

# Promoting the Quality of Medicines (PQM) Program

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

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

As of July 2018, USAID supports PQM's work in 18 countries, 1 regional mission, 1 Cross Bureau program, and 3 core health programs.

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# Acronyms

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

# Executive Summary

The Promoting the Quality of Medicines (PQM) program provides technical assistance in partnering countries to strengthen quality assurance (QA) systems to sustainably ensure medical products quality and safety and to protect public health. PQM's assistance helps to build the capacity of medicines regulatory authorities (MRAs) and QA systems. PQM supports the manufacture of quality-assured priority essential medicines for malaria; HIV/AIDS; tuberculosis (TB); neglected tropical diseases (NTDs); and maternal, newborn, and child health (MNCH). PQM also provides support to increase the utilization of medical product quality information for decision-making. This report summarizes results achieved during the third quarter (Q3) of FY 2018, from April 1 to June 30, 2018.

Quality is paramount to ensuring that the safety and efficacy of medical products are maintained from the moment a product is manufactured, across the entire supply chain, until it reaches the patient. By strengthening systems that help ensure quality—from developing effective and enforceable legislation, policies, and workforce capacity to helping implement regulations, guidelines, and operational procedures—PQM aims to reduce and eliminate substandard and falsified products that pose serious risks to patients' health and undermine global health and development efforts. PQM also supports the adoption of data standards and integrated regulatory information management to ensure that accurate, up-to-date, and reliable data inform regulatory actions and are disseminated to all stakeholders. In Ethiopia, a Recall Directive, which was discussed through a workshop in Q2, was reviewed by the Ethiopian Food, Medicine and Health Care Administration and Control Authority's management team and approved in Q3. Serving as a legally binding enforcement tool, this Directive will facilitate removal of poor-quality medicines from the market and the implementation of pharmaceutical recalls as outlined in the recall guidelines; in addition, it will help improve compliance of responsible stakeholders with regulatory requirements. In Indonesia, evaluations are underway on (1) the effectiveness of incorporating Minilab™ into post-marketing surveillance (PMS) (from a cost-effectiveness perspective, as well as Minilabs™ enabling an expansion of the types and total numbers of pharmaceutical samples tested) and (2) the methodology for collaboration among the Provincial Health Office, District Health Office, and regulator (BPOM). In Pakistan, PQM is working with six laboratories and provided support to the Pakistan Drugs Testing and Research Center toward World Health Organization (WHO) prequalification; the accreditation audit for ISO 17025 is expected in July.

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 prequalification program. PQM also provides technical assistance and guidance to manufacturers for the local production of medicines, which may decrease reliance on international donations and help establish a sustainable local supply with national resources. In Indonesia, PQM is in discussions to develop a training-of-trainers methodology that will establish a pool of experts for providing bioavailability/bioequivalence trainings for clinical research organizations. PQM plans to support the next training workshop, planned for August 2018, which will focus on data integrity and data validation in bioequivalence studies. In Pakistan, PQM continued to support the industry to improve good manufacturing practice (GMP) standards; based on experience gained through a comprehensive training on the Common Technical Document and GMP for the industry in FY 2017, an advanced 4-day training course on GMP was held in Karachi and attended by 59 senior technical managers from selected manufacturers.

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 Q3, the Ghana Food and Drug Authority (GFDA) finalized and shared with PQM the report on PMS of antimalarial and analgesic medicines tested in Q2, which showed that 418 antimalarial medicines and 75 analgesics were tested: 1.4 percent of antimalarials and 5.3 percent of analgesics samples tested did not meet quality specifications. GFDA took regulatory actions to remove the substandard medicines from the market. PQM subsequently shared this final report with USAID/Ghana and the U.S. President's Malaria Initiative. Additionally this quarter, in an effort to increase information in the public domain related to the manufacture of quality-assured medicines, PQM finalized and made available on PQM's website the first publication of a product information report (PIR) for rifapentine, an anti-TB medicine. The PIR contains a summary of available literature and expert opinion on the active pharmaceutical ingredient, analytical methods, toxicology, and formulation and process of the solid dosage form for the product. This publication will provide manufacturers and MRAs with centralized, relevant information on the product to help them in their decision-making.

Through PQM's Cross Bureau project, the development of a surveillance tool (MedRS) that complements PQM's "Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low and Middle Income Countries" has been finalized. MedRS, which will enable countries to design sound sampling strategies based on risk and statistical considerations, is expected to be posted on the PQM website by the end of Q4. Once posted, it will be freely available for use by interested countries. Lastly, PQM's proposal to developing an introductory e-course on

medicines' QA was submitted to the Global Health e-Learning Center. A revision of the scope and module content was suggested by the Agreement Officer's Representative team, and a proposal with a detailed module outline will be submitted to the Global Health e-Learning Center during Q4.

# Program Background

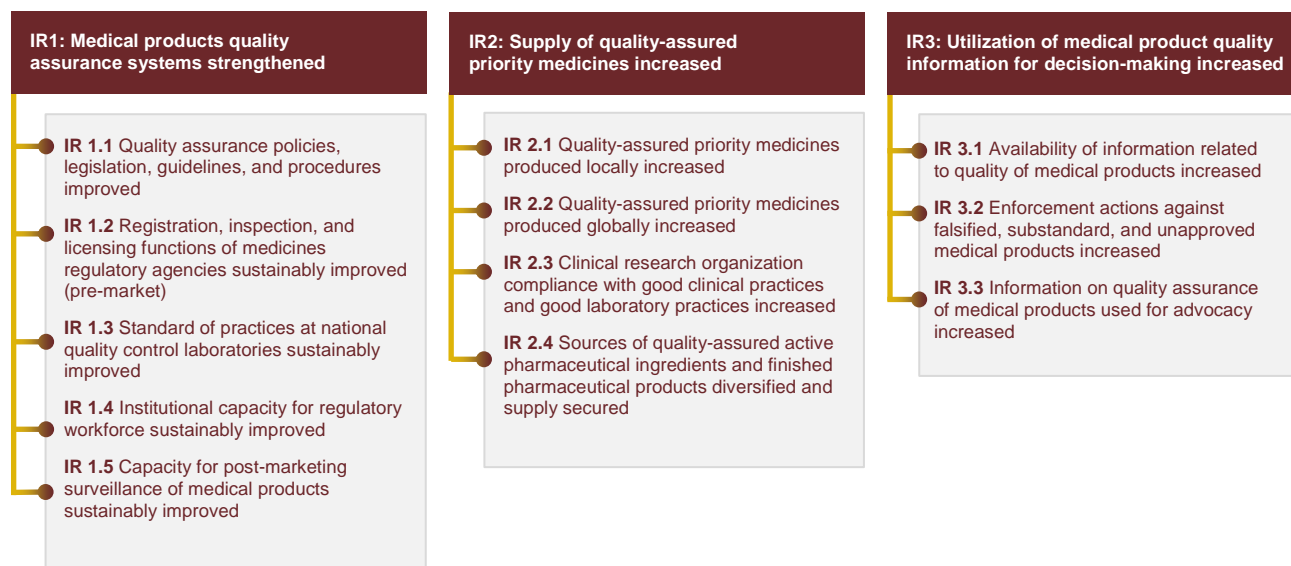
The Promoting the Quality of Medicines (PQM) program is a cooperative agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). Since 1992, USP has worked with USAID to support low- and middle-income countries (LMICs) in addressing critical issues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

This quarter, PQM implemented projects for 18 USAID country missions, 1 regional mission, 1 Cross Bureau program, and 3 core health programs.

## Results Framework

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

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



This report highlights the results achieved by PQM, organized by result area representing multiple countries where the program works, as well as by country and core portfolio for the April–June 2018 period.

# Result Highlights





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

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## Description of Sub-IRs

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

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

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

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

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

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

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

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

### **Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved**

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

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

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

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

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

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## **Overview of FY 2018 Third Quarter IR1 Achievements**

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### **Key Results and Highlights**

This quarter in Ethiopia, three guidelines on specialized areas of medicines registration (Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products, and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology) were completed and posted on the Ethiopian Food, Medicine and Health Care Administration and Control Authority's (EFMHACA) website (<http://www.fmhaca.gov.et/standardsdirectivesguidelines.html>). PQM provided technical assistance throughout the development of these guidelines. EFMHACA management's strong follow-up and expedited approval process formed a clear example of the leading role they assumed in this process. Approval of the guidelines for registration of specialized products is expected to increase access to new and innovative essential medicines and better address existing and emerging diseases. The guidelines will help facilitate registration of priority medicines, including vaccines and other biological products, and increase access to such medicines. In addition to their contribution to the alignment with international best practices, these guidelines will help in the review of dossiers for these types of products. PQM helped to establish efficient mechanisms for the development of guidelines that enabled the timely completion of these new guidelines. In addition, EFMHACA was able to use systems and processes PQM had earlier developed to facilitate the review of these guidelines.

Also in Ethiopia, a Recall Directive, which was discussed through a workshop in Q2, was reviewed by EFMHACA's management team and approved during in Q3. Serving as a legally binding enforcement tool, this directive will facilitate removal of poor-quality medicines from the market and the implementation of pharmaceutical recalls as outlined in the recall guidelines; in addition, it will help improve compliance of responsible stakeholders with regulatory requirements.

In Nigeria, following the accreditation of the National Agency for Food and Drug Administration and Control's (NAFDAC) Kaduna Laboratory in 2017, the laboratory in this quarter maintained existing test methods and also expanded scope to include microbiology test methods. The expansion to microbiology test methods will aid pharmaceutical microbiological analytical testing of products for sterility and enumeration of microorganisms in the northern part of the country. As part of NAFDAC's commitment to sustainability, all costs associated with equipment calibration, proficiency tests, and other laboratory supplies were paid for by the agency. Minimal technical assistance was provided by PQM during the preparation for surveillance audit that led to scope expansion, as the laboratory staff exhibited technical competency and took the lead during the process. With the scope expansion, three PQM-supported NAFDAC laboratories can now conduct pharmaceutical microbiology testing. Next steps include providing remote technical assistance to resolve minor nonconformances identified during the third-party audit. The laboratory's accreditation certificate is expected next quarter.

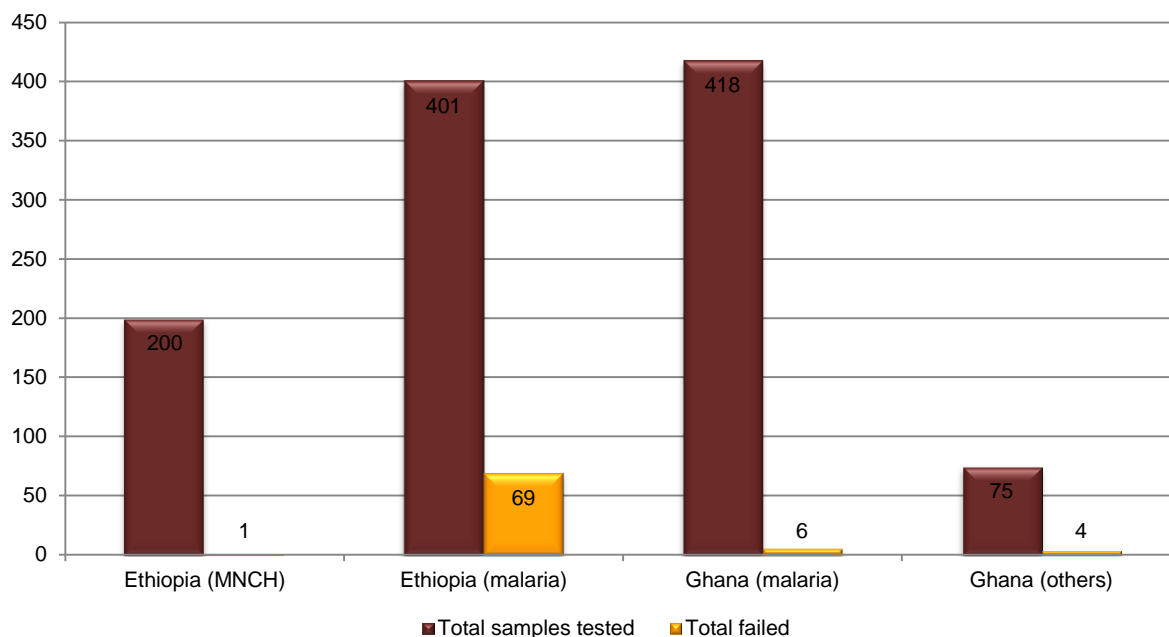
In Indonesia, Minilab™ screening has been officially adopted within the regulatory authority's (Drug and Food Control Agency; BPOM) routine sampling guideline for PMS in nine provincial BPOM institutions since the beginning of 2018. In these provinces, plans are underway to procure equipment and train staff for Minilab™ screening through a cooperative activity between PQM and the KNCV Tuberculosis Foundation's (KNCV) Challenge TB program. An evaluation of the effectiveness of incorporating Minilab™ into PMS (from a cost-effectiveness perspective, as well as Minilabs™ enabling an expansion of the types and total numbers of pharmaceutical samples tested) and an evaluation of the methodology for the Provincial Health Office (PHO)–District Health Office (DHO)–BPOM collaboration is underway. PQM will conduct focus-group discussions and assessments of the trainees from the Ministry of Health (MOH) and BPOM on the effectiveness of this type of collaboration and the best way forward for data-sharing and joint enforcement actions when out-of-specification products are identified. This assessment will

help to establish action plans as PQM rolls out additional procurement of equipment (under Global Fund technical assistance activities), training, and implementation of field screening for BPOM institutions nationwide.

### Key IR1 Indicators for FY 2018 Q3

|  |                             |
|--|-----------------------------|
| Number of quality control laboratories accredited or reaccredited                                  | 1 (Nigeria)                 |
| Number of quality control laboratories that have passed the proficiency test/inter-laboratory test | 3 (Bangladesh, Nigeria)     |
| Number of medical products' samples tested   | 601 (200 MNCH, 401 malaria) |

**Number of Samples Tested and Failed  
April–June 2018**



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

### Description of Sub-IRs

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

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

In support of key USAID priority health programs, PQM provides technical assistance and guidance to manufacturers for the local production of priority essential medicines, including those used to treat newborn infections and maternal and child health products. Local production may decrease reliance on international donations and help establish a

sustainable local supply. In addition, developing local manufacturing capacity where feasible and appropriate, and enhancing regulatory oversight, can improve both national and regional capabilities for sustainable sourcing of quality-assured medicines.

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

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

#### **Sub-IR 2.3 CROs' compliance with good clinical practices and good laboratory practices increased**

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

#### **Sub-IR 2.4 Sources of quality-assured API and FPP diversified and supply secured**

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

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## **Overview of FY 2018 Third Quarter IR2 Achievements**

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### **Key Results and Highlights**

PQM has been working with four manufacturers of chlorhexidine (CHX) 7.1% gel in Pakistan. The products of all four manufacturers are already in production and approved for domestic launch and are now freely available on the local market. During Q3, PQM supported the manufacturers to prepare for UNICEF submission by reviewing their dossiers and suggesting improvements to make the dossiers acceptable by UNICEF. As a result of this support, two manufacturers (Atco Laboratories and Aspin Pharmaceuticals) have submitted their dossiers to UNICEF.

PQM's support for two key maternal and child health products also saw significant progress this quarter. A dossier from a manufacturer in Pakistan for zinc dispersible tablet has been accepted for review by WHO PQ, and an audit visit to the manufacturer is planned. In Ukraine, the dossier for a PQM supported manufacturer for magnesium sulfate injection 500 mg/mL (10 mL) was accepted by WHO for review.

For tuberculosis, a manufacturer was able to complete its dossier compilation for clofazimine FPP with PQM's technical assistance. The manufacturer submitted the dossier for WHO PQ in June 2018. In addition to the submission of the clofazimine dossier, PQM also worked with the manufacturer Qilu Pharma to see the first WHO prequalification of amikacin FPP for the public health market.

In Indonesia during Q3, PQM supported a successful WHO audit of Kalbe Farma for prequalification of its levofloxacin 500 mg tablet, with a result of only three major observations. Audit findings are classified as critical, major, or minor. While critical observations are considered very serious and unacceptable, major observations are deviations that can be corrected. PQM had conducted a mock audit during Q2 that identified a number of key areas addressed by a rapid corrective and preventive action (CAPA) implementation in time for the WHO audit. Since there were less than six major observations by WHO, Kalbe Farma will be able to satisfy the auditors with its CAPA documentation without the need for a follow-up onsite visit. PQM anticipates successful prequalification of Kalbe Farma during FY 2018 Q4.

Additionally in Indonesia, PQM initiated collaboration with key Centers of Excellence universities in the country providing bioequivalence expertise to BPOM on developing a sustainable mechanism for high-quality technical assistance. PQM has shifted its focus from providing support to the Centers of Excellence to providing support for the Bioavailability/Bioequivalence Forum, a communication forum for CROs working in bioequivalence (in both the academic and private sectors) that builds capacity in Indonesia and regularly conducts training workshops for members. PQM is in discussions to develop a training of trainers (TOT) methodology that will establish a pool of experts for providing bioavailability/bioequivalence trainings for CROs as well as supporting the regulator BPOM. The next training workshop is planned for August 2018 and will focus on data integrity and data validation in bioequivalence studies; PQM plans to support this.

#### Key IR2 Indicators for FY 2018 Q3

|   |                       |
|---|-----------------------|
| Number of priority medicines that achieved WHO PQ, SRA, or ERP approval | 1 (amikacin solution) |
|---|-----------------------|

#### Number of Manufacturers Provided with Technical Assistance in FY 2018 Q3

| Countries/<br>Core Programs | Number of<br>Manufacturers | Product Types   |
|-----------------------------|----------------------------|---|
| Core MNCH                   | 1                          | Magnesium sulfate FPP   |
| Core TB                     | 13                         | Clofazimine FPP, clofazimine API, rifapentine API, rifapentine FPP, gatifloxacin API, gatifloxacin FPP, kanamycin API, kanamycin FPP, linezolid FPP, rifampicin/isoniazid/ethambutol/pyrazinamide (4 FDC) |
| Core NTD                    | 7                          | Praziquantel API, praziquantel FPP, albendazole API, albendazole FPP  |
| Bangladesh                  | 1                          | Chlorhexidine solution  |
| Ghana                       | 1                          | Artemether lumefantrine FPP   |
| Nigeria                     | 6                          | Sulfadoxine pyrethamine FPP, chlorhexidine gel, zinc sulfate FPP, artemether lumefantrine FPP, ready-to-use therapeutic foods   |
| Indonesia                   | 2                          | Levofloxacin FPP  |
| Pakistan                    | 6                          | Amoxicillin dispersible tablet (DT), chlorhexidine gel, zinc DT   |
| Uzbekistan                  | 1                          | Levofloxacin FPP  |

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

### Description of Sub-IRs

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

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

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



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

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

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

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

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

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

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

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## **Overview of FY 2018 Third Quarter IR3 Achievements**

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### **Key Results and Highlights**

In Ethiopia, a consolidated preliminary report of FY 2017 PMS results was drafted this quarter. The report showed a failure rate of 17.25 percent for 401 antimalarial medicines sampled. The findings showed an increase in failure rate as compared to FY 2016 PMS from 1.8 percent to 17.25 percent. The reason for this change is an increased failure rate of quinine sulfate tablets (55 samples from 11 batches). All of the failed samples were from one manufacturer and a single importer. The same product, quinine sulfate, failed quality test during FY 2016 PMS, although the number of samples failed during that year was significantly less than that of FY 2017. Similarly, there was an increase in the percentage of unregistered antimalarial medicines, from 8 percent in 2016 to 15.75 percent in 2017. In the previous quarter, EFMHACA took prompt regulatory measures on all of the failed samples, including recalling the products from the market, conducting further investigative inspections, and taking regulatory measures on the manufacturer of the failed quinine sulfate.

Also in Q3, the Ghana Food and Drug Authority (GFDA) finalized and shared with PQM the report for the PMS of antimalarial and analgesic medicines tested in the second quarter. Per the final report, a total of 418 antimalarial medicines and 75 analgesics were tested: 1.4 percent (6 of 418) antimalarials (4 quinine sulfate and 2 sulfadoxine pyrimethamine tablets) and 5.3 percent (4 of 75) analgesics samples tested did not meet quality specifications. GFDA also took regulatory actions to remove the substandard medicines from the market. PQM subsequently shared this final report with USAID/Ghana and the U.S. President's Malaria Initiative (PMI).

Additionally this quarter, in an effort to increase information in the public domain related to the manufacture of quality-assured medicines, PQM finalized and made available on PQM's website the first publication of a product information report (PIR) for rifapentine, an anti-TB medicine. The PIR contains a summary of available literature and expert opinion on the API, analytical methods, toxicology, and formulation and process of the solid dosage form for the

product. This publication will help manufacturers and MRAs have relevant information on the product in one place, which would help them in easier decision making.

**Key IR3 Indicators for FY 2018 Q3**

|   |                       |
|---|-----------------------|
| Number regulatory actions made by the MRA   | 6 (Ghana and Liberia) |
| Number of PQM-supported awareness raising or advocacy events promoting quality of medical products  | 8                     |
| Number of publications issued and presentations made on medical products quality assurance at national or international level that are presented or authored by PQM | 12                    |

# Africa





# Benin

## I. Quarter 3 Highlights

PQM procured and installed a power generator for the National Quality Control Laboratory (LNCQ). The laboratory also had its high-performance liquid chromatography (HPLC) instrument repaired. LNCQ is now ready to receive training on the HPLC and participate in a proficiency testing.

PQM is discussing details for the implementation of PMS activities with LNCQ. The PMS protocol includes elements of a risk-based approach for sampling and testing.

## II. Country Context

Malaria is the leading cause of morbidity in Benin, which is a high malaria transmission country according to WHO. In 2016, there were 1,324,576 reported and confirmed cases of malaria and 1,646 reported deaths. Benin adopted artemisinin-based combination therapy (ACT) in 2004 and began large-scale implementation of artemether–lumefantrine combination as a first-line treatment in 2007.

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

## III. Quarter 3 Progress by Objective

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

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PQM completed the procurement of a power generator to support LNCQ operations. The power generator was successfully installed to the satisfaction of LNCQ. LNCQ completed electrical rewiring of the laboratory to accommodate changes in the new power sources. Due to the rampant power outages prior to the generator's installation, the HPLC system would break down and could not sustain work processes. With the installation of the stable power source, the vendor was able to repair the HPLC, and it is now up and running, contributing to smooth operation of the laboratory. PQM is scheduled to provide advanced training in HPLC in early Q4 and will subsequently participate in proficiency testing.

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

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PQM collaborated with LNCQ to develop a PMS protocol (with a detailed budget) that incorporates elements of PQM's risk-based approach for sampling and testing. This approach will reduce the burden on LNCQ by limiting the number of samples to be collected and tested. It will also allow the laboratory to strategize its sampling plan. Sampling of antimalarial medicines will target the public sector and "pharmaceutical depot" outlets in remote areas that are managed by non-pharmacist staff under the supervision of the nearest pharmacist. Initial screening of most samples will be conducted in the field using a handheld Raman spectrometer. Other samples will be screened in the laboratory using Minilab™ kit. Samples that failed screening will undergo confirmatory testing as needed. PQM will facilitate the testing to enable timely laboratory submission of the results to the Directorate of Pharmacy, Medicine and Diagnostics for further action, as needed.

# Burkina Faso

## I. Quarter 3 Highlights

PQM continues to strengthen the Directorate of Medicine Control (DCM) laboratory. The following achievements were completed this quarter:

- Trained eight laboratory staff on calibration of ultraviolet-visible spectrophotometers (2 spectrometers).
- Procured a proficiency testing panel for DCM. The laboratory is currently carrying out the tests.
- DCM participated in USP-led inter-laboratory testing.

As next steps, PQM will closely monitor the performance of the laboratory in proficiency testing and inter-laboratory testing.

## II. Country Context

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

PQM was selected by USAID/Burkina Faso to strengthen the capacity of the country's national MRA (Direction Générale de la Pharmacie, du Médicament et des Laboratoires (DGPML)), NQCL (Laboratoire National de Santé Publique (LNSP)), and other major pharmaceutical systems with the primary goal of improving its QA/QC of medicines.

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

## III. Quarter 3 Progress by Objective

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

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To continue strengthening the analytical capacity of the DCM laboratory, PQM trained staff on the calibration and use of ultraviolet-visible (UV-Vis) spectrometer. Laboratory testing of medicines following international standards requires the use of several methods and instruments. UV-Vis spectrometer is among the instruments frequently used in the testing. Prior to the training, PQM procured a UV-Vis calibration kit for training and future use. Eight staff members received the training, and then PQM staff observed the trainees as they applied their new skills to calibration of two spectrophotometers and testing a sample. PQM also held a short training on Fourier transform infrared (FTIR) spectroscopy, how it works, and what the data can be used for. This was the first training that the staff received on this instrument procured last year through Sahel Women's Empowerment and Demographic Dividend project.

To prepare the laboratory for ISO 17025 accreditation, PQM is facilitating its participation in a proficiency testing activity managed by an external provider and an inter-laboratory testing organized by USP. The laboratory has successfully participated in previous USP inter-laboratory testing. Proficiency testing and inter-laboratory testing are usually used during the ISO 17025 accreditation process to demonstrate the ability of the laboratory to carry out the tests according to the standard.

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

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In collaboration with the National Pharmaceutical Regulatory Agency (ANRP), PQM developed a budget for the upcoming round of PMS of antimalarial medicines quality.

As next steps, PQM will collaborate with ANRP to develop a sampling and testing protocol and facilitate its implementation.

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## Objective 3 – Support the creation of the National Pharmaceutical Authority

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In Burkina Faso, ANRP has the mandate to organize pre- and post-marketing surveillance of medical products. However, quality control testing is carried out by LNSP. One of the challenges of PMS implementation in Burkina Faso is the lack of coordination between ANRP and LNSP. This issue has been clearly stated in the national pharmaceutical policy. PQM discussed with ANRP and DCM a plan to draft a regulatory provision that clarifies the mechanism of collaboration between ANRP and DCM for the implementation of PMS activities to avoid delays in management of noncompliant products.

# Ethiopia

## I. Quarter 3 Highlights

In Q3, PQM continued its technical assistance to EFMHACA in the development and completion of four guidelines/manuals, assessment of the medicine registration system for compliance with international standards, review of standard operating procedure (SOPs) for ISO 17020 accreditation of the inspection system, and the ongoing improvement and implementation of the Medicine Registration Information System (MRIS). In addition, technical support was provided in maintaining the EFMHACA laboratory's QMS through proficiency test participation, supportive supervision, provision of hands-on training to branch EFMHACA laboratories, and training of the National Metrology Institute (NMI) so as to strengthen in-country sustainable resources to assist in the calibration of EFMHACA's laboratory equipment. The development of two teaching modules (Product Registration and Inspection and Regulatory Science and Compliance) for the regulatory affairs post-graduate program was also completed. Overall, the following achievements were made during Q3:

1. Development and completion of three guidelines and one manual, all of which are posted on the EFMHACA website. These guidelines include Guidelines for Registration of Vaccines; Guidelines for Registration of Similar Biotherapeutics Products; Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology; and Inspection Manual. PQM's technical assistance encompassed preparation of the draft guidelines and supervision until completion; EFMHACA was the lead in the development process. PQM helped to establish efficient mechanisms for the development of guidelines that enabled the timely completion of these new guidelines. In addition, EFMHACA was able to use systems and processes PQM had earlier developed to facilitate the review of these guidelines.
2. As part of implementing audit-based inspection, 41 medicine outlets from Amhara and 25 from Tigray regional states were inspected. PQM assisted with developing the proposal and supported the deployment of the inspectors by covering part of the expenses. The inspection will also facilitate mentoring of regional inspectors by experienced EFMHACA inspectors who are co-inspecting using the audit-based inspection manual developed with PQM's support. The audit-based inspection is a systematic and independent onsite examination and verification of processes, procedures, or systems available at retail outlets to ensure compliance with requirements set by the authority. It will also improve the traceability of retail outlets' operations with respect to the transactions they make in their day-to-day dispensing practices. The relevance also goes to contributing to improve the internal risk QMS and governance processes of retail outlets.
3. The development of two modules (Product Registration and Inspection and Regulatory Science and Compliance) was completed and approved by the School of Pharmacy. PQM assisted through review of the draft module and provided technical inputs to enrich the contents of the final module.

Preliminary results of FY 2017 PMS were also completed in Q3. The preliminary report showed a failure rate of 17.25 percent for 401 antimalarial medicines sampled. In addition, of 200 MNCH medicines sampled, only 1 sample of zinc

sulfate failed testing. The findings showed an increase in the failure rate of antimalarial medicines as compared to FY 2016 PMS (from 1.8% to 17.25%). The reason for this change is an increased failure rate of quinine sulfate tablets (55 samples from 11 batches) during this PMS round. All of the failed quinine sulfate samples were from one manufacturer and a single importer. The same product, quinine sulfate, failed quality testing during FY 2016 PMS, although the number of samples that failed was significantly less than that in FY 2017. Similarly, there was an increase in the percentage of unregistered antimalarial medicines, from 8 percent in 2016 to 15.75 percent in 2017.

## II. Country Context

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

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

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

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

## III. Quarter 3 Progress by Objective

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

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#### ***Sub-IR 1.1 Quality assurance policy, legislation, guidelines, and procedures improved***

During Q1 and Q2, PQM provided technical support in the development of three guidelines (Guidelines for Registration of Vaccines, Guidelines for Registration of Similar Biotherapeutics Products, and Guidelines for Registration of Biotherapeutic Protein Products Prepared by Recombinant DNA Technology). In the past quarters the guidelines were 90-percent completed. In addition, development of the Generic Medicine Registration guidelines was 50-percent completed. The recall directive has passed through a review process by stakeholders.

In Q3, the three guidelines on specialized areas of medicines registration were completed and posted on EFMHACA's website (<http://www.fmhaca.gov.et/standardsdirectivesguidelines.html>). PQM provided technical assistance throughout the development of these guidelines. EFMHACA management's strong follow-up and expedited approval process served as a clear example of the leading role EFMHACA assumed in this process.

Approval of the guidelines for registration of specialized products is expected to increase access to new and innovative essential medicines and better address existing and emerging diseases. In addition to contributing to alignment with international best practices, these guidelines will help in review of the dossiers for this type of product. The Recall Directive, which was discussed through a workshop in Q2, was reviewed by EFMHACA management and approved in Q3. Serving as a legally binding enforcement tool, this Directive will facilitate removal of poor-quality medicines from the market and the implementation of pharmaceutical recalls as outlined in the recall guidelines; in addition, it will help improve responsible stakeholders' compliance with regulatory requirements. PQM also provided support in the development of an inspection manual. The manual, approved by the authority and posted on the website, was prepared to guide inspectors in preparing for and performing various types of inspection activities. It also serves as a reference document for inspectors before, during, and after inspections of facilities involved in the storage, distribution, and dispensing of medicines. Effective implementation of this manual will help facilitate the proper handling, storage, recording, and documentation of medicines transactions, thereby improving the traceability of products circulating in the market and reducing the penetration of falsified medicines in the supply chain. PQM also provided support in the review of GCP guidelines in previous quarters, which was approved by EFMHACA and is currently posted on the website.

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

In Q2, PQM provided support on planning, providing orientation, and deploying 68 inspectors to carry out auditing and risk-based inspection in retail outlets in Addis Ababa. PQM also participated in the assessment of the medicine registration system.

In Q3, PQM provided technical support on audit inspection at other regional state retail outlets, including in the Tigray and Amhara regions. The support included provision of orientation to inspectors and facilitation of the overall inspection process. The inspection covered 41 medicine outlets in Amhara and 25 in Tigray regional states. The objective was to gather information on the practices of community pharmacies and drug stores with respect to the procurement, storage, distribution, and dispensing of medicines, by auditing past and current transactions on the basis of selected high-risk and/or priority medicines as tracer drugs.

PQM continued providing technical support on the ongoing implementation of the MRIS and orientation of new users. The support PQM provided in the assessment of the medicine registration system was completed in Q3, and the findings will help incorporate missing components and correct practices that are not in accordance with international practices. Once the write-up of the report is complete, it will be used to make corrections on the gaps identified.

In Q4, support will continue for the completion and implementation of SOPs for the ISO 17020 accreditation, and a report on the audit-based inspection will be completed. In addition, technical assistance will be provided to address gaps identified through the assessment of the medicine registration system.

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

During Q2, the EFMHACA QC laboratory's accreditation was renewed and the scope expanded to 3 additional test methods, bringing the total number of accredited test methods to 16 (11 for physicochemical testing and 5 for condom testing).

During Q3, as part of the ongoing maintenance of EFMHACA's laboratory QMS, PQM provided support for the supply of proficiency testing samples for physicochemical test methods. The laboratory completed testing of the proficiency testing samples and submitted test results to the provider; the results from the provider are forthcoming. The continuous participation of the laboratory on proficiency testing is not only a prerequisite for continuing accreditation; it also helps the laboratory measure its performance in terms of precision, accuracy, and reliability of test results.

Through the support PQM provided to NMI, laboratory equipment calibration of EFMHACA regional branches was initiated during Q3. In addition, through supplementary funding, USP supported the training in Germany of two NMI staff on dimension calibration on April 16–27, 2018. The trained staff will be instrumental in ensuring the sustainability of calibration activities by serving as a local resource to help EFMHACA get its equipment calibrated in those particular areas where gaps were identified. This practice will also result in significant cost savings for EFMHACA, since the fees paid to NMI will be much lower than those being paid for overseas services, currently supported by PQM. In addition, it avoids the issues attached to the need for hard currency to cover fees for services from overseas.

***Sub-IR 1.4 Institutional capacity for regulatory workforce sustainably improved***

In previous quarters, PQM worked with the School of Pharmacy to prepare two training modules: (1) Product Registration and Inspection and (2) Regulatory Science and Compliance.

During Q3, the development of these two teaching modules was completed and approved by the School of Pharmacy. PQM played a key role in the review of the draft modules and provision of technical input to enrich the contents of the final modules. Part of the cost of developing these modules is covered through supplemental funds provided by USP. The completion of these teaching modules is a major milestone, as it helps the school sustain the regulatory affairs master's program and addresses the challenges the school faced due to shortages of teaching materials for the specialized topics in the curriculum. Having such modules will help utilize existing faculty to teach the courses and not rely in the long term on overseas professors.

The regulatory science and compliance module consists of two parts (Part I: Fundamentals of regulatory science and Part II: Law and Regulatory compliance). This module is intended to introduce learners to the fundamental concepts of regulatory affairs, including principles of regulation; good regulatory practice; and the perspectives, interactions, interrelationships, complexities, and implications of regulation with the business, legal, social, economic, and political environments. It also enables learners to comprehend global and national regulatory norms, legal frameworks, standards, and guidelines in the regulation of health-related products and healthcare services. The product registration and inspection module covers the foundational concepts of inspection, dossier evaluation, regulatory writing principles, variations, and other requirements for pharmaceutical product and health-related products registration. These modules address issues related to inspection from the product's origin to end users.

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

During previous quarters, it was reported that EFMHACA completed testing of samples collected in FY 2017 as part of its PMS program, and regulatory measures were taken on products that did not meet quality requirements.

This quarter, compilation of the findings from FY 2017 PMS indicated that 55 samples of quinine sulfate tablet, 1 sample of primaquine tablet, and 13 samples of artemether injection did not meet quality requirements. The overall failure rate for sampled antimalarial medicines was 17.25 percent. On the other hand, assessment of the sampled medicines for marketing authorization revealed that 63 of the 400 samples (15.75%) were unregistered. With regard to MNCH medicines, of 200 samples collected, only 1 sample of zinc sulfate failed the tests.

**Table 1: Summary of PMS samples collected, tested, and failure rate**

| Ser. No      | Product                        | # Samples tested | # samples pass | # Samples failed | % Failure   |
|--------------|--------------------------------|------------------|----------------|------------------|-------------|
| 1            | Artemether injection           | 22               | 9              | 13               | 59.1        |
| 2            | Primaquine tablet              | 25               | 24             | 1                | 4.0         |
| 3            | Quinine sulfate tablet         | 58               | 3              | 55               | 94.8        |
| 4            | Quinine injection              | 10               | 10             | 0                | 0.0         |
| 5            | Artemether/lumefantrine tablet | 105              | 105            | 0                | 0.0         |
| 6            | Amoxicillin dispersion         | 30               | 30             | 0                | 0.0         |
| 7            | Zinc acetate tablet            | 13               | 13             | 0                | 0.0         |
| 8            | Zinc sulfate                   | 44               | 43             | 1                | 2.3         |
| 9            | Magnesium sulfate              | 37               | 37             | 0                | 0.0         |
| 10           | Artesunate injection           | 31               | 31             | 0                | 0.0         |
| 11           | Chloroquine tablet             | 123              | 123            | 0                | 0.0         |
| 12           | Oral rehydration salts         | 76               | 76             | 0                | 0.0         |
| 13           | Chloroquine syrup              | 27               | 27             | 0                | 0.0         |
| <b>Total</b> |                                | <b>601</b>       | <b>531</b>     | <b>70</b>        | <b>11.6</b> |

As indicated in the table, most of the sampled medicines that failed quality testing were antimalarials, particularly quinine sulfate and artemether injection. The larger number of failed samples of quinine were from a single manufacturer imported by one importer. All samples collected during this round of PMS were tested; of the 601 samples (antimalarials and MNCH medicines), 70 samples (11.6%) failed testing, all except 1 of which were antimalarials. Among these, 55 were samples of quinine sulfate from 11 batches. EFMHACA has taken prompt regulatory measures on all of the failed samples. Recall of the products from the market, conducting further investigative inspections, and taking regulatory measure on the manufacturer of quinine sulfate were among the measures taken by EFMHACA during the past two quarters.

PQM also conducted joint supportive supervision at the four branch laboratories from April 23 through May 15, 2018. Activities performed included evaluation of action points from previous supportive supervision, identification of gaps, and provision of technical support where gaps were identified. One of the findings of the supportive supervision conducted at the four branches was that staff were not competent to conduct verification of dissolution and UV spectrophotometry measurements. Accordingly, EFMHACA's laboratory staff provided hands-on training on performance verification of dissolution and UV spectrophotometry. A total of 10 staff (3 females and 7 males) from the 4 branches were trained by EFMHACA at Mekele on May 21–25, 2018. In continuation of the previous quarters, the branch laboratories have collected 85 medicine samples as part of their routine PMS from their catchment areas.

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

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During Q2, PQM provided technical assistance by reviewing the status of CAPA implementation by Cadilla Pharmaceuticals with respect to WHO findings. In addition, based on a request from EFMHACA to coordinate and lead large-scale training funded by EFMHACA, PQM developed a proposal detailing how the training should be organized at different levels. Besides the proposal, PQM helped EFMHACA in developing a Concept Note for submission to WHO to solicit expert trainers to conduct TOT training. The demand for this training was triggered by the anticipated expansion of pharmaceutical manufacturing industries in Ethiopia and the existing gaps in capacity of GMP inspectors.

In Q3, PQM participated in the technical working group for implementation of the National Strategy and Plan of Action for Pharma (NSPA-Pharma), where PQM attended the regular regulatory working group meeting. The technical working group identified the activities to be performed during 2018–2019. Preparation of proposals and an action plan for TOT on GMP and basic GMP training have been completed. The TOT training will be conducted in collaboration with EFMHACA, WHO, and PQM. WHO experts will support provision of the TOT training scheduled for August 2–11,



2018; participants include 20 staff from EFMHACA, universities, local manufacturers, and the Food Beverage and Pharmaceuticals Development Institute (FBPDI). The rollout of basic GMP training will be provided to 300 staff from regional regulatory bodies, MOH, FBPDI, and universities, among others. PQM has played a critical role in coordinating these activities.

PQM also provided technical assistance for Addis Pharmaceuticals (APF) on a design and layout review workshop on April 11–12 in Addis Ababa. PQM provided design and layout evaluation, as well as a review of premises and all utilities of the new pharmaceutical manufacturing facilities to ensure their compliance with international GMP requirements from the beginning of operations.

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

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

PQM continued provision of technical assistance in the Adverse Event Following Immunization (AEFI) by participating in capacity-building trainings in four sessions at the events organized in Bahirdar and Dessie. A total of 177 participants attended the workshop. Similar workshops were also organized in Gambela, Beninshangul, Addis Ababa, and Oromia, where PQM also provided technical support in the revision of AEFI Guidelines. PQM's technical support in generation and utilization of adverse drug reaction-related information has contributed to the entry of 198 adverse drug event data into a pharmacovigilance data monitoring system and sharing of 5 adverse drug reaction reports with the WHO Uppsala drug safety monitoring center. Of the 198 adverse drug event -related reports, 9 product defects were identified, all of which are currently under investigation for further action. So far, two regulatory measures were taken as a result of this investigation, through the pharmacovigilance forum, on ringer lactate infusion and sodium valproate tablet. A recall letter was issued for the regions and the manufacturer.

Other supported activities include:

- Assessment of the abuse of tramadol medicine through participation in the preparation of data collection tools, data collection, and analysis.
- Participation in training on the national drug safety monitoring system requirements for the active surveillance efforts related to TB treatment, organized by EFMHACA and Challenge TB program.
- Technical support to EFMHACA in their provision of in-service training to 10 health centers at Kolfe Wereda, where 26 healthcare providers participated.

PQM, represented by Chief of Party Hailu Tadeg, participated in the annual forum organized by Ecumenical Pharmaceutical Network (EPN) in Kampala, Uganda, on May 15–18. PQM made a presentation entitled “Ensuring Quality and Safety of Medicines in LMICs: PQM’s Approaches and Successes.” The EPN Forum is a unique platform for enhancing knowledge and capacity on best practices in pharmaceutical healthcare that presents great opportunities for networking with delegates from more than 20 countries.

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

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Activities under this objective were completed in previous quarters. No additional update for Q3.

## **IV. Key Challenges**

As the government proceeds with the active implementation of the National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia, the demand for technical assistance is growing from the Ministry of Industry, EFMHACA, and manufacturing industries. PQM Ethiopia will not be able to cope with the emerging needs using current resources.

## **V. Lessons Learned**

Strengthening the inspection of medicine outlets, storage, and distribution facilities can have a significant impact on preventing and/or reducing the circulation of falsified and substandard medicines. Understanding these benefits, EFMHACA has placed increasing emphasis on working with regional regulatory authorities and intensifying inspection activities at all levels of the supply chain. PQM has long advocated for this initiative, and it is now receiving wide acceptance by EFMHACA. As a result of the common understanding created with the regulatory authority on putting emphasis on this initiative, PQM was able to leverage resources with EFMHACA to support inspection at 66 medicine facilities in Q3. The approach provides the opportunity to promote good distribution and storage practices,

as well as good pharmacy practices at the retail outlets level. PQM's role in this aspect has had a catalyzing effect in this initiative, which ultimately will lead to institutionalization of the approach within EFMHACA and scale-up through regional regulatory bodies.

## Ghana

### I. Quarter 3 Highlights

In Q3, the Ghana Food and Drug Authority (GFDA) finalized and shared with PQM the report for PMS of antimalarial and analgesic medicines tested in Q2. Per the final report, a total of 418 antimalarial medicines and 75 analgesics were tested; of these, 1.4 percent (6 of 418) antimalarials and 5.3 percent (4 of 75) analgesics samples tested did not meet quality specifications. GFDA also took regulatory actions to remove the substandard medicines from the market. PQM subsequently shared this final report with USAID/Ghana PMI.

Planning for implementation of PMS of uterotonic medicines (oxytocin and ergometrine injections) continues to advance. In Q3, GFDA submitted a draft protocol for PQM's review. Logistics are currently being finalized for the implementation of the survey.

PQM continues to provide remote technical assistance to Entrance Pharmaceuticals Limited (EPL) to address the gaps identified during the assessment in Q1 and to progress toward improved GMP compliance. The manufacturer is looking forward to identifying a CRO for the bioequivalence study needed for the artemether–lumefantrine product and also the production of a bio-batch. PQM's review of the protocol for the study is expected in Q4.

### II. Country Context

Malaria is a leading cause of morbidity and mortality in Ghana. The goal of PMI in Ghana is to reduce malaria deaths and substantially decrease malaria morbidity, toward the long-term goal of elimination. Through PQM, since 2009 USAID has been assisting GFDA to strengthen the medicines QA and QC systems. Activities have focused on strengthening GFDA's capacity in drug registration, medicines QC, and PMS. PQM has also recently provided technical assistance to ensure locally manufactured ACTs meet internationally acceptable quality standards.

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

There are several local manufacturers of pharmaceutical products in Ghana. GFDA continues to build capacity for its GMP inspectors to ensure it can adequately inspect facilities and provide guidance to industry to address GMP gaps. This will help to ensure locally produced medicines meet internationally acceptable GMP standards.

### III. Quarter 3 Progress by Objective

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

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##### ***Advocacy with Ghana FDA for country ownership – Develop a sustainability plan to show increase in country contribution to PMS***

In Q3, GFDA shared with PQM its recently developed business plan, whose goal is to address the microbiology laboratory and not the physical chemistry laboratory. PQM is in discussions with the laboratory leadership on the need to develop a supplement to this business plan that addresses plans for sustaining laboratory accreditation and PMS testing activities. PQM will continue to collaborate with GFDA on this task.

##### ***Facilitate PMS for antimalarial products in a sustainable manner using a risk-based approach***

In Q3, GFDA shared the final report for the PMS of antimalarial and analgesic medicines, which indicated that 422 antimalarial samples were collected from all 10 regions in the country. Of these, 418 were tested, and 6 (1.4%) were found to be substandard. All failed samples did not meet quality specifications for dissolution test. Four samples were chloroquine, an oral monotherapy, which were excluded from testing, as the product is banned in the country. For the analgesic samples, a total of 75 samples were collected and 4 samples (5.3%) failed to meet quality specifications. GFDA took regulatory actions to remove the substandard medicines from the market.



### ***Facilitate PMS of MCH products***

In Q3, GFDA shared with PQM a first draft of the protocol for the sampling of oxytocin and ergometrine injections in preparation for the implementation of quality surveillance of uterotonics in Ghana. PQM reviewed and provided comments and is awaiting updates from GFDA. This survey will be a follow-on, as GFDA continues to monitor the quality of oxytocin injections and ergometrine injections available to patients in Ghana. Implementation of this activity is expected to occur in Q4.

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

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### ***Facilitate ISO 17025 accreditation surveillance and maintenance***

In April 2018, ANAB visited GFDA to perform a reassessment of ISO/IEC 17025:2005 accreditation status of the Physicochemical, Microbiology, and Medical devices (male condom testing) laboratories. A summary of the nonconformity report was issued by ANAB, and GFDA addressed the CAPAs. GFDA is awaiting the final report.

It is noteworthy that this is the second year that GFDA has demonstrated technical capacity for maintaining its laboratory accreditation with little technical involvement from PQM experts. This continues to demonstrate that PQM's efforts have built technical capacity for maintaining ISO 17025 accreditation status within the laboratory. It is also noteworthy that this year also marks the first time GFDA contributed 50 percent of the cost of the ISO 17025 accreditation reassessment in line with ongoing commitment by GFDA leadership for sustainability.

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## **Objective 3 – Strengthen facility inspection capacity of Ghana FDA**

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### ***Provide training to strengthen capacity of Ghana FDA to perform inspection of local manufacturing facilities for cGMP compliance and in response to gaps identified through GMP roadmap***

The Head of Department for the Drugs Industrial Support department continues to receive hands-on training by working closely with PQM GMP experts as technical assistance is provided to EPL. PQM GMP experts opted for this hands-on approach as it allows the GFDA inspector to learn from PQM experts while concurrently providing technical assistance to the manufacturer with PQM guidance. The GFDA inspector provides in-country visits to the facility and helps to address some GMP gaps. With this arrangement, the GFDA Inspector is gaining more experience while learning from the routine interactions with PQM GMP experts.

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

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### ***Facilitate multiple technical assistance visits to manufacturing facilities***

In Q1, PQM GMP experts, in collaboration with GFDA inspectors, assessed four local manufacturers (EPL, Amponsah Efah Pharmaceuticals, Phyto-Riker Pharmaceuticals, and Ernest Chemist) for their GMP compliance toward WHO PQ for the manufacture of ACTs. Following the assessment, EPL was selected to continue receiving technical assistance from PQM. Technical assistance from PQM will help toward improving EPL's GMP compliance and submission of a dossier to WHO PQ for artemether–lumefantrine, a first-line ACT in Ghana.

In Q3, PQM GMP experts working in collaboration with the GFDA Industrial Support department provided technical assistance to EPL to address some key GMP gaps. PQM supported by providing API source review and product development protocol review, contact information for comparator tablet sources, technical criteria for CRO selection, and CRO contact information. PQM facilitated discussions with multiple CROs to enable EPL management select a CRO for the required bioequivalence study. EPL obtained the comparator tablets and expects to receive the API from a WHO-approved supplier so that it can manufacture the bio-batch that is required for the study. The manufacturer is also expecting the draft bioequivalence study protocol from the CRO it selected.

PQM envisages that, based on the agreed-upon timeline, EPL is expected to submit a dossier for artemether–lumefantrine for WHO PQ in January 2019, ahead of the PQM program period of performance end date.

# Guinea

## I. Quarter 3 Highlights

The main highlights of Q3 are as follows:

- Reviewed the demolition of the existing laboratory and provided an amended demolition plan.
- Reviewed the renovation plan of the laboratory and provided an amended renovation plan.
- Recommended revisions of the partitioning and overall layout of the laboratory.
- Provided technical assistance to the National Commission to finalize the review of the pharmaceutical law project.
- Facilitated the adoption of the pharmaceutical law by responding to the inter-ministerial committee comments and questions on the draft law.
  - PQM provided remote assistance to the commission in addressing some comments made during the process of the adoption of the law by the Parliament. PQM's support and diligent work with the National Directorate of Pharmacy and Medicine (DNPM) and commission members contributed to the rapid adoption of the law by Parliament in less than 1 month.
  - The next step is the promulgation of the law by the president, and then the enactment of the newly revised pharmaceutical law.

## II. Country Context

Together with other donors and USAID partners, PQM supports efforts to strengthen the pharmaceutical system. Like other African countries, Guinea is often disproportionately affected by the burden of poor-quality medicines. PQM can play a key role in strengthening the pharmaceutical system and the capacity of the national drug regulatory authority to assure the quality of medicines in the supply chain through registration, inspection, and QC activities. Malaria is the primary cause of consultations, hospitalizations, and deaths in Guinea—it especially affects children under 5 years of age. In 2011, Guinea was included in PMI; USAID and partners in Guinea are not only procuring malaria commodities but also helping to strengthen the country's health and pharmaceutical systems.

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

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

## III. Quarter 3 Progress by Objective

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

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To advance the adoption of the pharmaceutical law, in Q3 PQM worked closely with the commission (a committee previously designated by MOH and in charge of reviewing the pharmaceutical law) and contributed to the following

- Finalizing the review of the law project pharmaceutical documents. The main documents reviewed and finalized were pertaining to:
  - Medicines quality assurance.
  - Regulations.

- Pharmaceutical activities and organization.
- Anti-falsification/medicrime and sanctions.
- Finalizing the introduction document to introduce the law to the Ministers Council and Parliament.
- Preparing the draft of the five decrees to be presented with the draft law before its adoption by Parliament.
- Prioritization of the list of articles to support adoption of the law.
- Preparing the National Directorate of Pharmacy and Laboratory (DNPL) to address the questions and comments following review of the law project.
- Assisting the commission and DNPL during the processes of approval by MOH, adoption of the law by the inter-ministerial committee (IMC), and passing (vote) of the law by the national assembly (Parliament).

The end of this quarter was marked by the adoption of the pharmaceutical law. Promulgation by the President and the enactment of the law are among the final steps.

PQM will support the enactment of the pharmaceutical law by working with the commission to develop the necessary regulatory policies (texts).

### **Objective 2 – Continue strengthening DNPL capacity in product registration**

There is nothing to report for this quarter.

### **Objective 3 – Enable DNPL to assume MQM responsibilities**

A notable development during Q3 was the restructure of MOH. A new director was appointed for DNPM, and new government employees were assigned new roles within the same entity. During Q3, DNPM was heavily involved in the process of adoption of the law project by the national assembly. Having a new director and new staff in addition to the priority given to the adoption of the law forced the DNPM directorate to postpone the official launch of the PMS and the validation of its protocol. PQM shared with the new director and his deputy the FY 2018 work plan and discussed the remaining activities for the rest of the year. As a next step, DNPM will conduct a meeting with stakeholders for PMS activities and review the protocol based on the risk-based PMS guidelines provided by PQM. Subsequently, PQM will review the draft protocol its adoption.

### **Objective 4 – Strengthen QC capacity of LNCQM**

Currently the laboratory is under renovation with support from the European Union. PQM visited the laboratory, reviewed the renovation plan, and provided recommendations that will help address safety and laboratory equipment installation. The main improvements include:

- Installing electric cables in the ceiling.
- Adding emergency exit stairs.
- Installing fire-proof electric room doors.
- Ensuring good ventilation.
- Including an emergency shower and sink in the laboratory.
- Improving laboratory security by providing a better partitioning and layout. The new layout will allow easy movement for laboratory staff in case of fire or other hazardous incidents.

Based on these recommendations, PQM provided an amended renovation plan.

# IGAD

## I. Quarter 3 Highlights

The work plan for PQM's technical assistance to support the Intergovernmental Authority on Development (IGAD) medicine regulatory harmonization (MRH) initiative work plan was approved this quarter in May 2018. Implementation of activities also began in Q3 with a workshop in Addis Ababa, Ethiopia. This is the first PQM regional work plan supporting priorities of the IGAD-MRH and funded by USAID/East Africa.

In Q3, activities centered on the kickoff meeting and implementation of some activities outlined in the work plan. The kickoff meeting was part of a 6-day workshop held in Addis Ababa on June 25–29, 2018. Participants included representatives from IGAD member states Djibouti, Ethiopia, Kenya, Somalia, and Uganda; representatives from Sudan, South Sudan, and Eritrea were absent. Other participants and stakeholders present at the workshop included representatives from USAID/Ethiopia, the New Partnership for Africa's Development, the World Bank, and IGAD.

Highlights from the workshop include the establishment of the expert working group (EWG) on pharmacovigilance and PMS and review and adoption of the terms of reference for the EWG. A brief review of activities in the USAID/East Africa-funded PQM work plan was also shared with the participants.

PQM, in collaboration with the newly established EWG, implemented some key activities, including the gap assessment of current pharmacovigilance/PMS manuals, technical requirements with some recommendations drafted for considerations, and development of a draft protocol for the survey of substandard and falsified medicines available to patients at cross-border sites within the region. Both activities are expected to be finalized in subsequent quarters.

## II. Country Context

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

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

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

## III. Quarter 3 Progress by Objective

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

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#### ***Review terms of reference (TOR) developed by IGAD towards the establishment of the EWG on PV/PMS and validate through a regional IGAD-MRH meeting***

PQM provided technical review of the terms of reference (TOR) developed by the IGAD secretariat for the proposed EWG pharmacovigilance/PMS. The TOR defines the roles, responsibilities, and expected deliverables for the EWG

pharmacovigilance/PMS. This draft was reviewed and validated by member state representatives during the workshop in Addis Ababa. A final version will be submitted by the secretariat to the IGAD steering for approval at the next steering committee meeting.

In line with the rules for establishing technical working groups for IGAD-MRH and as facilitated by the IGAD secretariat, an EWG on pharmacovigilance/PMS was established with representation from five IGAD member states: Djibouti, Ethiopia, Kenya, Somalia, and Uganda.

***EWG to conduct and PQM to facilitate the assessment of current PV/PMS manuals/guidelines, technical requirements and standards, tools, standard operating procedures for monitoring of safety and quality of registered medical products in IGAD member states***

Working with the EWG, PQM facilitated a gap assessment of pharmacovigilance/PMS documents and practices. The identified gaps and preliminary recommendations are included in the June 25–30 workshop report. EWG members are also expected to provide country-specific recommendations for pharmacovigilance activities that will be included in regional recommendations report to be finalized in Q4.

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

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***Facilitate a survey to determine prevalence of SF used in the MCH-FP/TB/HIV. PQM will work with the EWG to implement this survey***

Working with the newly established EWG at the June 2018 workshop, a draft protocol for the survey of substandard and falsified medicines was developed. With technical leadership from PQM, the EWG applied a risk-based approach to determine the medicines of focus for the cross-border regions that will help identify the quality of medicines available to patients within the target areas. Oxytocin injections were identified as the medicine of interest for the survey, and 12 cross-border regions were identified. To identify which facilities will be sampled from, additional information is required from the member state MRAs. PQM will help develop a final survey protocol once the requested information is received. Implementation of this medicines quality surveillance is expected to occur in Q4 and will be preceded by a training of sample collectors at a training meeting planned for September 2018.

PQM also used this workshop to present on the principles of risk-based PMS that can also be adopted by the PMS units within the member state MRAs. PQM envisages working with at least one MRA to adopt risk-based PMS principles into the national PMS strategy in the next few quarters.

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

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No activity to report this quarter.

## **Liberia**

### **I. Quarter 3 Highlights**

With the new government, the management of the Liberia Medicines and Health Products Regulatory Authority (LMHRA) has been under the oversight responsibility of the human resources director. This decision has drastically impacted on the implementation of PQM activities in the ground. In Q3, the government reinstated Mr. David Sumo as Managing Director of LMHRA and appointed 20 new staff to LMHRA and 5 staff to the QC laboratory. During Q3, PQM provided training on dossier evaluation to eight LMHRA staff, assisted the laboratory in the installation of selected laboratory equipment, and provided refresher training in preventive maintenance and troubleshooting.

Additionally, PQM helped LMHRA progress in the implementation of the fixed amount award (FAA) and shared the risk-based PMS guidance to be incorporated in the existing protocol before the execution of milestone 3 (sampling and testing of medicines).

### **II. Country Context**

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

prevention interventions as well as improve public–private partnership to increase access to quality-assured antimalarial medicines.

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

PQM activities in Liberia are focused on:

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

As part of the approved FY 2017 work plan, PQM provides technical assistance toward building the QC capacity of the existing LMHRA quality control laboratory and attaining compliance with international standards (ISO 17025), strengthening and expanding quality monitoring of antimalarials, promoting regulatory actions when falsified and substandard medicines are identified, and increasing awareness about the quality of medicines.

### III. Quarter 3 Progress by Objective

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#### Objective 1 – Rebuilding capacity of LMHRA QC laboratory

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While waiting to get the final approval from the Global Fund to build a permanent laboratory, LMHRA has secured a temporary laboratory that has been renovated using pool funding. During the renovation of this facility, PQM provided guidance on the partitioning of the physicochemistry area and on safety measures.

To assist in getting the new facility functional, PQM conducted the following activities in the laboratory:

- Inventory of key parts of equipment for maintenance and/or routine use.
- Installation, commissioning, and hands-on training for designated laboratory staff on the following equipment:
  - Ultra-sonicator.
  - Vortex mixer.
  - Mechanical shaker.
  - Hot plate/magnetic stirrer.
  - Disintegration tester.
  - Vacuum pump.
  - Water bath.
  - Water purification system.
  - Fume hood.
- Provision of preventive maintenance training to designated laboratory staff with a focus on the following equipment:
  - HPLC.
  - UV-Vis.
- Provision of recommendations on how to keep laboratory equipment operational and troubleshooting on major laboratory equipment.
- Hands-on training and proper use of the polarimeter
- Installation and filling of pH electrodes and commissioning of pH meters.
- Service for the water purification machine.

### **LMHRA QC Laboratory New Organizational Chart**

With the reappointment of Mr. David Sumo as LMHRA's Managing Director, there were a series of positive changes that affected the QC laboratory:

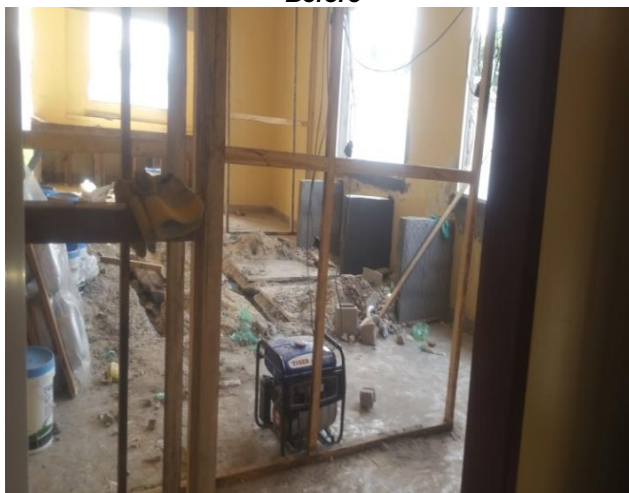
- The number of staff increased from 12 to 17 (5 newly recruited by MOH and seconded to the laboratory).
- The previous janitor/laboratory assistant has greater involvement in laboratory and office equipment maintenance.
- The QC Manager has been appointed as the Laboratory Director.
- One of the better qualified analysts became the QC Manager.
- Plans have been made to organize the QA Unit with a QA Manager.

### **Laboratory Challenges:**

- To meet ISO requirements for areas to be accredited, at minimum there must be a backup for the laboratory equipment, (e.g., two HPLC systems, two dissolution testers). Currently the laboratory has only one piece of equipment for each scope of testing.
- There is a need to calibrate the laboratory equipment and provide spare laboratory parts to avoid downtime in testing.

Below are photos of the laboratory during the renovation performed in Q2 and after renovation in Q3.

***Before***





After



**Next steps:**

- PQM will provide remote technical assistance to retrieve technical and managerial documents and assist the laboratory in reviewing/drafting missing SOPs and work instructions needed for ISO 17025 accreditation.
- LMHRA's QC laboratory will share with PQM the new organizational chart with roles and responsibilities of key laboratory personnel.

**Recommendations:**

- Explore the possibility of obtaining more pieces of equipment—at least two for each testing method.
- Provide more training for new staff and refresher training for experienced staff.
- Improve fire safety measures.
- Train selected staff in QA.

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

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As part of strengthening LMHRA capacities, PQM provided training to eight staff in dossier evaluation. This training was geared toward empowering the LMHRA staff to develop guidelines for implementation of the common technical document (CTD) format in Liberia. It will enable the staff also to carry out registration of medicines effectively to ensure the safety, quality, and efficacy of medicines available (or licensed for use) in the country.

The training took place during the last week of June. More information will be provided in the trip report.

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**Objective 3 – Build LMHRA capacity to take appropriate regulatory actions**

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Last year, in collaboration with NMCP and PQM, LMHRA conducted the first recall of monotherapies for malaria treatment in Nimba County. This exercise was very successful and led to the confiscation of over \$60,000 of medical products, including antimalarial monotherapies. In Q3, a plan was made with NMCP and LMHRA to conduct the second monotherapy recall in Lofa County. This exercise will be carried out in Q4.

LMHRA continues to take regulatory actions after conducting raids in hospitals and private pharmaceutical outlets. Inspections revealed that several clinics and outlets use and sell substandard medicines and illegal products that were not registered by LMHRA. These incursions identified medicines that had been banned by WHO for more than 10 years. Other medical products have been confiscated in Ganta, at the border with Guinea, thanks to the efforts of customs and police personnel that had been previously trained by LMHRA and PQM. LMHRA has sent warnings to the alleged facilities and will follow up with them according to LMHRA law.



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

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LMHRA was the awardee for the second FAA. The implementation of the first FAA milestone began in Q2. During Q3, PQM shared with NMCP and LMHRA that PQM recently developed risk-based PMS guidance for sampling and testing medicines. Both entities will review the existing PMS protocol and amend it according to the risk-based PMS guidance before launching the sampling and testing from the sites.

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

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

It is of note that in Q3 PQM shared with the Mission the PowerPoint presentation that was prepared with LMHRA and presented by LMHRA during the Malaria Operational Plan meeting in May.

### **IV. Key Challenges**

- Progress has been slow in getting approval from the Global Fund to build the permanent laboratory.
- The new government has appointed more than 20 staff to work with LMHRA. LMHRA must train the new staff to meet their job requirements for LMHRA activities and for the QC laboratory.
- Some new equipment procured by local vendors using World Bank finances did not meet the technical specification, which resulted in delays in the installation of the equipment.
- Delays in receiving laboratory reagents and consumables pushed the planned PQM trainings to Q4.
- Laboratory staff need refresher trainings on compendial methods because they have not been conducting routine analytical testing for over 6 months, after the fire incident, except for screening tests with Minilabs™.

## **Mali**

### **I. Quarter 3 Highlights**

In Q3, PQM reviewed the National Laboratory of Health (LNS) QMS. Following the review, a task force was formed to oversee the implementation of a plan for developing critical documents. Sixteen documents have been drafted.

In collaboration with the Directorate of Pharmacy and Medicine (DPM), Regional Directorates of Health (DRS), and National Malaria Control Program (PNLP), LNS has taken the lead in the implementation of 2018 PMS activities. The current protocol incorporated elements of PQM's risk-based approach for sampling, screening, and testing antimalarial medicines. The sampling teams have collected 511 samples so far. The activities are expected to be completed by August 2018.

In support of DPM, PQM drafted documents relating to governance and is working with the Directorate to develop procedures for medicines registration. The draft documents will be discussed and finalized with DPM in Q4.

ACT efficacy and seasonal malaria chemoprevention (SMC) studies carried out under two fixed-amount awards (FAAs) with the University of Science, Technology and Techniques have been completed. A follow-on SMC study is planned to start in Q4 with a new FAA.

### **II. Country Context**

Malaria is the primary cause of morbidity and mortality in Mali. The goal of PMI in Mali is to reduce malaria deaths and substantially decrease malaria morbidity, toward the long-term goal of elimination. Through PQM, since 2008 USAID has been assisting Mali's MOH to strengthen the medicines QA systems. Activities have focused on strengthening 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 3 Progress by Objective

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

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PQM is working with DPM to develop important documents relating to governance. Drafts of the DPM code of conduct, confidentiality, and management of conflict of interest have been shared with the Directorate. The documents will be discussed and finalized by DPM staff under PQM supervision in Q4.

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

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PQM assessed the LNS QMS as per the ISO 17025:2017 standard. As a result, a new roadmap for strengthening the LNS QMS has been developed in collaboration with the laboratory QA manager and key staff members. The roadmap included a 6-week action plan to kick off the strengthening of laboratory QMS to achieve ISO 17025:2017 accreditation. PQM verified existing draft SOPs and developed a list of QMS documents required for accreditation.

The Medicine Quality Control Laboratory (MQCL) of LNS participated in proficiency testing on HPLC and UV-Vis spectrophotometry. The aim of LNS participation was to obtain an external evaluation of the analytical capacity of the laboratory, but it was not able to submit the results in a timely manner, so the provider was not able to include the results from LNS. PQM reviewed the challenges faced and assisted LNS in developing a proficiency testing/inter-laboratory testing plan for 2018–2019.

With PQM support, the LNS drafted the following QMS documents:

- Instruction for the reception, inventory, installation, and operation of equipment.
  - Maintenance and calibration of equipment procedure.
  - Conflict of interest declaration form.
  - Staff training and monitoring procedure.
  - Communication policy.
  - Quality policy.
  - Privacy policy.
  - Impartiality policy.
  - Information policy.
  - Procedure for reviewing requests for tenders, contracts and subcontractor management.
  - Customer service improvement procedure.
  - Internal audits.
  - Control of samples.
  - Sampling procedure.
  - Procedure for facility management and control of environment and energy sources.
  - Procedure for the selection, validation of methods, estimation of measurement uncertainty, and control of data.
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#### Objective 3 – Strengthen sustainable local capacity to monitor the quality of medicines in the country

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The protocol for PMS of antimalarial medicines quality is being implemented. It incorporates elements of PQM's risk-based approach. The sampling plan targets specific products that have been identified as falsified (quinine sulfate and artemether–lumefantrine) or not recommended for malaria treatment (antimalarial monotherapies). So far, 2

teams composed of 1 representative each from LNS, DPM, Regional Directorate of Health, and PQM collected 511 samples from the District of Bamako (Communes 1, 2, and 3), and the regions of Koulikoro (Communes Koulikoro Ville, Banamba, Fana, Dioila, and Ouelessebougou), Mopti (Communes Mopti Ville, Koro, Bankass, and Bandiagara), Segou (Communes Ségou Ville, Tominian, San, and Bla), and Sikasso (Communes Sikasso Ville, Bougouni, Yanfolilla, Yorosso, and Koutiala). The team that collected samples in the District of Bamako included the PNLP pharmacist. This stage of PMS activities has shown close collaboration among the institutions involved. Screening and testing of samples is underway and expected to be complete by August 2018.

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#### **Objective 4 – Facilitate studies on resistance of antimalarial medicines**

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The Laboratory of Applied Molecular Biology (LBMA) completed the two studies and submitted related documents and reports for closeout of the FAAs for the ACT efficacy and SMC studies. The closeout of these FAAs is planned for July. A new FAA for a follow-on SMC study will be established in early Q4.

## **Mozambique**

### **I. Quarter 3 Highlights**

The PQM program provides technical support to the National Directorate of Pharmacy (DNF), to support transition to a robust MRA that has the organizational structure and technical know-how to promote and sustain availability of quality-assured, safe, and effective medicines in the country. PQM continues to play leading roles in ensuring that the national quality control laboratory for medicines (LNCQM) performs its statutory responsibilities of consistently generating accurate and reliable results on medicines quality to safeguard public health. Key activities in support of these goals in Q3 included the following:

- Continued to offer and provide technical support on regulation development. PQM received draft regulation from LNCQM for technical inputs.
- Established the need for a focal person for PMS and pre-shipment inspection and testing; these positions were subsequently appointed by the Head of DNF.
- Continued to build the capacity and skills of key laboratory staff to improve QMS practices. Seventeen SOPs were finalized and approved in Q3.
- Selected and shipped samples of oxytocin and magnesium sulfate injections for confirmatory test to an ISO 17025 accredited laboratory outside the country.
- Procured services to support calibration of analytical instruments in the laboratory.

### **II. Country Context**

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

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

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

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

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

### III. Quarter 3 Progress by Objective

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

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LNCQM aims to become compliant with international standards for GLP and QMS and attain ISO 17025 accreditation. PQM assessed the laboratory in Q2 and identified gaps for improvement. In line with outlined activities and corrective actions proposed after the previous assessment, PQM has procured stamps and pads for accurate labelling of SOPs used in the laboratory and provided technical support to finalize and approve 17 SOPs for laboratory functions.

Since the cost of procurement of service for qualification of analytical instrument is expensive, to achieve sustainability, minimize operation cost, and ensure that all NQCL laboratory equipment are qualified and functional, PQM provided hands-on job training and demonstration on Instrument Calibration & Qualification (AIQ) and preventive maintenance toward building in-house capacity and key laboratory staff skills to calibrate and maintain key laboratory equipment. The PQM training that was attended by 7 participants (4 females and 3 males) focused on building capacity and skills for the following:

- Verification performance of the balances
- Verification performance of the UV-Vis spectrophotometer.
- Verification performance of the Waters HPLC piece of equipment.
- Preventive maintenance of the Waters HPLC system.
- Troubleshooting of common hardware issues on the Waters HPLC.
- Development of performance verification SOPs for balances, UV-Vis spectroscopy, and HPLC.

With USP support, PQM supplied reference standards for medicines quality testing to LNCQM. PQM also procured the services of INNOQ (the local calibration body) for the calibration of volumes, weights, ovens, thermometers, and other analytical instruments in the laboratory. In addition, PQM procured reagents and performance verification kits.

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

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Preliminary results concluded and shared by LNCQM in Q2 showed that 21 samples of oxytocin and 4 samples of magnesium sulfate injections failed physicochemical testing. PQM advocated for information from the oxytocin study to be included in the DNF presentation to be made at an upcoming meeting with the Minister of Health. PQM also recommended to DNF that the following next steps be included in the presentation:

- Dissemination meeting for sharing preliminary and confirmatory results of PMS on oxytocin and magnesium sulfate injections in September 2018.
- Meeting with the central medical store (CMAM) and importers to discuss sourcing, transportation, and storage conditions throughout the entire supply chain system.
- Regulatory actions to address poor-quality medicines identified in the study.

Using specified criteria in the PMS protocol, 19 samples (5 magnesium sulfate and 14 oxytocin injections) were selected and sent to an external laboratory for testing.

Previously, performance of PMS in Mozambique was implemented by LNCQM. During the reorganization and transitioning from PD to DNF because of the newly approved pharmaceutical law, PMS function was subsumed under the pharmacovigilance, clinical trials, and rational medicine use unit at DNF. Upon close assessment of PMS responsibilities, it was concluded that the PMS function would not get the attention it required under that unit. Based on PQM's advice, the head of DNF appointed focal persons for PMS and pre-shipment inspection. PQM also

commenced discussions for training DNF and key stakeholders on the risk-based approach to PMS in Mozambique. This training would set the stage for a more cost-effective and efficient implementation of PMS activities in FY 2018.

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

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In Q3, PQM continued provision of technical support to DNF to support the transition to an MRA according to the newly approved national pharmaceutical law. PQM has consistently motivated DNF to develop robust regulations that would empower the directorate to deliver best service and quality-assured medicines to Mozambicans. Due to the strategic push from PQM during the visit in May 2018, the head of the NQCL for medicines sent LNCQM's draft regulation to PQM for review. During Q3, PQM review of this regulation was initiated. PQM encouraged DNF to finalize regulations, especially for LNCQM, as soon as possible to help the laboratory generate revenue and actualization of LNCQM sustainability plans, based on PQM recommendations.

As Mozambique depends on imports for medicines, PQM continues to support and strategically push DNF to fine tune pre-shipment inspections and testing requirements for products imported from India. In view of this, the DNF head nominated a focal person to ease communication and information-sharing between DNF and PQM. This focal point will work with PQM to plan for a meeting to engage and sensitize stakeholders on the new pre-shipment inspection requirements for medical products imported from India.

To strengthen the inspectorate unit of DNF, the head of DNF requested PQM to support the directorate with information on other screening technologies as alternatives to TruScan™. PQM shared detailed information on screening technologies used by different countries, including average cost and advantages they offer to generate results and support decision-making.

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

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No updates this quarter.

## **IV. Key Challenges**

Challenges highlighted previously have rolled over to Q3. Some major challenges impeding progress are:

- Slow progress in acquisition of the necessary additional space identified for the laboratory.
- Slow progress in development of necessary regulations.
- Total dependence on donor funding (USAID-PQM) for procurement of reagents, reference standards, analytical instrument qualifications, maintenance, service provision, and supplies.
- Insufficient number of trained personnel at DNF and LNCQM.

# **Nigeria**

## **I. Quarter 3 Highlights**

As a result of PQM's technical assistance, the National Institute for Pharmaceutical Research and Development (NIPRD) attained ISO 17025:2005 accreditations for six scopes by the third-party audit accreditation body ANSI-ASQ National Accreditation Board (ANAB).

In an effort to raise awareness related to the manufacture of quality-assured medicines and current medicines quality issues, the PQM Nigeria team made an advocacy visit to the Minister of Health. The visit helped bring burning issues surrounding the quality of medicines in Nigeria to his attention.

Technical assistance provided to Emzor Pharmaceuticals yielded an overall improvement in the company's production standards. Medical Export Group, an international distributor, is actively engaging Emzor toward the procurement of sulfadoxine–pyrimethamine.

Other accomplishments in Q3 included:

- NAFDAC's Kaduna Laboratory maintained ISO accreditation for existing test methods and also expanded its scope to include microbiology, giving the laboratory the ability to perform key quality control tests required for injectable medicines. The reaccreditation of Kaduna Laboratory will provide quality verification of medicines that are entering or currently circulating in northern Nigeria, allowing a more effective and quality-assured response to HIV/AIDS, malaria, TB, and other public health threats; securing the supply chain system; ensuring patients are safe from poor-quality products; and eliminating dependence on foreign or private laboratories to provide quality control testing services (which increases the costs and the turnaround time of results of sampled medicines).
- NAFDAC demonstrated its commitment to sustain activities previously supported by PQM through, paying for all costs associated with equipment calibration, proficiency tests, and laboratory supplies for the Kaduna Laboratory. Improved competency and skills of NAFDAC staff was also demonstrated during the preparation for surveillance audit for Kaduna Laboratory. PQM provided minimal support while NAFDAC staff took the lead.
- The PQM program has continued building a pipeline of professionals who will advance the country's capacity to support the manufacture of quality-assured priority medicines, review dossiers, and conduct PMS through three batches of training on the pharmaceutical quality system (PQS) curriculum at Nnamdi Azikwe University in Awka, Nigeria. Nnamdi Azikwe University is the first university to roll out trainings using the PQS curriculum in Nigeria. Implementation of the PQS curriculum will be extended to other Nigerian universities in subsequent quarters in FY 2018 and FY 2019.

## II. Country Context

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

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

The overall goal of PQM in Nigeria is 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 system strengthening of NAFDAC and PQM-supported local manufacturers.

## III. Quarter 3 Progress by Objective

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

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PQM conducted a mock audit and provided continuous technical assistance to the NIPRD laboratory ahead of the planned surveillance audit. The mock audit identified minor issues that were resolved ahead of the audit.

NIPRD received ISO accreditation for six test methods: HPLC, loss on drying, dissolution, spectrometry, pH measurement, and uniformity of dosage units (weight variation and content uniformity). NIPRD's institutional mission is to apply modern science and technology to increase local production of medicines by effective collaboration with the industry and experts that are within and outside of Nigeria, provide assurance of quality on all the medicines used in healthcare, and develop quality standards for phytomedicine. The accreditation of NIPRD better positions the advancement of local pharmaceutical research and development, increases interaction with local manufacturers, and supports third-party testing of locally manufactured medical products in Nigeria.

The next step is to include selected NIPRD staff in a PQM-planned advanced training on instrument maintenance in Q4. The selected staff will constitute the agency's meteorology team that will help sustain PQM's efforts at NIPRD. This capacity is critical for maintenance of equipment and will lead to cost savings for the agency as it takes over this necessary prerequisite for maintaining its laboratory accreditation status.



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## Objective 2 – Strengthen the national quality assurance and regulatory system

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Following the accreditation of the NAFDAC's Kaduna Laboratory in 2017, the laboratory was not only successfully reaccredited but also expanded its scope of testing to also include microbiology test methods (e.g., sterility and bacterial endotoxin test). This will allow the laboratory to perform quality control tests on products intended to be sterile, such as some injectable products, a capacity previously not available in northern Nigeria. The new test methods also include titrimetry, disintegration, hardness test, friability (Chemistry Scope) and microbial limit test, and sterility and bacterial endotoxin test (Microbiology Scope). As part of NAFDAC's commitment to sustainability, all costs associated with equipment calibration, proficiency tests, and other laboratory supplies were paid for by the agency. Minimal technical assistance was provided by PQM during the preparation for the surveillance audit that led to scope expansion, as the laboratory staff exhibited technical competency and took the lead during the process. Next steps include remotely providing technical assistance to resolve minor nonconformances identified during the third-party audit. The laboratory's accreditation certificate is expected in Q4.

PQM conducted a gap assessment of the NAFDAC National Control Laboratory for Biologics (NCLB) using the ISO/IEC 17025:2005 audit checklist. NCLB is the only laboratory in the country responsible for the quality control of vaccines and biologics in Nigeria. When accredited, the laboratory will provide quality testing for vaccines developed and imported into the country. The laboratory audit was conducted by witnessing the analysts perform different test methods in accordance with internal quality control documents. These methods include titrimetric analysis, pH measurement, HPLC, UV-Vis spectrophotometry, sterility test, microbial limit test, identity test on BCG vaccine, bacterial endotoxin test, safety/inoculation test, specific toxicity of DTP vaccine, virus titration, enzyme-linked immunosorbent assay (ELISA), and uniformity of dosage unit. Review of documents and key informant interviews were conducted to verify the laboratory's QMS. Key assessment findings included 1 critical, 16 major, and 6 minor nonconformances.

The next steps will include providing technical assistance to address the identified nonconformances, supporting the procurement of reagents and equipment calibration, and providing two QMS trainings for the laboratory staff scheduled for Q4 in preparation for ISO/IEC 17025:2005 accreditation.

PQM facilitated a meeting with the Director General of NAFDAC and some directors of the agency. The objective was to provide an update on the progress of implementing PQM activities. Key activities discussed during the meeting included:

- NAFDAC will lead the conduct of a countrywide assessment for all local manufacturers to ascertain the level of current GMP compliance of all local manufacturers in Nigeria with support from PQM.
- PQM will provide technical assistance to NAFDAC's tariff committee in designing a strategy that will ensure the sustainability of PMS activities.
- PQM will work with the NAFDAC Planning, Research, and Statistics directorate to conduct an initial baseline assessment of the monitoring and evaluation (M&E) system and develop indicators and template for data gathering, which will be vital to closely monitor intended and unintended results.
- PQM will work with NAFDAC to develop a comprehensive list of equipment of focus as well as an agenda for the performance verification training.

As a follow-up to the meeting with the NAFDAC Director General, another meeting was held with the Director and staff of NAFDAC drug evaluation and research directorate. The primary objective was to discuss further the modalities of executing the countrywide GMP roadmap. Key outcomes included for NAFDAC to support the provision of resources needed to implement the GMP roadmap. This will include data sharing on the local manufacturers in the country's pharma space and required capacity of NAFDAC staff to support the activity.

In line with efforts to use data for evidence-based decision-making, a PQM Nigeria M&E specialist commenced an activity start-up meeting with NAFDAC M&E champions to develop a roadmap for the pharmaceutical M&E plan for the regulatory agency. As part of the developed roadmap, a detailed assessment of the agency's M&E system will be conducted in Q4. Results of the assessment will help provide more insights in development of the pharmaceutical M&E plan. The M&E plan will detail what, when, how, and by whom the monitoring activities will be conducted, as well as how and when NAFDAC will evaluate its performance in pharmaceutical regulation. This will lead to improved performance monitoring of projects, programs, and policies through clearly articulated goals, targets, and methods of data collection and management. Especially when new approaches are used, such as innovative medicines quality detection programs, the M&E plan will be vital to closely monitor both intended and unintended results and to test and revise the assumptions on which the intervention is based.

A medicine dossier is a document that contains the administrative, quality, nonclinical, and clinical data of a pharmaceutical product submitted for approval and marketing in a country. Currently, the review process of this critical document is deficient within NAFDAC, and this could allow poor-quality medicines to enter the Nigerian market if not correctly reviewed. To address this deficiency, in Q3 PQM conducted a 5-day training on dossier evaluation, in CTD format for 26 NAFDAC staff and 2 pharmacy faculty members from Nnamdi Azikwe University Awka (11 females and 17 males), as part of building a pipeline of skilled professionals in Nigerian universities. The training session covered topics on API assessment, FPP data, and all other CTD modules. A hands-on training approach was deployed using WHO model dossier templates, which further strengthened participants' understanding of the requirements and reference materials used during dossier evaluation.

Also in Q3, PMS sample collection was concluded. The results of the PMS exercise are expected to be released in Q4 for both antimalarial and MNCH products.

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**Objective 3 – Provide technical assistance to selected manufacturers with strong interest and commitments to locally manufacture products of interest (zinc sulfate tablet, oral rehydration salts, chlorhexidine, amoxicillin dispersible tablet, artemether-lumefantrine, oxytocin injection, magnesium sulfate injection, and ready-to-use therapeutic food) to successfully register their products at NAFDAC**

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PQM continued to provide technical assistance to six local manufacturers, including Emzor Pharmaceuticals, to increase procurement interest for sulfadoxine 500 mg pyrimethamine 25 mg by the Medical Export Group (MEG). The tailored assistance has impacted positively on the overhaul of Emzor's QMS to comply with WHO GMP standards. This has yielded procurement order for clotrimoxazole 120 mg and 960 mg by MEG for relief programs all over the world.

Other activities carried out in Q3 included:

- PQM continued to provide technical assistance to Drugfield Pharmaceuticals in the compilation of its dossier for CHX gel in compliance with CTD format. Drugfield plans to make dossier submissions to the West Africa Health Organization.
- The PQM GMP team conducted startup activities for the GMP roadmap, which included meeting key NAFDAC staff to discuss key resources needed for the activities.
- As part of ongoing technical assistance provided to Pharmatex Pharmaceuticals, the GMP team conducted a reassessment of the current GMP status of the company. Next steps include providing technical assistance in resolving identified CAPAs and tailored trainings in analytical method development, validation, and annual product review.

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**Objective 4 – Strengthen human capacity of academia**

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In line with efforts to build capacity in the pipeline of professionals, PQM commenced a partnership with the Faculty of Pharmacy, Nnamdi Azikwe University Awka to provide technical leadership, experience sharing, and professional networking to both lecturers and students at the university. In Q3, PQM facilitated a 5-day current GMP training for 202 students and teaching staff of the faculty of Pharmaceutical Sciences. GMP topics covered during the training included the relationship between QA and GMP, building blocks of GMP, formulation and production of medicines, introduction to sterile dosage forms, introduction to pharmaceutical facilities, quality aspects of drugs, introduction to biologics, clinical trials, registration, intellectual property and patent rights of biotechnological products, FPP manufacturing, and process validation.

PQM attended a meeting with the Minister of Health and the director of the Food and Drug Directorate, Federal Ministry of Health (FMOH). The objective was to acquaint the Minister of Health with accomplishments in the pharma space as a result of USAID's contributions through the PQM program in Nigeria. The Minister applauded the program's achievements as it aligns with the Nigeria government's policy on local content for procurement. The visit helped bring forward burning issues surrounding the quality of medicines in Nigeria.

The key outcomes of the meeting included:

- The Minister of Health recommended continuous support to Juhel, as well as a fixed survey on the use of oxytocin manufactured by Juhel and its findings presented to the Society of Gynecology and Obstetrics of Nigeria (SOGON). An exhibition by Juhel at the next SOGON meeting was also recommended.



- The Minister requested PQM's support for WHO PQ for anti-TB, antiretroviral, and antimalarial medicines that will enable local manufacturers to participate in global tenders.
- The Minister requested technical assistance for WHO PQ of the ISO-accredited NAFDAC laboratories. As part of next steps, PQM will continue to provide technical assistance to local manufacturers to enable procurement of locally manufactured medicines in Nigeria.

## Senegal

### I. Quarter 3 Highlights

To prepare the National Drug Control Laboratory (LNCM) for the first official ISO 17025 accreditation audit by the Tunisian Accreditation Council (TUNAC), in Q3 PQM procured some laboratory supplies and made plans to conduct several activities at LNCM. PQM made plans to conduct a visit at the end of July to support DPM in strengthening its registration and importation functions. Due to the delay in the approval process of the FAA, PQM support of PMS activities were postponed until Q4.

### II. Country Context

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

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

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

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

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

### III. Quarter 3 Progress by Objective

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

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To follow on the activities conducted at LNCM in Q2 by Zef-Sci, PQM shared a detailed report on the qualification of the selected laboratory equipment with the Laboratory Director and his staff. The next step is to conduct a series of technical assistance activities and trainings to prepare the laboratory for the first official audit by TUNAC, taking into account the new ISO 17025:2017 requirements. The following will take place in Q4:

- Review the CAPAs implemented in response to the last assessment.
- Review authorization of activities.
- Review gaps/updates to ISO 17025 documentation (SOPs, work instructions, and managerial documents).
- Training on records and sample worksheets.
- Assess equipment status: qualification, calibration, and maintenance records.
- Perform a detailed ISO 17025 assessment and provide feedback on the laboratory readiness for the final audit.

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

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Due to the delayed approval for FAA, planned joint PMS activities could not take place. FAA approval is expected in Q4 to pave the way for sampling and testing. Details of this activity will be reported when completed.

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### **Objective 3 – Support DPM in improving its regulatory functions**

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At the request of DPM director, PQM will continue supporting the registration and importation functions of DPM. To this end, PQM is planning an intervention in early August to conduct the following activities:

- Deploy an online solution for submission of application files and easy access to the DPM database.
- Protect access to the DPM database via a backup system and establishment of user password.
- Train on the standardization of import procedures and ensure that only registered medical products are imported into the country.

## **West Bank and Gaza**

### **I. Quarter 3 Highlights**

During Q2, PQM conducted a 2-week assessment of the General Directorate of Pharmacy (GDP) using the Global Benchmarking Tool (GBT) and a 2-week assessment of the national quality control laboratory's (CPHL) QA/QC systems. The GBT tool assessment was conducted using a questionnaire on the legal framework and the GDP functions followed by validation of the records and activities conducted by GDP staff. In Q3, PQM shared the outcomes of both assessments with the Mission and key stakeholders and provided recommendations on how to address laboratory assessment findings and GDP assessment results.

While addressing gaps identified during the assessment, PQM provided a series of theory and hands-on trainings in the laboratory, delivered a presentation on risk-based PMS, and assisted GDP in reviewing current registration guidelines.

### **II. Country Context**

PQM has provided technical assistance in the areas of QA and QC, regulatory systems support, and current GMP. In 2015, the PQM program conducted an assessment of manufacturing services in the Palestinian Territory of West Bank and Nablus. However, due to continuous uncertainty in the region, after that visit the PQM program could not undertake additional activities in the area for more than 2 years. In FY 2017, the USAID Mission in Israel, with responsibility for West Bank programming, provided funding for PQM to initiate activities in the West Bank. The focus builds on past PQM efforts to provide a comprehensive systemic approach in building the capacity of the regulatory agency to protect people's health by ensuring the availability of quality-assured medicines.

### III. Quarter 3 Progress by Objective

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#### **Objective 1 – Strengthening the General Directorate of Pharmacy’s organizational structure and regulatory functions**

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To strengthen its capacity, PQM conducted an assessment of GDP using the GBT. In Q3, PQM presented the outcomes of the assessment and provided recommendations on how to improve the existing functions and address the gaps identified in GDP’s legal framework. The recommendations included the followings:

- Assist GDP in the establishment of a legal framework to support the institutionalization of a PMS program under GDP mandate.
- Develop guidelines to support the implementation of a PMS program using a risk-based concept.
- Align the national medicines policy with the health policy.
- Address the growing need for standards of practice, as per the WHO model law.
- Develop GDP’s QMS, including risk management principles.

In addition to the above recommendations, PQM reviewed GDP’s registration guidelines and provided guidance to GDP staff on how to conduct PMS using risk-based protocols for sampling and testing.

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

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GDP is in the process of adopting and installing SIAMED software for its registration activities. Following its installation of this software by WHO, PQM will provide the necessary technical support to optimize its use and improve the registration processes to meet international standards.

Training on inspection using WHO and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines is planned for Q4.

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

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Nothing to report this quarter.

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

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Following PQM CPHL’s QA/QC assessment, PQM shared in Q3 the detailed findings report with the Laboratory Director and his staff and provided an action plan on how to address those findings.

To support CPHL toward developing a QMS that is compliant with international standards, such as ISO/IEC 17025:2005 and/or WHO PQ, PQM developed training manuals and conduct hand-on training courses on:

- Analytical methods within the scope of the ISO 17025 accreditation.
- Effective/proper use of pharmacopeias (USP, British Pharmacopoeia, and International Pharmacopoeia).
- Laboratory corrective, preventive, and risk management actions.
- Good laboratory practices.
- Good documentation practice.

PQM also reviewed the existing QMS and assisted the laboratory in developing lists of annual reference standards and essential chemicals required to support CPHL testing needs.

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

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Nothing to report this quarter.

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

# Asia



# Bangladesh

## I. Quarter 3 Highlights

PQM's activities during FY 2018 Q3 were focused on the implementation of objectives 1, 3, and 4 in the approved work plan and remaining activities of the FY 2017 work plan. The Q3 highlights include the following:

- National Control Laboratory (NCL) submitted an application to ANAB in April 2018 to conduct an audit of NCL's physicochemical laboratory toward achieving ISO 17025:2017 accreditation on 10 analytical method scopes. PQM provided technical assistance to NCL to prepare the required documentation (47 SOPs and 24 quality documents) for application submission to ANAB for review.
- NCL analysts performed proficiency testing on five analytical method scopes (HPLC, UV-Vis, pH, Karl Fischer, and FTIR) and successfully passed all.
- PQM staff and NCL management jointly conducted a mock gap assessment focusing on the 10 analytical method scopes to assess the readiness of the laboratory for ISO 17025:2017 accreditation requirements. The assessment report was prepared by PQM and submitted to the Directorate General of Drug Administration (DGDA) and NCL on May 6, 2018. PQM organized a meeting in the same month to discuss and address the issues from the gap assessment in preparation for the upcoming ISO 17025:2017 inspection by a third-party assessor.
- On May 20–24, PQM staff conducted a mock inspection, landscape, and gap analysis on QMS and ISO 17025:2017 understanding. During this time, PQM also held a practical demonstration on compendial methods at NCL to assess the preparedness of NCL staff in participating in an upcoming ANAB inspection.
- DGDA established a core committee on risk-based PMS in April 2018 to lead risk-based PMS activities and the development of PMS guidelines and a sampling and testing protocol. A draft guidance and protocol were developed and are currently under review by DGDA.
- PQM developed and implemented 2 new SOPs in Q3 and closed 19 CAPAs toward achieving compliance with international standards (ISO 17025:2017).
- In order to prepare laboratory staff to be ready to meet competency requirements for ISO 17025:2017 accreditation, the capacity and skills of 122 staff (79 male and 43 female—aggregate number from 9 separate trainings) from NCL were built on various key operational areas and analytical test methods by PQM.

As a follow-on to the November 2017 workshop for updating the graduate pharmacy syllabus to incorporate regulatory and quality assurance topics at the Centre for Advance Research in Science (CARS) of the University of Dhaka, PQM organized a consultative workshop to discuss recommendations to adopt changes in pharmacy curriculum of pharmacy schools/departments in Bangladesh.

## II. Country Context

PQM's goal in Bangladesh is to strengthen institutional capacity for sustainable regulatory and QA/QC systems that meet international standards. To achieve this, 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 was working—including product registration (dossier format and registration software), GMP training, and PMS—PQM provided technical support to SIAPS, as the lead agency, to provide technical support to DGDA.



### III. Quarter 3 Progress by Objective

#### Objective 1 – Continue to provide technical assistance to the DGDA laboratory – NCL in Dhaka and DTL in Chittagong towards achieving international ISO/IEC 17025:2017 accreditation or WHO PQ

PQM has been providing technical guidance and capacity building of NCL staff to strengthen its QMS toward achieving the ISO 17025:2017 accreditation standards.

PQM worked alongside NCL management and technical staff to follow up on its CAPA implemented to address findings from the internal audit and the PQM audit. In Q3, CAPAs were addressed, and ongoing support was provided to close some CAPAs.

With the assistance of PQM technical staff in Bangladesh, NCL staff developed SOPs to improve internal processes toward achieving international standards. Some key accomplishments during Q3 include the following:

- PQM HQ staff visited NCL on May 20–24 and conducted a landscape and gap assessment of NCL's QMS. Details of activities included:
  - Conducted a 2-day training on ISO 17025:2017 for NCL staff to increase their knowledge and understanding of the ISO 17025:2017 requirements.
  - Reviewed policies and processes and observed all procedures on 10 analytical method scopes to comply with international standards of medicines QC for HPLC, UV-Vis, dissolution, pH, Karl Fischer, loss on drying, uniformity of dosage unit, FTIR, disintegration, and thin-layer chromatography.
  - Reviewed all QMS documents and calibrations/qualifications, installation qualification, operational qualification, and performance qualification information to assess laboratory readiness toward ISO 17025 requirements.
  - Built the capacity of laboratory staff on compendial testing using hands-on interactive approach to promote compliance with international standards.
- NCL received five proficiency test samples in May 2018 from the accredited proficiency test provider, Sigma Aldrich. Proficiency testing determines the performance of an individual laboratory for specific tests and measurements and is used to monitor the continuous performance of a laboratory. Using the knowledge and skills for compendia testing received through PQM's technical support to the laboratory, NCL staff performed proficiency testing on the five analytical method scopes (HPLC, UV-Vis, pH, Karl Fischer, and FTIR) and successfully passed all of them.
- PQM staff conducted a gap assessment of the laboratory with NCL staff; which focused on evaluating laboratory competence for 10 analytical method scopes. Following sharing of the final report with DGDA and NCL in May, PQM organized a meeting titled "Readiness of NCL towards ISO 17025:2017 accreditation" to debrief DGDA management about the 10 analytical method scope readiness of NCL for the upcoming ISO 17025:2017 audit by ANAB; and to obtain clear leadership direction on the way forward to address gaps. The meeting was very participatory and highly motivating to NCL staff.

#### Summary of Laboratory Progress from April 1 to June 30, 2018

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

| Items   | Number of Items completed  |
|---|--|
| Approved and implemented SOP through PQM review   | 02 (SOP for Good Documentation Practices (GDP) & SOP for operation, cleaning and calibration of Radweg analytical balance) |
| <b>CAPA status in Q3 FY18:</b>  |  |
| CAPA generated during Q3 (Apr to Jun-2018) based on the observations by internal audit on April-2018 (16) | Completed: 08, Remaining 08 CAPA under follow up   |
| <b>Total remaining CAPA up to Jun-2018:</b>   |  |
| CAPA from PQM audit (2017) (24)<br>(CAPA No.: CAPA/CD/004/17)   | Completed: 21 (01 in Q3). Remaining 3 CAPA in process.   |
| CAPA from NCL Internal Audit – March 2017 (28)<br>(CAPA No.: CAPA/MB/003/17)                              | Completed: 25 (01 in Q3); Under follow up: 03  |

| Items  | Number of Items completed                                 |
|--|---|
| CAPA from NCL Internal Audit - June 2017 (26)<br>(CAPA No.: CAPA/CD/005/17)                        | Completed: 23 (02 in Q3); Under follow up: 03             |
| CAPA from PQM assessment on November 2017 (13)<br>(CAPA No.: CAPA/CD/(001,002,004,006,013)/FEB/18) | Completed: 09 (1 in Q3) Pending: 1 to be followed up      |
| CAPA from NCL Internal Audit on November 2017 (09)<br>(CAPA No.: CAPA/NCL/009/17)                  | Completed: 08 (1 in Q3) Pending: 1 to be followed up      |
| CAPA from NCL Internal Audit on March 2018 (09)<br>(CAPA No.: CAPA/NCL/009/17)                     | Completed: 08 (1 in Q3) Pending: 1 to be followed up      |
| Calibration performed by NCL   | Electronic balance (03 balance)<br>pH Meter (2 pH Meters) |

**Summary of training conducted in Q3 FY18  
(Laboratory area -ALS & QMS)**

| SL/ No. | Training  | Date           | Laboratory Designation | Gender        | Total Trained | Technical Areas   | Training conducted by |
|---------|---|----------------|------------------------|---------------|---------------|-------------------|-----------------------|
| 01      | Hands-on training on the analytical technique of Disintegration (DT)  | 03-April/2018  | 23 NCL                 | 15 M, 8F      | 23            | ALS               | Local staff           |
| 02      | Hands-on training on User Requirement Specification (URS) for the laboratory equipment: dissolution tester, DT, UV, thin-layer chromatography & Balance | 05-April/2018  | 10 NCL                 | 8M, 2F        | 10            | QMS               | Local staff           |
| 03      | Hands-on training on the procedure of Training Needs Assessment (TNA)   | 12-April/2018  | 11 NCL                 | 8M, 3F        | 11            | QMS               | Local staff           |
| 04      | Refresher training on Analyst validation  | 12-April/2018  | 2 NCL                  | 2F            | 2             | ALS               | Local staff           |
| 05      | Hands-on training on User Requirement Specification (URS) for the laboratory equipment: HPLC, LOD, KF titrator, PH meter, FTIR.                         | 16-April/2018  | 09 NCL                 | 6M, 3F        | 9             | QMS               | Local staff           |
| 06      | Training on general Standard Testing Procedure (STP)  | 08-May/2018    | 14 NCL                 | 10M, 4F       | 14            | ALS               | Local staff           |
| 07      | Theoretical training on landscape and gap assessment of QMS, ISO 17025:2017 understanding and proficiency testing                                       | 20-21-May/2018 | 23 NCL                 | 15M, 8F       | 23            | QMS               | HQ staff              |
| 08      | Hands-on training on analytical technique of LOD  | 27-June/2018   | 15 NCL                 | 9M, 6F        | 15            | ALS               | Local staff           |
| 09      | Refresher theoretical training on Pharmacopeial use   | 27-June/2018   | 15 NCL                 | 9M, 6F        | 15            | ALS               | Local staff           |
|         | Total in Q3   |                |                        | M=79<br>F= 43 | 122           | ALS= 69<br>QMS=53 |                       |

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

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In Q3, PQM conducted a GMP assessment of Advanced Chemical Industries (ACI) Limited's Narayanganj manufacturing site as part of PQM's technical support for CHX gluconate 7.1% solution for umbilical cord care. The purpose of the assessment was to evaluate the manufacturing operation of ACI Limited against WHO GMP requirements with manufacturing of CHX gluconate 7.1%. Based on the observations found during the assessment, ACI Limited submitted its CAPA plan for PQM's review.

In June 2018, HQ GMP staff and PQM BGD staff reviewed the CAPA and provided review comments for next steps and the way forward.

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

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Several activities were implemented to enhance DGDA’s regulatory capacity. These include strategic planning, human resources, international standards, and improved PMS.

- DGDA established a core committee on risk-based PMS in April 2018 following a 3-day long workshop and a 4-day practical demonstration workshop for key stakeholders by PQM. The committee’s TOR include leading risk-based PMS activities, as well as developing PMS guidelines and a sampling and testing protocol toward establishing an effective risk-based-PMS system. A draft guidance and protocol has already been developed and is undergoing review to be finalized by DGDA.
- PQM organized a consultative workshop on recommendations to adopt changes in the pharmacy curriculum of pharmacy schools/departments in Bangladesh in May 2018. This workshop was a follow-on event after the plenary meeting on updating graduate pharmacy syllabus relevant to the regulatory functions at CARS by a selected core group in November 2017. The main output of the November workshop was a draft strategic report prepared by PQM with recommendations for the revision of the existing course curricula of the pharmacy schools/departments. The workshop in Q3 involved a wider stakeholder consultation to finalize the draft report and recommendations. Meeting participants included University Grants Commission, University of Dhaka, Jahangir Nagar University, North South University, East West University, DGDA, Pharmacy Council of Bangladesh (PCB), Regulatory Society Bangladesh, USAID and USP-PQM program. A draft final strategic report was prepared by PQM and will be submitted for review and finalization.
- PQM finalized the first draft report on support to DGDA on the revision of legislation, organization, and management of medicine regulation in Q4. The report is undergoing internal review.

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

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Since April 2018, the PQM technical team has been providing support to the National QA/QC Policy (NQAP) committee. DGDA established the NQAP Committee in March 2018 following a consultative workshop organized by DGDA and PQM to deliberate on a national QA/QC policy for quality-assured medical products in February 2018. The workshop aimed to provide clear policy directions to public healthcare authorities and professionals regarding quality of medicines and medical products and to support implementation of National Drug Policy 2016 in relation to the medicines quality issues. PQM is preparing for the next committee meeting to be held on July 23, 2018.

## **IV. Key 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 is a global issue. The country office is closely working with the USP global security team to monitor security situation.
- The upcoming Parliament election in December 2018 may affect PQM project implementation activities and achievement of some project deliverables.
- During the planning process for FY 2018, PQM took into consideration planned financial contributions from the Government of Bangladesh to augment the support provided by USAID. If government resources do not materialize as anticipated, it could hamper the achievement of the overall program objectives.

## **V. Lessons Learned**

Program performance is limited by the shortage of critical staff with relevant skills and experience at DGDA and NCL/drug testing laboratory (DTL). The availability of highly motivated, skilled personnel is the key to success. Motivation of existing NCL and DTL staff emerged as a concern in different observations. Special attention to identifying and resolving demotivation factors is key to achieving NCL strategic goals. In support of this, PQM arranged a successful meeting of DGDA top management and the NCL staff to resolve the factors on May 8, 2018.

## VI. Sustainability, Partner Contributions, and Ownership

DGDA, NCL, national priority health programs, and the pharmaceutical industries are the primary stakeholders of the PQM program in Bangladesh. PQM has been working closely with these partners. In the process, PQM is providing technical assistance to MRA, NCL, and essential medicines manufacturers toward achieving international standards for the long-term public health benefits.

## Burma

### I. Quarter 3 Highlights

With PQM's technical assistance and supervision, the Department of Food and Drug Administration's (DFDA) Nay Pyi Taw laboratory has begun testing deltamethrin-coated long-lasting insecticide nets (LLINs) collected by VectorWorks/PSI as part of an ongoing PMI-funded study. The laboratory has agreed to test 60 samples of LLINs (5 tests/sample).

PQM and DFDA conducted a training workshop on QMS as part of the preparations toward maintenance of ISO 17025 accreditation of Nay Pyi Taw laboratory. PQM-trained trainers led the workshop and trained 34 of their counterparts from Nay Pyi Taw and Mandalay laboratories.

PQM and DFDA welcomed Dr. Nu Nu Khin, new activity program management specialist for PQM from PMI/USAID-Burma, to Nay Pyi Taw laboratories and briefed her on PQM's work and achievements in the country. After the briefing, Dr. Nu toured around the current Pharmaceutical Chemistry Laboratory, which achieved ISO 17025 accreditation with PQM's technical assistance in 2016. Dr. Nu also visited the new laboratory construction project and the newly opened National Reference Laboratory for Food, both of which received PQM assistance in interior design and configuration with PMI's support.

### II. Country Context

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

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

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

### III. Quarter 3 Progress by Objective

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

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This activity is ongoing. In Q3, PQM provided feedback to DFDA on structuring the testing fees for LLIN testing. The fees initially calculated at 80 USD/test (5 tests/sample) and was reduced to 60 USD/test upon PMI's request to accommodate funding limitations faced by VectorWorks project implemented by PSI.

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

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PQM delivered training on testing of deltamethrin-coated LLINs in FY 2018 Q2, and the laboratory continued its practice in FY 2018 Q3. The laboratory encountered a problem during the practice, and PQM provided assistance in identifying the root cause of the problem, which was found to be a technical issue with the column used for HPLC analysis. After the problem was solved, the laboratory continued its practice testing, and the results were found to be satisfactory.

The laboratory began the actual testing of 60 samples of LLINs collected by VectorWorks/PSI at the end of May 2018. By the end of FY 2018 Q3, 24 out of 60 samples were tested as PQM continued to supervise.

As part of the preparations toward maintenance of ISO 17025 accreditation, DFDA and PQM conducted a training workshop on QMS in June 2018. The team trained 34 laboratory staff (33 female and 1 male) from Nay Pyi Taw and Mandalay laboratories on the new requirements for ISO 17025-2017 standards. The training content included building capacity and skills for document control and SOPs writing, GLP, good documentation practices, laboratory safety, internal audit, root cause analysis, corrective action, and risk management. PQM utilized the collaborative learning model whereby DFDA staff who received advanced training in the past led and supported the very practical and interactive training to promote a sustainable learning environment at DFDA.

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

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Due to the changes in DFDA senior management, the construction projects in Nay Pyi Taw and Mandalay were halted in June 2018. This activity is delayed.

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

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Nothing to report this quarter, as the Mandalay laboratory is currently under construction.

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

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Nothing to report this quarter, as the Mandalay laboratory is currently under construction.

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

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Nothing to report this quarter—activity on hold by DFDA.

## Indonesia

### I. Quarter 3 Highlights

As of FY 2018 Q3, the 2017 BAST<sup>1</sup> has been completed and signed by BPOM and USAID for submission to the Ministry of Finance. In anticipation of the completion of the FY 2018 BAST, PQM will continue to collect the relevant financial and implementation information for inclusion in the upcoming BAST and finalize it during Q1 2018 (FY 2019) at the end of the calendar year.

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<sup>1</sup> The BAST (*Berita Acara Serah Terima*) is a document that is required by the government of Indonesia to capture all financial and activity contributions handed over to the government from donor programs. Legally, the reporting is from USAID to BPOM, which then collates and submits the BAST to the Ministry of Finance. In practice, PQM provides the detailed information to USAID who then approves, signs and submits to BPOM on an annual basis per government fiscal year cycle (calendar year Jan-Dec).

During Q3, PQM supported a successful WHO audit of Kalbe Farma for prequalification of its levofloxacin 500 mg tablet, with a result of only three major observations. Audit findings are classified as critical, major, or minor. While critical observations are considered very serious and unacceptable, major observations are deviations that can be corrected. PQM had conducted a “mock audit” during Q2 which identified a number of key areas addressed by a rapid CAPA implementation in time for the WHO audit. Since there were less than six major observations by WHO, Kalbe Farma will be able to satisfy the auditors with their CAPA documentation without the need for a follow-up, onsite visit. PQM anticipates successful Prequalification of Kalbe Farma’s levofloxacin 500 mg product during FY 2018 Q4.

Three provincial BPOM institutions were supplied and trained on the use of Minilabs™, which have been incorporated into the BPOM national sampling strategy as part of its risk-based approach to include screening to complement compendial medicines testing. PQM will be further rolling out training to six more provincial laboratories during FY 2018 as part of a collaborative co-financing between KNCV’s USAID Challenge TB and PQM in response to official requests by the government of Indonesia. Further plans include supplying all 34 provincial institutions with Minilabs™ through a TB and HIV Global Fund grant for 24 Minilabs™ during the next year (pending GF scheduling).

PQM also continued to support Sanbe Farma in its bid to have its levofloxacin 500 mg tablet prequalified by WHO, targeting product dossier submission to WHO by August 2018.

The BBPOM Denpasar provincial laboratory is also on track for submission of the laboratory information file (LIF) documents to WHO for prequalification of the medicines quality control laboratory, with LIF submission planned for early 2019.

Additional activities include initiating collaboration with the Global Fund–TB and WHO Indonesia to support BPOM in pre-market and post-market surveillance for medicine and in-vitro diagnostics and rapid diagnostic tests; participation in an annual symposium and partnership initiation with the International Society of Pharmaceutical Engineers; development of potential collaboration on oxytocin quality control with the DAI Jalin project in Indonesia; and further development of the technical assistance program as implementing partner with the Global Fund TB and HIV projects.

## II. Country Context

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

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

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

## III. Quarter 3 Progress by Objective

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

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As part of the ongoing support to provincial QC laboratories (BBPOM) for the development and dissemination of technical review and recommendations following Minilab™ Pilot Study (FY 2017) implementation in Jakarta DKI, Minilab™ trainings and field testing were conducted for the following provincial QC laboratories: DKI Jakarta, Balai POM Jayapura, and Denpasar. The BBPOM Denpasar training also included the introduction of two additional field screening technologies (Trek and Target ID) using infrared and near-infrared spectroscopic methods. Based on brief evaluations, the Minilabs™ were the preferred method for both sensitivity and specificity for field-based screening for medicines quality.



The Minilab™ trainings were unique in that they focused mostly on hands-on implementation of sampling and testing as a collaborative approach between the Provincial Health Offices (PHO), District Health Offices (DHO)—including pharmacies, warehouses, storage, units and clinical sites—and BPOM focusing on the public-sector program medicines in addition to private sector. The PHO–DHO–BPOM collaboration at the pharmacy installations ensures real-time data-sharing of screening results and encourages relationship-building and establishing formal connections for medicines quality control. Using the field screening collaborative activities will continue to be a key strategy that the government can use to routinely implement requirements under the PMK 75/2016 regulation on ensuring medicines quality in public sector facilities.

Minilab™ screening has been officially adopted within the BPOM routine sampling guideline for PMS in nine provincial BPOM institutions since the beginning of 2018. In these provinces (Medan, Serang, DKI Jakarta, Surabaya, Denpasar, Mataram, Kupang, Jayapura, and Makassar), plans are underway to procure equipment and train staff for Minilab™ screening through a cooperative activity between PQM and KNCV's Challenge TB program. An evaluation of the effectiveness of incorporating the Minilab™ into PMS (from a cost-effectiveness perspective, as well as Minilabs™ enabling an expansion of the types and total numbers of pharmaceutical samples tested) and an evaluation of the methodology for PHO–DHO–BPOM collaboration are underway. PQM will conduct focus-group discussions and assessments of the trainees from MOH and BPOM on the effectiveness of this type of collaboration and the best way forward for data-sharing and joint enforcement actions when out-of-specification products are identified. This assessment will help to establish action plans as PQM rolls out additional procurement of equipment (under Global Fund technical assistance activities), training, and implementation of field screening for BPOM institutions nationwide.

PQM supported three BPOM officers to attend the Evaluation of Medicines Field Screening Devices workshop, held in Vientiane, Lao PDR, on April 9–10, 2018. This workshop was a joint project among the Wellcome Trust-Oxford Research Unit in Lao PDR, Asian Development Bank, and USP with the objective to assess specificity and sensitivity of a variety of field-based screening technologies that could have potential use in LMICs to support risk-based approaches to pre- and post-marketing surveillance strategies.



Onsite sampling/testing with Minilab™ at public medicines storage facility with MOH-BPOM staff in Jayapura, Papua



Training on Minilab™ at Jayapura, Papua BPOM laboratory

PQM continues to provide technical assistance to PTBB QC laboratory (BPOM) in preparation for WHO PQ. Following PQM's "mock audit" of the BPOM PTBB national QC laboratory, WHO conducted an audit of the laboratory for prequalification of the national laboratory on May 2–4, 2018, in Jakarta. Following the audit, the PTBB laboratory was given 6 months to develop, submit, and implement its CAPA plan. Upon satisfaction of the CAPA activities, WHO will likely conduct a follow-up assessment at the PTBB laboratory prior to listing the laboratory on the WHO Public Inspection Report as being prequalified. PQM hopes to have the PTBB laboratory prequalified by WHO prior to the end of FY 2019. A CAPA plan in response to WHO's request was prepared, submitted to, and accepted by WHO in June 2018 (see Table 1 below).

**Table 1** WHO PQ timeline for NQCL (PPOMN) of BPOM RI

| Activity  | Timeline               | Status      |
|---|------------------------|-------------|
| NQCL submitted LIF to WHO   | August 31, 2017        | Submitted   |
| WHO PQ On-site Inspection (visit)   | May 2-4, 2018          | Done        |
| Received Inspection Report from WHO   | May 21, 2018           | Received    |
| Preparation CAPA Plan by NQCL   | May 22 – June 11, 2018 | Prepared    |
| Submit CAPA Plan by NQCL (due date: 30 days after inspection report received) | June 12, 2018          | Submitted   |
| Received Feedback on CAPA Plan with comments from WHO                         | July 16, 2018          | Received    |
| Review CAPA Comments by NQCL  | July 30, 2018          | in progress |
| CAPA Completion and Closed  | End of September 2018  | in progress |
| Compile all the CAPA supporting document and evidence                         | October 1 – 13, 2018   | TBD         |
| Submit completed CAPA Response and evidence                                   | October 15, 2018       | TBD         |
| CAPA Verification by WHO (follow on inspection) – Visit                       | November 2018          | TBD         |

PQM supported 20 BBPOM laboratories to participate in the Network of Official Medicines Quality Control Laboratories (NOMCoL) inter-laboratory testing medicines quality assurance program. As part of this support, two laboratory officers from the national Center for Development of Drugs and Food Testing (PPOMN, or *Pusat Pengembangan Pengujian Obat dan Makanan Nasional*) attended the Annual NOMCoL workshop at Kuala Lumpur, Malaysia, May 14-16, 2018. Also in attendance were regional NRAs, WHO, ADB, and other partners to harmonize and promote regional cooperation within the Association of Southeast Asian Nations for medicines QA.



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

During Q3, PQM provided technical assistance to Sanbe Farma/Caprifarmindo to finalize the levofloxacin 500 mg product dossier for submission to WHO for PQ, with a target submission date of the product dossier by FY 2019 Q1 (during October–December 2018). PQM also plans to conduct a final product dossier assessment and facility/documentation/practices “mock audit” depending on the WHO schedule once finalized (likely during FY 2019). A follow-up visit to evaluate the readiness of the product dossier of levofloxacin 500 mg was conducted during May 17–18, 2018, onsite at Sanbe Farma. PQM has intensified its focus on providing technical assistance to Sanbe Farma in anticipation of the PQM project closeout. PQM plans a second product dossier evaluation in the coming months.

PQM provided technical assistance to Kalbe Farma to finalize levofloxacin 500 mg product dossier. WHO conducted an extensive facility, documentation, and personnel inspection at Kalbe Farma to evaluate the levofloxacin 500 mg manufacturing processes on May 24–29, 2018. The inspection was successfully closed with no critical findings and only three major observations. Based on this, WHO will accept the submission of documents as evidence of the closed CAPA implemented by Kalbe Farma within 60 days of CAPA submission (by August 2018). PQM continues to provide technical assistance on developing, submitting, and implementing the CAPA plan to address the audit findings and to provide additional data on the Quality Part of the product dossier as requested by WHO. PQM has conducted several onsite meetings, teleconferences, and internal evaluations during this support.

**Table 2** Timeline for Kalbe Farma's WHO Prequalification of levofloxacin 500 mg

| Activity   | 2018 Timeline      | Status               |
|--|--------------------|----------------------|
| WHO PQ Inspection of Kalbe Farma                                   | 24-29 May          | Complete             |
| Official Inspection Report   | 1 June             | Received             |
| Drafting CAPA based on Inspection Report                           | 2 June-23 June     | Submitted to WHO     |
| Feedback/comments from WHO inspectors on CAPA                      | 28 June            | Re-submitted WHO     |
| Conducting training on CSV according to CAPA plan                  | 11-12 July         | Training Report done |
| Drafting, reviewing, compiling all documents and SOP-related CAPAs | 2 July-end of July | In progress          |
| Submit all evidence addressing CAPA for major observations         | 24 July            | TBD                  |
| CAPA submission reviewed by WHO inspectors                         | 26 July- 3 August  | TBD                  |
| WHOPIR published, WHO Prequalified                                 | 7-10 August        | TBD                  |



Photo of GMP inspection at Kalbe Farma

PQM initiated collaboration with key Centers of Excellence universities in Indonesia providing bioequivalence expertise to BPOM on developing a sustainable mechanism for high-quality technical assistance on GLP and GCP. PQM has shifted its focus from providing support to the Centers of Excellence to providing support for the Bioavailability/Bioequivalence Forum, a communication forum for CROs working in bioequivalence (for both the academic and private sectors) that builds capacity in Indonesia and regularly conducts training workshops for members. PQM is in discussions to develop a TOT methodology that will establish a pool of experts for providing bioavailability/bioequivalence trainings for CROs as well as support the regulator BPOM. The next training workshop is planned for August 2018 and will focus on data integrity and data validation in bioequivalence studies, and PQM plans to support this.

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**Objective 3 – To enhance the technical capacity of the government of Indonesia to develop and implement inter-agency (MOH, BPOM, donors, professional associations, other stakeholders) policies and procedures for medicines quality assurance (coordination, advocacy, and developing appropriate public awareness tools), and to support the National TB Program, National AIDS Program, and FARMALKES to ensure quality and production is in line with procurement policy/new treatment guidelines**

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PQM developed and convened the MOH–BPOM National Joint Sampling and Testing Data Dissemination Workshop, held on May 14 in Jakarta. The meeting was attended by national and 11 provincial MOH, PHO, and BPOM (central and provincial) officers, including several Directors from the Center for Disease Control (CDC) (Oblik, Subdit HIV and TB), Farmalkes, and BPOM with the aim of disseminating key data from the joint sampling and to develop recommendations to the Minister of Health. The BPOM Directorate for Safety and Quality of Imported and Exported Medicines, Psychotropics, Precursors, and Addictive Substances (BPOM Directorate KMEI), the directorate responsible for the national PMS program of BPOM, was the official government sponsor of the workshop. The joint sampling activity was a PQM-initiated activity funded by the Global Fund with USAID technical assistance as provided by PQM.

The workshop resulted in several key recommendations that will be summarized and submitted by three directorates (CDC, Farmalkes, and KMEI) to the Minister of Health and other high-ranking officials. Main takeaways included the need to:

- Identify needs and establish official planning and engagement plan for sampling activities, including the mechanisms to prevent stock-outs from sampling and replacement of sampled products.
- Identify mechanism for rapid communications among stakeholders at the provincial and district levels regarding test results to prevent out-of-specification products from being dispensed to patients.
- Develop the quality assurance system for Special Access Scheme (SAS) supply management. SAS medicines are high-priority medicines imported by MOH that do not currently fall under the jurisdiction of BPOM. The current national PMS system must include SAS medicines, and PQM is working with MOH and BPOM on the mechanism to do so, including a potential shift in jurisdiction from MOH to BPOM.

The Director of KMEI agreed to submit the workshop recommendations to all key stakeholders for comprehensive follow-up action.

PQM Indonesia will continue to work with the KNCV Challenge TB project on a co-financing mechanism to support the expansion of the Minilab™ projects to six additional provincial BPOM institutions to support the national PMS system. This activity is planned for FY 2018 Q4.

A meeting was held with the head of the National HIV/AIDS Program (NAP) to discuss USP's capacity to provide technical assistance for supporting the HIV/AIDS program. The NAP requested PQM to assist on the PMS of rapid diagnostic tests or in vitro diagnostics used by the programs. PQM was actively involved in Global Fund TB meetings to establish the Technical Assistance Plan for supporting TB program implementation, as developed and submitted by all implementing partners in Indonesia. PQM proposed 37 activities, particularly around supporting the national QA system of medicines in pre- and post-market in the technical assistance matrix for supporting TB and HIV programs. The final matrix has been submitted to the Global Fund following approvals by the National TB Program (NTP) head, the director of the MOH CDC, and the person in charge of the Global Fund program and the Global Fund Country Team in Geneva.

Discussions were held with NTP, the Global Fund Technical Working Group, and other implementing partners to include PQM in the national technical assistance plan along with other implementing partners (USAID partners, WHO, and others). Discussions on potential areas of technical assistance to be provided to NTP and NAP with Global Fund support include procurement of 24 additional Minilab™ kits to be operated at the provincial BPOM

quality control labs and related trainings to strengthen PMS as BPOM has officially requested. Other activities include providing GMP technical assistance to local manufacturers that have expressed interest in producing a 2FDC for TB treatment as the daily regimen (RH 150/75) as well as second-line drugs used in the treatment of drug-resistant TB. As the national disease programs shift funding to domestic government sources, MOH needs to anticipate lead times for developing medicines to be made available to the government's public procurement mechanism.

PQM was invited by WHO Indonesia to develop the quality assurance system for the in vitro diagnostics used by the MOH disease control programs, including the rapid diagnostic test units for HIV/AIDS. PQM will follow up with this request in coordination with WHO, Chemonics Procurement and Supply Management, and the national disease control programs of MOH.

PQM also participated in the annual International Society for Pharmaceutical Engineering (ISPE) conference "BEYOND COMPLIANCE – Protecting Patients, Support Innovation" on May 8, 2018, in Jakarta to discuss potential partnering with ISPE, which requested PQM's support for an upcoming training workshop during FY 2018 Q4.

PQM also initiated discussions with DAI's Jalin project on Maternal Neonatal and Child Health concerning QA and QC testing of oxytocin in the public and private sectors in Indonesia, based on stated concerns about suboptimal storage and distribution practices in the government and private sectors. There was initial interest in collaborating on this following PQM's web publication of "Revisiting the Stability and Storage Specifications of Oxytocin Injection: A Literature Review." A collaborative study would include reviewing primary data from BPOM collected during PMS activities, as well as designing a quality survey for oxytocin in various health facilities in Indonesia.

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#### **Objective 4 – Monitoring and Evaluation for specific activities**

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Nothing to report this quarter.

### **IV. Key Challenges**

The Global Fund partners' technical assistance plan to support NTP has been approved for PQM-proposed activities. However, the funding mechanism for Global Fund–TB funding is still pending and will hopefully be resolved during FY 2018 Q4. In addition, PQM is still awaiting final signoff by the KNCV Challenge TB's USAID Agreement Officer's Representative (AOR) to support the collaborative activity on Minilab™ training. There were also significant delays in the approval of the Chief of Party's work permit and official resident visa, which was finally granted by the government of Indonesia in FY 2018 Q3 (after a year of processing).

### **V. Sustainability**

The most significant area for sustainability of the PQM program is the official incorporation of the use of Minilab™ screening technology into the BPOM national PMS program policy. This adoption of the use of screening to support a risk-based approach to regulation will ensure that these activities will continue beyond the life of the PQM program in Indonesia, providing a more comprehensive approach to medicines quality surveillance. PQM is also collaborating with different partners to ensure pertinent country activities continue to be funded and implemented. These include leveraging of funds from KNCV's Challenge TB program to support the equipping and training of six additional BPOM provincial institutions for Minilabs™; a proposal (in the final stages of approval) to the Global Fund via the BPOM KMEI Directorate to have Global Fund financing (NTP and NAP) of 26 Minilabs™ for final coverage of all BPOM provincial institutions (this will ensure widespread coverage of screening for medicines quality nationwide in Indonesia, fulfilling requirements of the Presidential instructions and BPOM's own strategic goals); PQM's partnership with WHO in developing QMS for the external quality assessment (EQA) system for IV Diagnostics and rapid diagnostic tests to support the public-sector disease control program; and partnerships with DAI for initiating QA of maternal health products and with ISPE for working with local manufacturers on expanded GMP and other areas.

## **Pakistan**

### **I. Quarter 3 Highlights**

During FY 2018 Q3, PQM continued to provide technical assistance to strengthen the drug regulatory system by building the capacity of laboratory staff on laboratory instrumentation and supporting selected manufacturers of priority products, including the four local manufacturers (Atco Laboratories, Aspin Pharmaceuticals, Zafa Pharma, and Akhai Pharmaceuticals) that launched CHX 7.1% gel with the support of PQM. All four manufacturers made the products available in all four provinces and regions of Pakistan as over-the-counter medicines, readily accessible by

the general public. It is a success story for PQM Pakistan to facilitate locally manufactured, quality-assured, and safe CHX 7.1% gel in a short span of 2 years. Additionally, these products are now available for procurement by provincial governments, where they are already included in the list of essential medicines for lady health workers<sup>2</sup> working under the Prime Minister's Program for Family Planning and Primary Health Care (a program launched by the government in 1994).

During Q3 Atco Laboratories and Aspin Pharmaceuticals completed dossiers for CHX 7.1% gel that were submitted to UNICEF. A positive review by UNICEF would enable both manufacturers to become potential UNICEF suppliers.

An advanced 4-day training course on GMP was held in Karachi for technical managers from the industry. The technical personnel from local manufacturers, 59 of them (49 male, 10 female), were selected and invited to attend this workshop on the basis of their qualifications, expertise, and functional role at work.

PQM continued providing support to the Drug Regulatory Authority of Pakistan (DRAP) to strengthen its regulatory system, especially in the QMS for regulatory functions and preparation of its institutional development plan to address findings from the second self-assessment that was conducted in FY 2017 with PQM support. In Q3, PQM hired a full-time Regulatory Specialist tasked to focus on DRAP regulatory support and work toward achieving WHO's GBT Level 3 for DRAP. This was a specific request by the DRAP CEO and is a very significant PQM endeavor to help strengthen DRAP's regulatory capabilities.

In Q3, PQM conducted a hands-on capacity and skills building training at the Drug Testing Laboratory (DTL) Lahore for a selected group of analysts to improve their use of laboratory equipment. PQM also reviewed the Pakistan Drugs Testing and Research Center (PDTRC) to prepare for the WHO PQ inspection planned in July 2018. Two other DTLs from Faisalabad and Multan also attended and benefited from the hands on training at DTL Lahore, making final preparation for their ISO17025 preparation expected to take place in Q4.

## II. Country Context

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

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

## III. Quarter 3 Progress by Objective

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

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### **CHX 7.1% Gel**

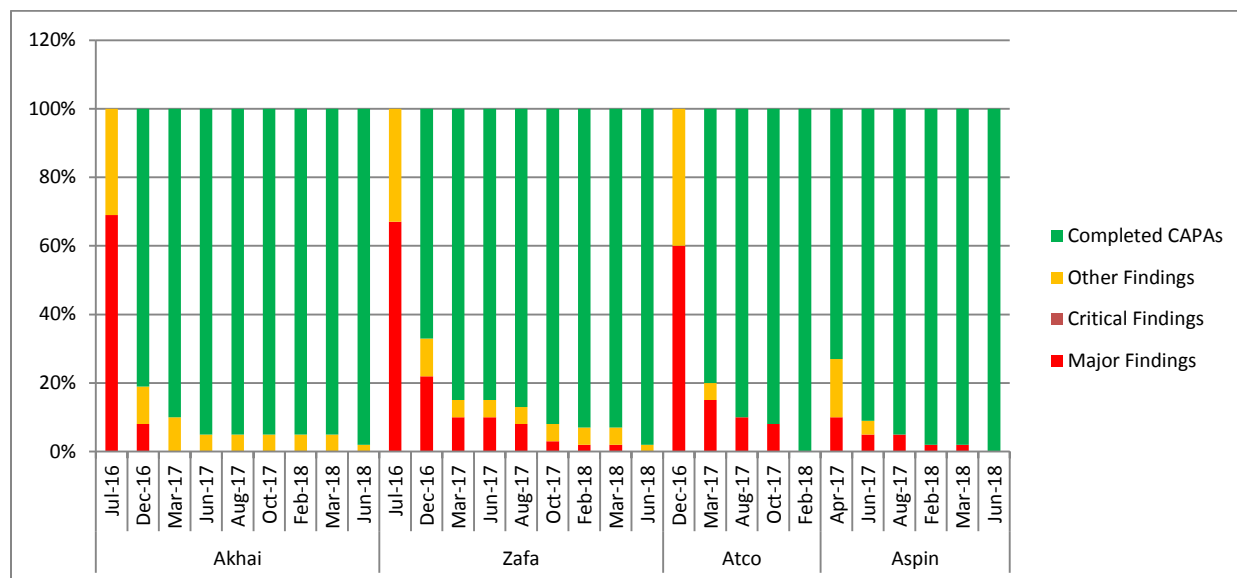
PQM has been working with four manufacturers of CHX 7.1% gel—Zafa Pharmaceuticals, Akhai Pharmaceuticals, Atco Laboratories, and Aspin Pharmaceuticals—to assess the implementation of the recommended CAPA plans and to identify areas where the manufacturers need further PQM support to address the remaining CAPA items. The progress of manufacturers on CAPA implementation is shown in the chart below. All the manufacturers have been able to complete the CAPA implementation plan prepared under PQM's technical assistance. The products of all four manufacturers are already in production, approved for domestic launch, and now available on the local market.

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<sup>2</sup> The Lady Health Worker Program was introduced in Pakistan in order to make primary healthcare accessible to women who are confined to their homes, and to effectively administer immunization among children.



During Q3, PQM supported the manufacturers in preparing for UNICEF submission by reviewing their dossiers and suggesting improvements to make the dossiers acceptable by UNICEF. As a result of this support, two manufacturers (Atco Laboratories and Aspin Pharmaceuticals) have submitted their dossiers to UNICEF.



### Amoxicillin Dispersible Tablets (DT)

PQM conducted a baseline assessment of Macter International’s penicillin manufacturing facility in FY 2018 Q1 and prepared a comprehensive assessment report already communicated with the company’s management. The manufacturer has since prepared a CAPA plan based on PQM’s input and the plan was shared, reviewed, and agreed upon with PQM for implementation. PQM provided technical assistance to the manufacturer to close its non-compliances.

Considering the importance of this product and its potential demand, PQM has identified an additional manufacturer, M/s CSH Pharmaceuticals, as another potential manufacturer of amoxicillin DT. A comprehensive GMP assessment of CSH Pharmaceuticals will be conducted in FY 2018 Q4.

### Other Essential MCH Products

PQM consulted with the USAID Mission in Pakistan to identify other essential MCH medicines with public health impact needing PQM support; identified products included amoxicillin DT, oxytocin injection, zinc DT, and zinc DT/oral rehydration salts co-pack.

Amoxicillin is an effective broad-spectrum antibiotic, especially for the treatment of children with bacterial pneumonia. Its availability and use as a first-line treatment for pneumonia in countries with a high burden caseload remains limited, despite higher effectiveness than existing alternative treatments.

Diarrhea remains a leading cause of death globally among children under 5 years of age. Zinc (micro nutrient) supplementation has been shown to reduce the duration and severity of diarrhea and to prevent subsequent diarrheal episodes (frequency). At the present time in Pakistan, zinc DT (recommended for children under 5 years of age) are not manufactured locally. PQM identified the following manufacturers as potential local producers of these products (based on their GMP compliance data with PQM and DRAP):



PQM team reviewing QMS at PDTRC

1. Amoxicillin DT: Macter International (Karachi) and CSH Pharmaceuticals (Lahore). During Q3, PQM worked with Macter International to develop a stable formulation of amoxicillin DT. Support was also extended to prepare the dossier for WHO PQ of the product. A suitable formulation has been developed by the manufacturers and plans are underway to start stability studies.

2. Zinc DT: Pharmedo, Aspin Pharmaceuticals, and Atco Laboratories were selected for the manufacturing of the product. With PQM support, M/s Atco has developed a stable formulation of zinc DT and is now waiting for the raw material to prepare larger batches for stability testing. Two pilot scale batches will be placed on stability testing by August 2018 as part of the pre-launch preparation.

Aspin Pharma is also in the process of developing a stable formulation of zinc DT and zinc syrup is also supported by PQM to prepare the registration dossier for DRAP application submission. The submission to DRAP is expected in November 2018. The dossier from Pharmedo for zinc DT was accepted by WHO for review and the experts from WHO for a PQ audit visit expected in the third week of July 2018.

3. Zinc DT/oral rehydration salts co-pack (for diarrhea): Atco Laboratories prepared a formulation with PQM technical support; the stability study is ongoing. The manufacturer is also preparing its dossier for WHO PQ submission. Once completed, PQM will review the dossier and provide input to ensure compliance and acceptance by WHO for PQ.

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

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PQM conducted two sessions of hands-on training on instruments at the premises of DTL Lahore. Two groups of analysts from all five DTLs of Punjab and PDTRC Lahore were invited to attend. The 3-day training was conducted by PQM technical expert from Rockville and was attended by the newly recruited analysts from DTL Lahore. The second training lasted 5 days, was conducted by another PQM technical expert from Rockville, and was attended by analysts from the DTL Laboratories situated at Faisalabad, Multan, Bahawalpur, and Rawalpindi, in addition to the selected staff from PDTRC and DTL in Lahore. The objective was to train the new laboratory staff to improve their skills in use of equipment such as HPLC, ultra-performance liquid chromatography, and UV-Vis spectrophotometry. It is important to note that all the laboratories involved in the training are working toward ISO 17025 certification followed by WHO PQ. These trainings aimed at helping the laboratories improve their standard of performance, meet regulatory requirements, and ensure the availability of quality-assured safe medicines in the market. These trained analysts will serve as master trainers for their remaining analysts who could not attend the training.



**PQM staff discussing GLP**

### **CDL Karachi**

The QMS of CDL was reviewed by Rockville experts and shared with the laboratory management. The laboratory is preparing its final QMS document, including the LIF to be submitted to WHO.

The infrastructural work at this laboratory has been completed. Pending activities include installation of the newly procured equipment, including HVAC. Once installation is completed, PQM will review the system and prepare the laboratory for WHO LIF submission. PQM also proposed to the DRAP management to precede WHO PQ of the laboratory with ISO 17025, as the ISO system will have leveraging effects on the WHO PQ.

### **DTL Lahore**

During Q3, PQM Pakistan maximized the presence of the technical expert from Rockville in conducting a hands-on training session on instruments; on special request after the daytime work hours, the analyst conducted an extended review of DTL Lahore’s QMS. PQM was able to provide valuable guidance to the management regarding the laboratory QMS and SOPs in place. This support aims at helping the laboratory better prepare for ISO 17025 certification by the Pakistan National Accreditation Council (PNAC) and subsequent WHO PQ for the facility to meet international standards.

### **PDTRC Lahore**

PQM has been working with PDTRC for WHO PQ since last year and has provided support with preparations of QMS documents and with improvement of laboratory working standards. PQM helped the laboratory develop a LIF for WHO that was accepted, and a WHO peer audit was conducted by a WHO-appointed audit team in December 2017. PDTRC was also supported in developing CAPA



**PQM staff provide hands-on training on HPLC**

based on the peer audit report. PQM supported the closure of various observations mentioned in the CAPA. In Q3, PQM arranged for final review of PDTRC preparedness before the WHO inspection visit in July 2018. A technical expert from HQ traveled to Pakistan and, with the local PQM team, conducted a detailed review of the laboratory's preparedness and provided valuable inputs to management to address other outstanding gaps before the WHO visit.

In line with the work plan for 2018, PQM began work with two provincial laboratories in Punjab (Faisalabad and Multan). Both are preparing for ISO 17025 and are also aiming for WHO PQ. A desktop review of QMS was done remotely, and the required improvements were communicated to the laboratories.

#### **DTL Faisalabad**

While the analysts from DTL Faisalabad were taking part in the hands-on training at DTL Lahore, the Punjab government, on behalf of DTL Faisalabad, requested PQM to support the review of its QMS, as they were expecting the PNAC visit in a few weeks' time. Therefore during the hands-on training at Lahore, PQM reviewed the QMS documents and provided the required input. PQM expects that, with the support provided, DTL Faisalabad will achieve successful outcomes during the PNAC visit for ISO 17025 certification in Q4.

#### **DTL Multan**

The analysts from DTL Multan also participated in the hands-on training at Lahore, and they have updated that the improvements suggested by PQM in the QMS were already implemented. The pre-audit by PNAC was completed, and the accreditation audit is expected in July for ISO 17025.

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

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**Inauguration ceremony of advance GMP training**

During FY 2018 Q3, PQM continued to support the industry to improve the standards of GMP. Based on the experience gained through a comprehensive training on CTD and GMP for the industry during FY 2017, an advanced training course on GMP was prepared, and technical managers from selected manufacturers were invited to this 4-day training course in Karachi. The selection of such technical personnel was made on the basis of their qualifications, expertise, and functional role at work. A strict set of criteria was maintained to include only participants with relevant expertise and competencies to further develop and maximize knowledge gained from the training to ensure sustainability. The training was completed by 44 technical professionals (37 male, 7 female) from the industry. The importance of training can be gauged from the

fact that many manufacturers sent their senior technical managers with years of experience to attend. These technical personnel attended the training for all 4 days. On the last day during evaluation, one senior staff member from the industry among the trainees came forward to the stage to thank USAID and PQM for arranging such training session, which improved participants' knowledge and skills in many new aspects of GMP, despite the years of actual practice experience they had. The trainees expressed they felt more confident to implement the new concepts learned through the training in their respective work places.

With the addition of the newly recruited Regulatory Specialist to the Pakistan PQM Team, PQM plans to focus and work with DRAP on organizational QMS (based on the GBT). The first assessment and internal audit team of DRAP will be preparing an "institutional development plan" (IDP), which will contribute to achieving WHO Maturity Level 3 as defined by the GBT. A detailed IDP has been developed and will be followed through from now through FY 2019.

As part of the transformation and modernization process, DRAP has also signed on as a member of the Collaborating Registration Procedure (CRP) program with WHO. This program was also supported and facilitated by PQM. This registration procedure will allow DRAP to accelerate the registration of WHO prequalified medicines,



**PQM expert team responding to questions of participants**

thus removing barriers to register quality medicines and making essential medicines more accessible to the public more quickly (<http://extranet.WHO.int/prequal/news/pakistan-joins-collaborative-registration-procedure>).

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

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During FY 2018 Q3, PQM continued to liaise with stakeholders to finalize a national framework/policy on PMS to develop an information-sharing mechanism. The draft guidance document will be presented at the next stakeholders meeting in order to develop consensus on its contents, implementation schedule, and logistics; achieve the objective of establishing a robust risk-based PMS; and train the regulators on the three-level approach.

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

USP office registration in Pakistan is still pending. With the recent Ministry of Interior's (MOI) request for submission of revised Annual Plan of Action (APA), the progress seemed to get a bit more optimistic. Once office registration in the country is granted, the government policy allows for 1-year multiple-entry visas for officials traveling for program-related work. This would greatly facilitate and ease the travel restriction of PQM HQ staff traveling to Pakistan to undertake and support the PQM work. In the meantime, the technical gap were mostly addressed and mitigated through the engagement of local-based consultants.

PQM has been working collaboratively and striving to maintain open communication with key regulatory strengthening stakeholders in Pakistan (e.g., DRAP, MOH, provincial government, WHO).

At the federal level, the Appellate Laboratory at the National Institute of Health in Islamabad is pivotal in Pakistan's QC system; however, its equipment is 25 years old, and the building that is housing the laboratory is not adequate based on current international standards. This laboratory requires financial support from the government to upgrade both the equipment and facilities.

#### **V. Lessons Learned**

PQM works closely with DRAP to strengthen its regulatory capacity. However, a review of provincial health authorities has established that they require more technical assistance, especially in the smaller provinces; this support in the smaller provinces is necessary to protect public health by promoting the standardization of processes and actions countrywide. The technical assistance that the provinces require is in the area of PMS and strengthening of the provincial QC laboratories. Therefore, PQM's assistance at the provincial level will help strengthen the regulatory and QA/QC system of the country.



# Eastern Europe & Central Asia



# Kazakhstan

## I. Quarter 3 Highlights

During Q3, PQM provided remote technical assistance to Karaganda laboratory in preparation for WHO inspection. PQM began preparing for a visit by a consultant specializing in risk assessment of cross contamination and risk management to the Nobel Almaty Pharmaceutical Factory.

PQM continued to provide technical assistance to Karaganda NQCL of the National Center for Expertise of Medicines, Medical Devices, and Medical Equipment of Kazakhstan (NCEM) to strengthen its QMS in preparation for WHO PQ. As a result of this technical assistance, the laboratory will be better equipped to conduct QC of medicines. Eventually, this will contribute toward ensuring the quality of medicines in the Kazakhstan market. PQM also started preparation for a visit to Nobel Almaty Pharmaceutical Factory for assessment of cross contamination between the products manufactured at the new site and the products manufactured at the adjacent facility. Mitigation of cross contamination is critical for compliance with international GMP standards, essential for manufacturing of quality-assured products.

## II. Country Context

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

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

Kazakhstan has a well-established national 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), about 40,000 units of falsified medicines in 40 cases were withdrawn from the market by the Kazakhstan FDA.

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

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

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

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



### III. Quarter 3 Progress by Objective

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

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PQM continued remote technical assistance to NCEM NQCLs. It was agreed that PQM will focus its assistance on Karaganda NQCL; other laboratories will learn from the experience of the Karaganda laboratory. Since January 2018, Karaganda NQCL had been waiting for WHO PQ inspection; PQM recommended the laboratory to participate in a WHO peer audit scheme, which would give representatives of Karaganda NQCL an opportunity to observe a WHO PQ inspection in another country. As a result, Karaganda specialists will better understand WHO inspection requirements and be better get prepared for WHO inspection of their laboratory. In Q3, PQM assisted Karaganda NQCL in applying to the WHO PQ team for participation in the peer audit scheme. In Q3, the Karaganda laboratory also made a decision to go through a WHO PQ pre-inspection process. This will allow the laboratory to have a mock WHO inspection, get relevant observations, and eliminate possible deficiencies prior to actual WHO inspection. The pre-inspection is scheduled for Q4. PQM will continue providing technical assistance to Karaganda NQCL. A PQM QMS consultant will attend the WHO pre-inspection as an observer and provide follow-up support to the laboratory to respond to the observations of the WHO PQ team.

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

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In Q3, PQM provided to Nobel Almaty Pharmaceutical Factory a confidential assessment report on the GMP gap assessment of the new facility conducted in February 2018. One of the critical issues identified during the assessment was potential cross contamination between the products manufactured at the new site and the products manufactured at the adjacent facility. In Q4, a PQM consultant specializing in risk assessment and management will come to Nobel Almaty Pharmaceutical Factory to assess the risk of cross contamination and advise the staff on how to mitigate the risks and prepare appropriate documentation to comply with the international GMP standard.

## Uzbekistan

### I. Quarter 3 Highlights

In Q3, PQM continued technical assistance to Nobel Pharmsanoat in preparation for participation in the WHO PQ program. PQM conducted an ISO 17025:2017 training for the staff of the QC laboratories of the Agency for Development of Pharmaceutical Industry and assessed QMS of Tashkent QC laboratory for compliance with the new ISO 17025:2017 standard. PQM also conducted a PIC/S QMS and GMP Inspection Methodology training for representatives of the Agency for Development of Pharmaceutical Industry. After, the National Medicines Regulatory Authority became a structural unit of the Agency for Development of Pharmaceutical Industry.

PQM continued remote technical assistance to Nobel Pharmsanoat, following up the results of the GMP gap assessment conducted in February 2018. PQM conducted a training on the new ISO 17025:2017 standard for the staff of QC laboratories of the Agency for Development of Pharmaceutical Industry. The training was followed up by assessment of the Tashkent QC laboratory for compliance with the ISO 17025:2017 standard. PQM conducted a PIC/S and GMP training for the GMP inspectorate of Uzbek MRA (State Center for Expertise and Standardization of Pharmaceutical Products, Medical Products, and Medical Equipment). PQM continued to work on equipment procurement for the QC laboratory of the Agency for Development of Pharmaceutical Industry.

### II. Country Context

Uzbekistan is classified as a high MDR-TB burden country; MDR-TB reaches 23 percent among new cases and 62 percent among previously treated cases.

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

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

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

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

### III. Quarter 3 Progress by Objective

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

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In Q3, PQM provided to Nobel Pharmsanoat a confidential assessment report on the GMP gap assessment of the new facility conducted in February 2018. As a follow-up, PQM will continue providing technical assistance to the manufacturer. In Q4, a PQM consultant specializing in risk assessment and management will come to Nobel Pharmsanoat to assess the risk of cross contamination and provide technical assistance in cross-contamination risk management.

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#### Objective 2 – Strengthen the medicines quality control system

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In Q3, PQM provided 3-day training on a new ISO/IEC 17025:2017 standard: General requirements for the competence of testing and calibration laboratories. The training was completed by 25 participants from different laboratories of the State Center for Expertise and Standardization of Pharmaceutical Products, Medical Products, and Medical Equipment under the Agency for Development of Pharmaceutical Industry. The training was followed by an assessment of the physical chemical laboratory activities against ISO/IEC 17025:2017 in Tashkent NQCL. The assessment report is being developed and will be provided to the laboratory in Q4. Based on the assessment findings, the priorities for future PQM technical assistance to the laboratory will be defined. In Q3, PQM continued work on equipment procurement for the Uzbek MRA's QC laboratory. The procurement will be executed in Q4.

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#### Objective 3 – Strengthen GMP inspection system

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In Q3, PQM provided a 7-day training to 18 representatives from the Agency for Development of Pharmaceutical Industry on the PIC/S QMS and GMP Inspection Methodology. The training of Uzbekistan GMP inspectors was divided into two essential parts. The first 3 days were dedicated to basic information about PIC/S, including its accession procedure, detailed information about QMS requirements, and a description of the content of Quality Manual and related SOPs. The remaining 4 days were focused on GMP training, including inspection methodology, virtual inspection from inspection preparation to report writing, and a workshop on classification of GMP deficiencies. The Agency for Pharmaceutical Development confirmed its interest in accession to PIC/S and will start preparation for PIC/S accession and establish working team responsible for preparation for PIC/S. The Agency will work on self-assessment as trained by PQM. Based on the self-assessment, PQM will develop a PIC/S accession roadmap and prepare further recommendations concerning improvements and readiness for the PIC/S membership application.

# Core Portfolio



# Core MNCH

## I. Quarter 3 Highlights

A magnesium sulfate manufacturer in Ukraine was able to submit its FPP dossier with assistance from PQM.

PQM also collaborated with the University of Minnesota to conduct and publish “Revisiting the Stability and Storage Specifications of Oxytocin Injection: A Literature Review,” which was made available on the PQM website in May 2018: <https://www.usp-pqm.org/sites/default/files/pqms/article/stability-storage-oxytocin-jul2018.pdf>

## II. Health Element Context

In 2015, the Sustainable Development Goals were adopted by world leaders to build on the success of the Millennium Development Goals. Goal 3, “Ensure healthy lives and promote well-being for all at all ages,” encompasses targets similar to USAID’s Ending Preventable Child and Maternal Deaths (EPCMD) initiative. The EPCMD initiative focuses resources on 24 priority countries toward 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 assures an uninterrupted supply of quality-assured medicines, but also strengthening medicines regulatory capacities to protect populations against poor-quality medicines, which is the essence of PQM’s technical expertise.

## III. Quarter 3 Progress by Objective

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

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

- **Magnesium sulfate FPP:** The manufacturer supported by PQM completed the dossier and submitted to WHO PQ in June 2018. PQM’s technical assistance contributed significantly to achieving this important milestone. PQM’s assistance included GMP assessment of the manufacturer in 2017, which resulted in development and implementation of the CAPA plan, allowing the manufacturer to achieve better compliance with the internationally acceptable GMP standards. In addition to this, PQM reviewed the dossier and provided recommendations for improvement before its submission to WHO for PQ review. PQM also agreed to a plan for further technical assistance with the manufacturer, including technical assistance in preparation of responses to WHO queries, training on data integrity in preparation for the GMP audit by WHO, and a mock audit prior to the WHO audit.

PQM’s Manufacturing Services Group is continuing to provide technical assistance at various stages to ensure that manufacturers are making progress toward WHO PQ for global procurement eligibility. This assistance includes providing responses to WHO PQ for dossier queries and a GMP mock audit of the magnesium sulfate FPP manufacturer in preparation for WHO inspection. PQM is also planning to provide training on data integrity for the manufacturer of magnesium sulfate FPP as requested by the manufacturer.

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

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Based on the discussion with the USAID MNCH team, PQM is in the process of revising the work plan in order to focus on high-impact activities. Particularly, in order to achieve higher impact during the lifetime of the PQM program, PQM is considering an alternative to conducting a workshop on use of WHO CRP for registration on MNCH products: PQM may propose to work closely with the regional registration harmonization mechanisms, countries, and manufacturers to facilitate review and approval of at least one oxytocin and one magnesium sulfate finished product dossiers by the regional registration bodies in Africa and potentially in southeast Asia. During Q3, PQM worked to explore feasibility of this idea and will propose it to USAID in Q4.

A questionnaire has been drafted to conduct a survey of oxytocin and magnesium sulfate registration status analysis in USAID's priority countries. The questionnaires are specific to MRAs and industry to engage in further discussion on the successes and challenges of product registration. Based on the findings, further actions will be defined to facilitate the registration of these products in the countries, thus increasing access to the lifesaving medicines.

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

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PQM has actively collaborated with the Concept Foundation and USAID on development of the procurement manual for use by countries as they carry out their own procurements of MNCH commodities. Particularly, PQM reviewed and provided comments on the QA part of the document. PQM also completed work with the University of Minnesota on a systematic literature review and meta-analysis of the quality of oxytocin supply globally, specifically as it relates to shelf life and stability. The final report titled "Revisiting the Stability and Storage Specifications of Oxytocin Injection: A Literature Review" was published and made available on the PQM website in May 2018: <https://www.usp-pqm.org/sites/default/files/pqms/article/stability-storage-oxytocin-jul2018.pdf>.

## **Core NTD**

### **I. Quarter 3 Highlights**

In Q3, PQM continued to provide technical assistance to manufacturers at various stages to ensure that they are making progress toward WHO PQ.

### **II. Health Element Context**

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

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

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

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

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



### III. Quarter 3 Progress by Objective

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

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During Q3, PQM provided technical assistance to manufacturers of the following NTD products:

- **Praziquantel API:** PQM continued to provide technical assistance to two manufacturers in their response to WHO PQ dossier queries for praziquantel API. One manufacturer will no longer receive technical assistance due to lack of response.
- **Praziquantel FPP:** PQM continued to provide technical assistance to manufacturers at various stages toward WHO PQ of praziquantel FPP. PQM's technical assistance included review of an in vitro dissolution study protocol and review of CAPAs as a result of PQM's GMP assessment.
- **Albendazole API:** PQM was notified by the albendazole FPP manufacturer that one API manufacturer is not interested in the sale of albendazole API. This API manufacturer has not been in communication with PQM during Q3. PQM will re-engage the manufacturer to identify its reason for not selling its API.
- **Albendazole FPP:** The manufacturer is in the process of conducting process validation. PQM has reached out to confirm a date for GMP assessment of the facility.

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

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

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Manufacturers of praziquantel are continuing to complete the CAPAs and submitting the evidence to PQM for review. Simultaneously, the protocols for the bioequivalence study are in the process of being finalized for submission to WHO for final review. PQM is also working with the manufacturer to source and procure the comparator product for the in vitro dissolution study and bioequivalence study.

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

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This activity is not yet approved for FY 2018.

## Core TB

### I. Quarter 3 Highlights

During Q3, a manufacturer that was supported by PQM successfully submitted the clofazimine FPP dossier to the WHO PQ team on June 22, 2018. PQM's technical assistance played a vital role from the beginning of formulation development and research and development strategy to review of bioequivalence protocols to ensure a successful study. PQM also provided GMP support to the contract manufacturing site to bring it up to the international compliance level. In addition, PQM reviewed the dossier and provided recommendations for improvement prior to submission to WHO. As next steps, PQM will provide further technical assistance to the manufacturers in their preparation of responses to WHO queries and response to GMP audit by WHO.

In addition to the submission of the clofazimine dossier, PQM also worked with the manufacturer Qilu Pharma to see the first WHO prequalification of amikacin FPP for the public health market.

PQM also participated in two workshops: Regional Pharmacovigilance Workshop—Implementation of Active TB Drug-Safety Monitoring and Management for New Drugs and Shortened Treatment Regimens for MDR-TB. The workshops were held in South Africa (for Africa region) in May 2018 and Kazakhstan (for Eastern Europe and Central Asia (EECA) region) in June 2018. On both workshops PQM facilitated the plenary discussion session with representatives of national MRAs. The plenary sessions discussed national MRAs' roles in support of NTP needs for quicker uptake of new anti-TB medicines and novel MDR-TB treatment regimens. The discussion helped in further work in developing of the Active Drug Safety and Monitoring (aDSM) plans by the country teams during the workshop.



Additionally in Q3, in an effort to increase information in the public domain related to the manufacture of quality-assured medicines, PQM finalized and made available on PQM's website the first publication of a product information report (PIR) for rifapentine. The PIR contains a summary of available literature and expert opinion on the API, analytical methods, toxicology, and formulation and process of the solid dosage form for the product. This publication provides manufacturers and MRAs with relevant information on the product in one place, which would help them in easier decision-making. This will further serve to help manufacturers in their development of the new product of interest, rifapentine and isoniazid fixed-dose combination. This is another high-priority product of interest, and PQM has initiated discussions with two manufacturers to discuss development and initial timelines. One manufacturer has submitted its initial timeline, and PQM will review and provide assistance in ensuring that this very important medicine is soon available on the market.

## II. Health Element Context

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

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

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

## III. Quarter 3 Progress by Objective

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

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During Q3, PQM provided technical assistance to manufacturers of the following anti-TB products:

- **Clofazimine FPP:** PQM visited the manufacturer and worked with the regulatory team to review and update the dossier for submission to WHO PQ. The dossier was finalized and submitted for PQ on June 22, 2018.
- **Clofazimine API:** The manufacturer submitted a response to the dossier query in late February 2018. PQM advised the manufacturer to reach out to the WHO PQ team to follow up on the status of the review.
- **Rifapentine API:** One manufacturer, supported by PQM, completed the renovation to reach a higher level of GMP compliance. In addition, the manufacturer is compiling its API Master File for submission to PQM for review. A second manufacturer has not been responsive to PQM during Q3; PQM will continue to reach out to the manufacturer.
- **Rifapentine FPP:** PQM conducted an initial GMP assessment and provided the report to the manufacturer. A second manufacturer will not be receiving PQM technical assistance due to lack of response and interest.
- **Gatifloxacin API:** PQM reviewed and provided comments for the API Master File, and the manufacturer is incorporating the comments and will resend the updated API Master File for review.
- **Gatifloxacin FPP:** PQM and the manufacturer are still awaiting WHO PQ and WHO TB teams' decision on a path forward for prequalification of this product, as no quality-assured comparator product is available on the market.
- **Kanamycin API:** PQM has been waiting to receive CAPAs from the initial GMP assessment conducted in late February 2018. CAPAs are expected to be received in early Q4. Other API manufacturers will no longer receive technical assistance from PQM due to lack of response and interest.
- **Kanamycin FPP:** There was no activity in Q3 for this manufacturer. PQM and the manufacturer are awaiting the WHO PQ team's final approval and issuance of WHO Public Assessment Report.

- **Linezolid FPP:** The manufacturer received the last round of request for information and responded in May. The manufacturer is awaiting final approval of the application from the U.S. FDA.
- **Rifampicin/Isoniazid/Ethambutol/Pyrazinamide (4 FDC):** For one of the manufacturers, PQM is continuing to provide technical feedback on overage in formulation. The bioequivalence protocol was also received for PQM's review in June 2018. A second manufacturer received local regulatory approval of the new facility in May/June 2018. PQM will need to conduct a GMP assessment of the new facility.

PQM also worked with the manufacturer Qilu Pharma to see the first WHO prequalification of amikacin FPP for the public health market.

In Q3, PQM worked on completing the due diligence process for the manufacturer that was selected for PQM's assistance for U.S. FDA approval of its product, rifampicin. As a next step, PQM is working with the manufacturer to confirm a visit date for the GMP assessment. This activity intends to contribute to ensuring an uninterrupted supply of anti-TB medicines on the U.S. market: bringing new suppliers to the U.S. market will decrease the risk of a medicines shortage and may also have a positive impact on medicines price reduction.

The PQM GMP team will continue to provide technical assistance to the manufacturers. PQM staff will continue to work with the manufacturer for the U.S. FDA submission for rifampicin. The sub-award documents will be gathered and submitted to USAID in Q4, and technical assistance to the manufacturer will be initiated thereafter.

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

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PQM was able to publish the first PIR for rifapentine on the PQM website. This report contains pertinent information useful for manufacturers and regulators to ensure that quality-assured rifapentine is manufactured and available for patients.

PQM placed a call for proposals to select a candidate for developing online training modules for GMP, dossier, and GCP requirements. The online training modules will be a free resource for industry and MRA representatives, specifically in LMICs, where they can get up-to-date information on current GMP, dossier, and GCP requirements. Eleven proposals were received and are in the review stage with the technical and the program teams. Selection of the candidate will occur in early Q4.

PQM conducted an orientation for technical consultants in early April 2018. The objective of this orientation was to onboard consultants to the PQM program, technical goals and objectives, and technical processes, and help them learn from the various field experiences on regulatory landscape and bioequivalence study design and protocol development. This orientation has helped onboard the consultants on the PQM policies and processes to ensure smooth execution of the activities.

USAID organized two regional pharmacovigilance workshops: Implementation of Active TB Drug-Safety Monitoring and Management for New Drugs and Shortened Treatment Regimens for MDR-TB in Cape Town, South Africa (for Africa region) and Almaty, Kazakhstan (for EECA region). There were representatives from 12 countries on Africa and 10 countries on EECA regional participated in the workshops. Taking into account PQM's experience in terms of strengthening medicines regulatory system, PQM was invited to lead a panel discussion session with representatives of the national MRAs at both workshops. PQM facilitated a panel of regulators addressing the role of national MRAs in the introduction and uptake of new drugs and a shorter MDR-TB regimen. The goal of the panel session was to discuss a role of MRAs in terms of introduction of new anti-TB medicines and ways of improving collaboration between MRAs and NTPs. It was discussed that two important areas where there is a need for active collaboration between MRAs and NTPs are market authorization of the new medicines to ensure that registration does not create barriers in terms of access to these medicines and another aDSM. At the sessions, all countries had an opportunity to share their experiences and discuss specific challenges in these areas. As a follow-up of these discussions, during the workshop each country team—which included representatives of both MRAs and NTPs—worked on developing country plans for strengthening their aDSM systems.

PQM will review the proposals received and select an appropriate candidate to develop the training modules.

# Cross Bureau

## I. Quarter 3 Highlights

Media reports on medicines quality collected throughout the year have been analyzed, and the results are presented in a dashboard that will be updated quarterly and posted on the PQM website.

The development of a surveillance tool (MedRS) that complements the PQM “Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low and Middle Income Countries” has been finalized. MedRS, which will enable countries to design sound sampling strategies based on risk and statistical considerations, is expected to be posted on the PQM website by the end of Q4. Once posted, it will be freely available for use by interested countries.

## II. Cross Bureau Context

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

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

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

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

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

## III. Quarter 2 Progress by Objective

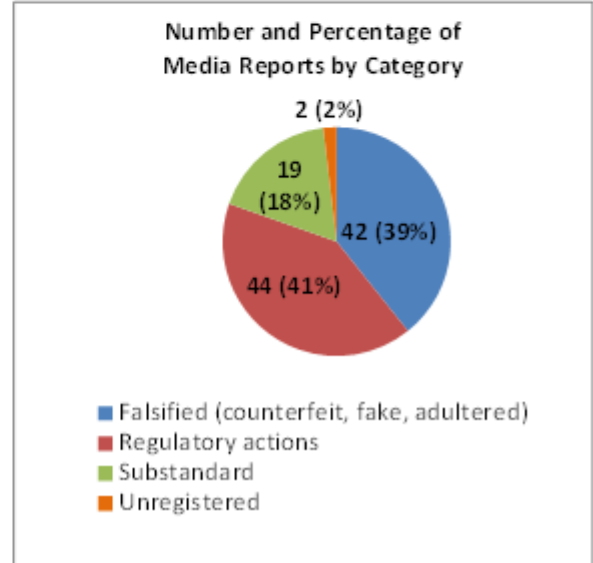
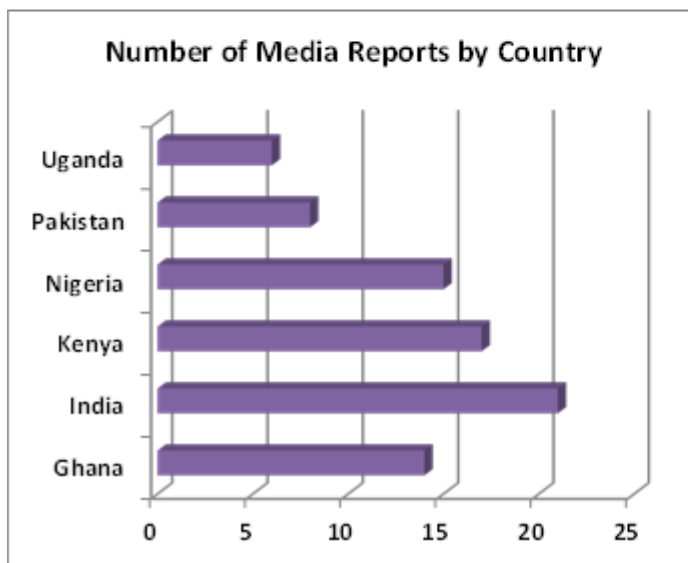
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### Objective 1 – Increase awareness of the importance of medicines quality

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Media reports on poor-quality medicines in EPCMD countries were gathered for the October 2017–June 2018 period. The following is a summary of the analysis of the data. Information will be posted in PQM website during Q4.

## Mapping of EPCMD countries with media reports during October 2017-June 2018



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

Development of the risk-based web tool (MedRS) associated with the “Guidance for Implementing Risk-Based Post-Marketing Quality Surveillance in Low- and Middle-Income Countries” was completed, and the User Guidance was finalized. Test data from Ethiopia were uploaded during Q3. Validation of the online tool will take place in Q4, and launching at the PQM website is expected by late Q4.

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

No updates this quarter.

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

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

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

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PQM's proposal for developing an introductory e-course on medicines' quality assurance was submitted to the Global Health e-Learning Center; though initially denied, it was subsequently accepted. A revision of the scope and module content was suggested by the AOR team, and a proposal with a detailed module outline will be submitted to the Global Health e-Learning Center during Q4. Modules completion based on the revised outline is expected during FY 2019 Q1.

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

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Revision of the profiles developed by a consultant for Bangladesh, Malawi, and Nigeria was finalized. Suggested changes will be submitted in early Q4, and the final profiles will be completed by the end of Q4.

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

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No updates this quarter.

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

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No updates this quarter.

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# Management Overview

During Q3, PQM worked with the USAID missions and core health element teams to obtain outstanding approvals for FY 2018 work plans. By the end of the quarter, 19 out of 22 work plans (86%) had been approved. This includes the approval of the newly drafted work plan for USAID's Kenya and East Africa Regional Missions to provide support to IGAD's regional health system priorities.

During Q3, PQM held a Program Review and Closeout Planning Workshop. The workshop brought together staff from PQM's Rockville office and key staff from each of the PQM field offices. The objectives of the workshop were to commence development of FY 2019 work plans and to share tools and approaches for PQM's global program closeout that will take place in September 2019. By having staff participate in the workshop, PQM plans for the last year of implementation to be well coordinated and looks forward to a streamlined and efficient closeout process. USAID's OHS Director, Kelly Saldana, kicked off the workshop with a presentation of "Health Systems Strengthening and the Office of Health Systems," and members of PQM's USAID AOR team were able to partake in select sessions of the workshop as well.

PQM Director, Jude Nwokike participated in two key meetings during Q3. In April 2018, Director Nwokike had the opportunity to attend the 2018 Generic Drugs Forum that was organized by the FDA's Small Business and Industry Assistance program in the Center for Drug Evaluation and Research (CDER SBIA), which provides guidance and information to regulated domestic and international small pharmaceutical business and industry. The forum covered updates on the implementation of the FDA's Generic Drug Program and updates from the Office of Pharmaceutical Quality (OPQ). Part of the OPQ strategic objectives is to elevate awareness and commitment to the importance of pharmaceutical quality. FDA speakers discussed several topics including Generic Drug User Fee Amendments (GDUFA) II Commitment Letter, review timelines and user fees, Integrated Quality Assessment Process, bioequivalence studies, generic safety and surveillance, and microbiology quality review.

Director Nwokike also attended the World Health Assembly 71 in Geneva, which included several sessions that focused on access to medicines in achieving global health goals. The sessions provided opportunities for more insights into the draft thirteenth general program of work, 2019–2023 proposed by the WHO. Sessions attended focused more on topics around access to essential medicines. The Director held several bilateral meetings including with the WHO Regulation of Medicines and other Health Technologies leadership and team members. The Global Public Health division of USP sponsored a side event on Incentivizing Investments in Access to Quality Medicines where a high level panel that included Dr. Alma Golden discussed issue of incentivizing investment in quality medicines and collaborative solutions to improve access, build local capacity, share best practices and knowledge, and coordinate on a global level.