacity of the national stakeholders

Study tour for Uzbek participants at USP headquarters
On August 15–18, 2017, three representatives from the national MRA and the Uzbek State Joint Stock Concern of Pharmaceutical Industry (Uzpharmsanoat) visited USP headquarters in Rockville. During the visit, Uzbek participants met with USP/PQM staff, learned about PQM and its technical approaches, visited USP's laboratories, and became

familiar with the role of public quality standards in the pharmaceutical supply chain and international quality standards for laboratories. They were also briefed about the WHO PQ program, Pharmaceutical Inspection Co-operation Scheme, and WHO Collaborative Registration Procedure. In addition, participants visited Sanaria, Inc., a biotechnology company in Rockville that is developing vaccines for malaria. They had an opportunity to discuss with PQM staff the implementation of the program in the country, as well as future plans. The visit allowed the participants of the tour to acquire additional knowledge and experience, which will help them in their future work

Core Portfolio

Cross Bureau

I. Quarter 4 Highlights

To advocate for the importance of medicines quality assurance systems, PQM cohosted a workshop on building sustainable medicine regulations through risk-based quality assurance and improved regulatory information management, and participated in a discussion panel at Triangle Global Health Consortium Conference.

The PQM program began drafting three medicines quality assurance country profiles. PQM also drafted two e-learning course modules on medicines quality and medicines life cycle and is developing a web-based version of its tool for generating a risk-based sampling plan. PQM submitted to the Agreement Officer's Representative team the final document on the risk-based quality assurance framework and an updated version of the risk-based PMS implementation guidelines document.

II. Cross Bureau Context

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

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

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

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Increase awareness of the importance of medicines quality

To advocate for the importance of medicines QA systems, PQM participated in and presented at a consultative workshop on building sustainable medicine regulations through risk-based quality assurance and improved regulatory information management. The workshop was took place September 25–28 in Bangkok, Thailand. The Asian Development Bank, USAID, USP, and PQM co-hosted the workshop in collaboration with WHO, Global Fund, Asia Pacific Leaders Malaria Alliance, and Centre of Regulatory Excellence at Duke-NUS Medical School. The workshop examined policies, guidelines, frameworks, and best practices important to effective medicines regulations, and discussed approaches to strengthen governance and improve transparency, coordination, and communication with MRA functions. In working groups, participating countries determined their priority gaps in terms of Information Management Systems and a risk-based approach to PMS. PQM also participated in the Triangle Global Health Consortium Conference held September 28 in Raleigh, NC. A PQM representative was a speaker in the discussion panel on the global pandemic of falsified medicines and presented a recent incident of falsified medicine found during training of NQCL staff in Benin on screening medicines for quality using a handheld Raman spectrometer.

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

No updates this quarter.

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

PQM developed a tool that helps develop sampling plans using a risk-based approach. To make this tool user friendly, PQM is in the process of making the tool web-based. An online mock-up has been developed. The completion of this work is expected by early Q1 FY 2018.

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

The tool has been finalized in previous quarters of FY 2017. This activity is complete.

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

PQM has started drafting content of the course. So far, two modules have been drafted and are undergoing internal review. Module 5 deals with the definition of falsified and substandard medicines, current efforts to address the need for the availability of information on medicines quality, and the impact of poor-quality medicines. Module 2 covers life cycles of medicines, including medicine development, market authorization, and post-market safety and quality surveillance throughout the supply chain.

Objective 6 – Establish regulatory system country profiles

PQM began drafting quality assurance profiles of Bangladesh, Malawi, and Nigeria. Assessments of medicines quality assurance of these countries are used as a basis to develop the profiles. Draft profile documents will be available by early Q1 FY 2018.

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

No updates this quarter.

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

No updates this quarter.

Core TB

I. Quarter 4 Highlights

The joint Core TB/NTD workshop for manufacturers and MRAs was held in July 2017, where almost 90 representatives from MRAs, manufacturers, NTPs, and other key stakeholders gathered in Bangkok, Thailand, to discuss how they could individually and collectively help increase the supply of quality-assured anti-TB and NTD medicines. Through the workshop, PQM was able to disseminate information on the WHO PQ program and the valuable technical assistance available to manufacturers to help ensure the availability of priority medicines. The workshop drew participants from 17 countries, including 27 manufacturing companies from 14 countries and MRA officials from 9 countries. Of the 27 manufactures that attended, 14 manufactured anti-TB medicines. PQM conducted an analysis of the manufacturers based on a survey and identified two new manufacturers for further assessment to receive technical assistance under the core TB portfolio.

PQM has worked with NCPC International in the past to help it achieve WHO PQ for streptomycin FPP and capreomycin FPP. NCPC received WHO PQ for streptomycin FPP last quarter and for capreomycin FPP in September. NCPC became the fourth manufacturer to receive WHO PQ for capreomycin FPP, and with its own API source, there is potential for a drop in price. This is another example of how the initial work that PQM conducts in

providing technical assistance to a manufacturer can be applied to multiple products for the manufacturer—another sustainability success.

II. Health Element Context

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

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

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

III. Quarter 4 Progress by Objective

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

PQM has worked with NCPC International in the past to help it achieve WHO PQ for streptomycin FPP and capreomycin FPP. NCPC received WHO PQ for streptomycin FPP last quarter and for capreomycin FPP in September. NCPC became the fourth manufacturer to receive WHO PQ for capreomycin FPP, and with its own API source, there is potential for a drop in price. This is another example of how the initial work that PQM conducts in providing technical assistance to a manufacturer can be applied to multiple products for the manufacturer—another sustainability success.

During Q4, PQM provided technical assistance to manufacturers of the following anti-TB products:

- **Capreomycin FPP**
  - NCPC International received WHO PQ in September 2017.
- **Clofazimine API**
  - PQM provided remote assistance on responding to WHO's queries on the API Master File (APIMF) submitted in Q2.
- **Clofazimine FPP**
  - The contract manufacturing organization continued working on CAPA implementation, which was developed based on PQM and WHO audit and risk mitigations. PQM also provided remote assistance in reviewing the crossover bioequivalence study protocol and providing recommendations to ensure high probability of success for the study. PQM is planning to visit the CRO to conduct an assessment and/or monitoring of the bioequivalence study.
- **Cycloserine API**
  - PQM provided remote technical assistance to the manufacturer in solving stability issues. This manufacturer is still in the product development phase.
- **Rifapentine API**
  - PQM conducted a GMP assessment of one manufacturer in August 2017. PQM will continue technical assistance to the manufacturer in development and implementation of the CAPA plan.
  - PQM is working with a second manufacturer where the CAPAs from PQM's audit have been completed. PQM is now working with the manufacturer to compile the APIMF for submission to the WHO PQ team.
- **Rifapentine FPP**
  - PQM provided remote technical assistance to the company in product development.

- **Gatifloxacin API**
  - PQM is working with the manufacturer to develop the APIMF for submission to WHO PQ; particularly in Q4, PQM provided technical assistance to the manufacturer on impurity analysis based on the USP monograph.
- **Gatifloxacin FPP**
  - As there is no originator or another comparator product on the market, PQM is providing assistance through communication with the WHO PQ team in sourcing of the comparator product.
- **Kanamycin API**
  - With PQM's assistance, the company conducted a cross contamination assessment and is in the process of implementing PQM's recommendations to mitigate the risks related to potential cross contamination. The manufacturer also initiated a process study to reduce impurity with a different source of starting material, and PQM provided remote technical assistance in that.
- **Kanamycin FPP**
  - PQM provided input on addressing additional queries from WHO PQ's assessment of the finished product dossier. The manufacturer is currently waiting for response from the WHO PQ team.
- **Linezolid FPP**
  - The manufacturer had its dossier accepted for review by the WHO PQ team and the U.S. FDA in June 2017. PQM will provide assistance as requested on the queries received from both agencies.
- **PAS Na API**
  - PQM assisted the manufacturer on development of the CAPA plan as a result of the WHO PQ inspection. The CAPA plan was submitted, and the manufacturer is awaiting response from the WHO PQ team.
- **Pyrazinamide API**
  - Implementation of CAPA developed as a result of PQM's audit is in progress.
- **Rifampicin/Isoniazid/Ethambutol/Pyrazinamide (4FDC)**
  - One manufacturer is continuing to implement CAPAs as a result of PQM's GMP assessment in April 2017. PQM provided remote technical assistance in CAPA implementation as needed, and the company completed about 30 percent of the CAPAs. Next steps include identification of a CRO to conduct a bioequivalence study that will be accepted by WHO, conducting of an in vitro dissolution study, and evaluation of the stability data to reduce overage in the formulation. PQM will provide guidance to the company in this process.
  - A second manufacturer is working on submitting CAPAs to PQM. This company was also assessed in April 2017 and needs to work on reformulating its 4FDC not to include organic solvents. The company is also looking to identify a CRO to conduct a bioequivalence study for its 4FDC product. The company is building a new facility for processing of anti-TB medicines, such as the 4FDC product.

To contribute to ensuring an uninterrupted supply of anti-TB medicines on the U.S. market, the PQM team advertised a Request for Applications (RFA) for rifampicin submission to the U.S. FDA. 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 Stop TB Partnership's Global Drug Facility, so the intervention potentially can increase the number of international quality-assured suppliers not only in the United States but also on the global public health market, particularly for the countries benefiting from the Global Drug Facility mechanism. The RFA was advertised for 1 month in August, and six applications were received. PQM is currently evaluating the applications, and candidate selection is expected to take place in Q1 FY 2018.

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

The joint Core TB/NTD workshop for manufacturers and MRAs was held in July 2017. Almost 90 representatives from MRAs, manufacturers, NTPs, and other key stakeholders gathered in Bangkok, Thailand, to discuss how they could individually and collectively help increase supply of quality-assured anti-TB and NTD medicines. The workshop drew participants from 17 countries, including representation from 27 manufacturing companies from 14 countries and officials from 9 separate government MRAs.

During this workshop, PQM was able to meet and engage potential new manufacturers to receive technical assistance toward WHO PQ of priority anti-TB medicines. In addition, PQM was able to meet with the MRAs and NTP members of the Southeast Asian countries to engage in discussion for registration of new anti-TB medicines and

potential participation in WHO's Collaborative Registration Procedure with the assistance of PQM. As next steps from the workshop, the PQM GMP team will continue the discussion and assessment of the identified manufacturers to potentially receive technical assistance. PQM also proposed to continue working with the MRAs and NTP members in Southeast Asian countries on registration of new TB medicines and participation in the WHO Collaborative Registration Procedure.

Participants at the "Ensuring the Quality of Medicines on the Public Health Market" workshop

In Q4, PQM submitted an abstract to the USAID Global Health Mini University conference held on September 14, 2017. Dr. Archil Salakaia conducted a presentation titled, "Quality-Assured Medicines: A Key Factor for TB Elimination." Participants asked many questions, and there were healthy discussions on PQM's work to assure the quality of medicines for TB elimination.

Core NTD

I. Quarter 4 Highlights

The joint Core TB/NTD workshop for manufacturers and MRAs was held in July 2017, where almost 90 representatives from MRAs, manufacturers, NTPs, and other key stakeholders gathered in Bangkok, Thailand, to discuss how they could individually and collectively help improve access to quality-assured anti-TB and NTD medicines. PQM was able to disseminate information on the WHO PQ program and the valuable technical assistance available to the manufacturers to help ensure the availability of priority medicines. The workshop drew participants from 17 countries, including representation from 27 manufacturing companies from 14 countries and MRA officials from 9 countries. The workshop emphasized the importance to ensuring the quality of medicines for TB and NTD programs and discussed and provided information on available resources for strengthening quality assurance systems for both the manufacturers and MRAs.

During the quarter, PQM also worked to complete the review of EOI submissions for bioequivalence study support to manufacturers. Evaluations were conducted on five applications, and the top two manufacturers, S Kant and Medopharm, were selected for PQM's financial and technical assistance toward conducting a praziquantel bioequivalence study. Contracts are drafted and scheduled to be finalized in October 2017. By finalizing the contracts with the two manufacturers, PQM can initiate work with the manufacturers and CROs to develop, review, and execute the bioequivalence study protocols in the coming months. PQM's support to the selected manufacturers will help to accelerate their preparedness for submission for WHO PQ of praziquantel, which is greatly needed on the public health market at this time.

Lastly, PQM-supported manufacturer Hisun Pharma obtained WHO PQ for praziquantel API. Hisun Pharma is the first manufacturer to become prequalified for praziquantel API. Praziquantel is an important medicine for treating NTDs, and having a quality-assured API source is vital for production of quality finished products.

II. Health Element Context

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

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

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

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

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

III. Quarter 4 Progress by Objective

Objective 1 – Increase availability to quality-assured NTD medicines

PQM-supported manufacturer Hisun Pharma obtained WHO PQ for praziquantel API. Hisun Pharma is the first manufacturer to become prequalified for praziquantel API. Praziquantel is an important medicine for treating NTDs, and having a quality-assured API source is vital for production of quality finished products.

During Q4, PQM provided technical assistance to manufacturers of the following NTD products:

- **Praziquantel API**
  - Hisun Pharma submitted its APIMF, and WHO completed its second inspection in April 2017. PQM provided remote assistance, and the manufacturer obtained WHO PQ for the product in September 2017.
  - A second manufacturer received site acceptance by WHO (WHO Public Inspection Report) in Q4. PQM also provided remote assistance in addressing WHO's queries on the APIMF regarding starting material.
  - A third manufacturer submitted its APIMF for WHO PQ, and it was accepted for review in Q3. In Q4, PQM provided remote assistance in the first round of queries received by the manufacturer from WHO PQ.
  - PQM identified a fourth manufacturer that is considering developing praziquantel API for human use and its submission for WHO PQ. This manufacturer already has U.S. FDA and Certificate of Suitability of Monographs of the European Pharmacopoeia (CEP) approval for praziquantel API, but it is for animal use.

- A fifth manufacturer received CEP approval for praziquantel API with the assistance of PQM and is now considering submission to WHO PQ for this API.

- **Praziquantel FPP**
  - PQM provided assistance in product development for one manufacturer. A PQM GMP assessment is tentatively scheduled for Q1.
  - A second manufacturer is completing the CAPA implementation as a result of PQM's GMP assessment. PQM will continue to provide technical assistance on dossier compilation while the manufacturer works with Gates Foundation for its bioequivalence study.
  - A third manufacturer recently moved its praziquantel line to a new facility, and PQM plans to conduct a GMP assessment in Q1 FY 2018. The manufacturer is also preparing for the bioequivalence study of its finished product.
  - Two manufacturers were identified to receive financial and technical assistance toward their bioequivalence studies. PQM will conduct GMP and dossier assessments of both manufacturers in Q1 FY 2018.

- **Albendazole API**
  - One manufacturer is in the process of implementing the CAPAs from PQM's audit in Q1. A PQM onsite technical assistance visit will be scheduled with the manufacturer.
  - A second manufacturer has completed product development and is now conducting process validation with PQM's remote technical assistance. PQM plans to make an onsite visit to conduct a GMP assessment in Q1 FY 2018.

- **Albendazole FPP**
  - One manufacturer is in the product development stage. PQM has been working with the manufacturer and WHO to source the comparator product.

- **Mebendazole FPP**
  - One manufacturer is in the product development stage with the assistance of PQM. PQM is also working with the manufacturer to source the comparator product.

During the quarter, PQM also continued its work on the situation analysis on the availability of quality-assured priority NTD medicines in five high NTD burden countries (Nigeria, Ethiopia, Tanzania, India, and Indonesia). The draft report of analysis was developed in Q4. The report will be finalized and shared with USAID for review in Q1 FY 2018. Subsequently, a decision on selection of the manufacturers of NTD products in these countries will be made in discussion with USAID.

Objective 2 – Technical support for bioequivalence study

Thorough evaluation of the five EOI applications received for PQM's support of praziquantel bioequivalence studies was conducted in Q4. PQM's conducted the evaluation based on preset scoring criteria and selected the two top manufacturers. These manufacturers will receive PQM's financial and technical assistance to help them prepare for submission of their products for WHO PQ.

Selecting manufacturers to receive financial and technical assistance toward the bioequivalence study of their praziquantel finished product will motivate the manufacturer to complete the process for WHO PQ submission. The selected manufacturers have been notified, and contracts were drafted for review by the manufacturers. These contracts are planned to be fully signed by PQM and manufacturers in October 2017.

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

The joint Core TB/NTD workshop for manufacturers and MRAs was held in July 2017. Almost 90 representatives from MRAs, manufacturers, NTPs, and other key stakeholders gathered in Bangkok, Thailand, to discuss how they could individually and collectively help improve access to quality-assured anti-TB and NTD medicines. The workshop drew participants from 17 countries, including representation from 27 manufacturing companies from 14 countries and officials from 9 separate government MRAs; 12 of the 27 manufacturers that attended the workshop are already manufacturing or developing the priority NTD medicines.

After detailed analysis of the surveys submitted by the manufacturers, it was determined that PQM could potentially engage with four manufacturers for technical assistance toward WHO PQ of priority NTD medicines. The PQM GMP team will continue the technical assistance process for the new manufacturers identified.

Core MNCH

I. Quarter 4 Highlights

PQM continued to provide technical assistance to manufacturers of priority MNCH medicines during Q4. PQM worked with one manufacturer, ACI Pharmaceuticals, to address corrective actions as a result of an audit conducted for chlorhexidine solution by Save the Children. The manufacturer has completed all of the CAPAs and will be working to provide an update to the organization and become a future supplier. The manufacturer is also supplying approximately 40,000 units of chlorhexidine solution per month to the local markets in Bangladesh and Burma. PQM's work with ACI Pharmaceuticals aims toward having a quality-assured source of this product in the local market and eventually available to global procurement agencies as well.

II. Health Element Context

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

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

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

III. Quarter 4 Progress by Objective

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

During Q4, PQM provided technical assistance to manufacturers of the following MNCH products:

- **Chlorhexidine solution**
  - PQM continued remote assistance to ACI Pharmaceuticals to address corrective actions as a result of an audit conducted by Save the Children. The manufacturer has completed all of the CAPAs and will be working to provide an update to the organization and become a future supplier. The manufacturer is also supplying approximately 40,000 units per month to the local markets in Bangladesh and Burma.
- **Chlorhexidine gel**
  - Work with the CHX gel manufacturer has been temporarily put on hold due to suspension of activities in Kenya.
- **Magnesium sulfate FPP**
  - One manufacturer is still in the product development stage with the assistance of PQM.
  - PQM conducted a GMP assessment of a second manufacturer in Q2, and the assessment report was provided to the manufacturer in Q3. PQM is awaiting CAPAs from the manufacturer. During the March audit, the magnesium sulfate line could not be assessed due to renovation. A trip is planned for Q1 or Q2 of FY 2018 to assess the renovated area
- **Oxytocin FPP**
  - PQM continues to provide technical assistance to the manufacturer in product development.
- **Oxytocin API**
  - PQM conducted a GMP assessment, and the manufacturer is in the process of implementing CAPAs.

- **Amoxicillin FPP**
    - PQM identified a new manufacturer in May 2017. PQM plans to conduct a full GMP assessment in Q1 of FY 2018. PQM is also working with the manufacturer to identify a new API source.
    - A second manufacturer is implementing the CAPAs as a result of PQM's GMP assessment. PQM is also working to facilitate discussion between the manufacturer and procurement agencies on the availability of this product.

Objective 2 – Provide technical leadership on MNCH medicine quality assurance

PQM worked on drafting a product information report on amoxicillin DT finished product, which consolidates much of the needed information for manufacturers to help with producing quality-assured medicines. The product information report contains a summary of available literature for the API, analytical methods, toxicology, and formulation and process of the solid dosage form for the product. PQM will continue to work on finalizing the product information report to be available to manufacturers.

Core Malaria

I. Quarter 4 Highlights

The profiles for Ethiopia and Nigeria were finalized, including initial feedback received from USAID. Profiles were subsequently submitted to the rest of the PMI team, and their comments have been addressed.

PQM is waiting for the PMI team's recommendation to develop additional profile(s) with the remaining pipeline.

Quarterly activity update reports for Q2 and Q3 FY 2017 were submitted to the PMI team. Feedback received for Q3 FY 2017 was addressed, and the report was resubmitted.

II. Health Element Context

Although tremendous progress has been made in the fight against malaria, the disease continues to affect the health and economy of endemic countries globally. Current treatments may be rendered ineffective if proper measures are not taken to ward off the threat of resistance. The mainstay for malaria control recommended by WHO is ACTs, which have demonstrated good efficacy against the malaria parasite. However, resistance of the malaria parasite to ACTs has been reported in Southeast Asia, raising concerns about the possibility of the spread of the drug-resistant parasite to Africa. Certain practices favor the development of resistance, including unregistered medicines of unknown quality and efficacy, as well as diversion of donated medicines to the private sector where those medicines may be used irrationally and without proper prescription.

III. Quarter 4. Progress by Objective

Objective 1 – Provide technical leadership & global advocacy to raise awareness about the potential dangers of using substandard or counterfeit antimalarial medicines

The country profiles developed for Ethiopia and Nigeria provide updated information on regulatory aspects of countries' medicines quality assurance systems. The information includes an up-to-date status of countries legal and regulatory frameworks, emphasizing specific key functions (e.g., registration and post-marketing quality surveillance), the status of NQCLs, and the corresponding sustainability plans. The country profiles include comprehensive information on malaria medicines in the country, as well as information on PQM technical assistance to strengthen quality assurance systems, the outcomes of the assistance, current gaps, and planned activities to address them. Quarterly activity update reports for Core Malaria and PMI-funded countries were also delivered.

Planned Activities for Q4 included the following:

- Country Profiles
    - Finalize information gathering for Nigeria profile
    - Submit Nigeria profile to USAID
    - Update Ethiopia and Nigeria profiles based on USAID feedback
    - Submit final profiles to PMI

- Quarterly Reports
    - Gather information from PMI funded countries
    - Deliver to PMI team quarterly report on Core Malaria and PMI funded countries

Major deliverables/milestones:

- Ethiopia and Nigeria profiles submitted to PMI team

Summary of upcoming activities:

- Identify in consultation with PMI adviser additional countries to develop profiles
- Gather information for identified countries
- Develop and submit profiles to PMI

Management Overview

The PQM team successfully submitted all FY 2018 work plans by the USAID deadline of August 31. PQM drafted FY 2018 work plans for 15 country Missions, 3 directed Core portfolios, and the Cross Bureau project. The works plans outlined the background and rationale, key accomplishments, PQM's strategic approach, and planned activities for the fiscal year, as well as highlighted the associated program management, monitoring and evaluation, knowledge management and communication, and budgetary information. Each work plan also included a performance monitoring plan, activity monitoring matrix, and environmental mitigation and monitoring plan (if applicable). These comprehensive documents provide USAID with a considerable amount of information that allows USAID activity managers to clearly understand the plan for the upcoming fiscal year. By submitting the work plans at the end of August, PQM anticipates many work plans receiving USAID approval early in the new fiscal year and swift implementation thereafter. As of the end of October, 8 of the 19 work plans (42%) had already received full approval.

PQM Director Jude Nwokike attended two key meetings during Q4. The first was presenting at the Boston University School of Public Health "Short Course on Quality of Medical Products and Public Health" an overview of the PQM program. Director Nwokike also participated in the Joint UNICEF, UNFPA, and WHO meeting in Copenhagen, Denmark.

In addition to the key meetings, Director Nwokike paid a management visit to Bangladesh in July 2017. The visit provided the opportunity to engage with the PQM Bangladesh team and provide guidance from the leadership level. During his visit, Director Nwokike participated in the WHO Coalition of Interested Partners meeting, at which an update on PQM's activities since March 2016 and detailed justification of the DGDA proposed organogram were presented. Mr. Nwokike provided suggestions and gave a pragmatic outline on the new DGDA organogram to reflect its mission and strategic vision, as well as to gradually align it with the international standard of a fully functional regulatory agency.